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How the west has won? Evidence from the Indian Diet Heart Study

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The geographical distribution of CVD in different parts of the world is far from uniform. CHD is less common in oriental countries and Mediterranean countries than in westernised countries. In Japan, China, Korea, Thailand, Malaysia, India and Sri Lanka, mortality due to CHD was lowered; but now for the last two decades, it is increasing. Italy, France and Greece have less CHD mortality. While CHD mortality is decreasing in USA, Belgium, Finland, Netherlands, Australia, New Zealand and Portugal, several European countries such as Germany, UK, Sweden, Denmark, Poland, and Hungary have the highest CHD mortality in the world (1,2). In USA, and in other western countries CHD was least common around 1920, it started increasing after the year 1930 and decreased after the world war II (1947) in several countries. A further increase was noted after 1950s with a peak rise in CHD in 1968.

There is a continuing trend of a decrease in CHD after 1968 in USA. The decrease in CHD mortality (1-2%) is associated with decreased prevalence of stroke, hypertension, hyperlipidemia, obesity, physical inactivity and smoking in most of these countries in association with dietary and lifestyle changes and improved medical care (3,4). Thus it is not clear, how the west has won or the east has lost having a decrease or increase in CHD incidence and mortality respectively. There is a need to find out what Americans are doing or not doing causing a decrease in CHD and what Asians are doing or not doing having a increase in CHD because Swedish and British having the same medical care as Americans do not have a decrease in CHD mortality. Similarly developing countries have improved medical care but CHD is still increasing. While improved medical care has been suggested to cause decrease in case fatality rate, changes in dietary habits, an enormous increase in physical activity and recreation and cessation of smoking have been demonstrated to cause overall decrease in CHD in the communities and in patients with CHD (3-6). Secondly, in every randomised and controlled intervention trial (7, 8), aimed at reduction of risk factors by improved medical care, such as drug therapy for hypertension, hyperlipidemia and diabetes, there was no influence on CHD mortality and moreover drug therapy may have adverse influence on metabolic changes leading to decreased capability of adaptation(6).

A risk factor seems to be a protective response of our body which develops in an attempt of the body to adapt and fight against the dietary and lifestyle changes, eg. obesity; if energy intake is more than expenditure,

hyperlipidemia; if it is saturated fat and cholesterol; hypertension; if it is salt, energy, stress and alcohol. The underlying mechanism is a decreased capability of the body leading to unsuccessful adaptation. While physical inactivity further decrease such a capability of our body, exercise and weight loss may be enhancing the capability of our body to adapt. The adaptations could to biological or genetic, metabolic or physiological behavioural or social(6). Pathological or structural adaptations may also occur such as obesity or a lowered muscle mass due to lowered energy intake. Indeed CHD may also be a result of maladaptation, however more studies would be necessary to provide proof for this hypothesis. Although several prospective population studies (3,4) have provided evidence but, there is no scientific proof, that the west has won or the east has lost because of dietary and lifestyle changes. There is clinical evidence that dietary changes (9), exercise (5) and weight loss can independently modulate several metabolic factors including blood pressure, blood lipids and diabetes and decrease CHD (10).

We have provided evidence possibly for the first time that a joint strategy with comprehensive dietary changes, increased physical activity, weight reduction and modification of behaviour can modulate the major risk factors of CHD leading to decreased cardiovascular events including CHD and total mortality.

Methods and results

Of 430 patients initially randomised, 30 patients lost in the followup, 8 in group A and 22 in group B. The dietary specifications, clinical and laboratory data in 214 group A and 216 group B patients participants at entry to study were similar. Incidence of risk factors such as hypertension (55 vs 47), hypercholesterolaemia (33 vs 26), diabetes mellitus (34 vs 32), smoking (73 vs 65), obesity (77 vs 78), physical inactivity (107 vs 108) and CHD (92 vs 86) were comparable. There were 198 males in group A and 196 in group B and age varied between 25-65 years, complications and drug therapy at entry to study were also similar.

Group A patients received a diet with comprehensive changes, characterised by 28% calories from fat, P:S ratio 1.8, dietary fibre 24.3g, cholesterol 108mg per 1000 kcal per day in association with vitamins and minerals in the form of fruits, vegetables, cereals, nuts and oils. Group B patients received 27.5% calories from fat, P:S ratio 0.73 diet, 13.2g dietary fibre and 159mg cholesterol per 1000 kcal per day for 2 years. Group A patients also did more brisk walking (25.5 vs 6.5 km/week), and jogging (91.2 vs 20.2 min/week) compared to group B.

Risk factors

Risk factors at entry to study were similar. After 2 years there was a significant decrease in mean body weight in group A subjects compared to group B (5.8 vs 2.3 kg). The decrease in mean systolic and diastolic pressures, mean total cholesterol, LDL cholesterol, triglycerides and fasting blood sugar were significantly more in group A compared to group B after 2 years. Smoking cessation and reduction of tea, coffee and alcohol were similar in both the groups. In group A, subjects, doing the adequate exercise, had greater decrease in blood pressures, total cholesterol and triglycerides and a rise in HDL cholesterol.

Complications and cardiovascular end points

Initial complications such as angina, arrhythmias, ECG changes were similar in both the groups (434 vs 429) at entry to study. After 2 years, there was a significant decrease (52.8%) in these complications in group

A compared to group B (113 vs 242).

Nonfatal myocardial infarction (7 vs 16), fatal myocardial infarction (4 vs 8), sudden death (4 vs 6), total cardiac mortality (8 v 14), and total mortality (8 vs 15) were higher in group A than in group B. However due to less number of cases, statistical significance was not observed. Total cardiac end points were significantly ($P < 0.001$) less (60.8%) in group A compared to group B (15 vs 30). In group A, end points were less common in a subset of patients who followed the exercise programme compared to those who did not follow or did less exercise (8 vs 15 cases).

Comments

The present study provides scientific proof for the first time, that a combined strategy with comprehensive dietary changes, moderate physical activity and weight reduction in patients with major risk factors or with CHD can modulate blood pressures, blood lipids and blood glucose leading to significant ($P < 0.001$) decrease (60.8%) in total cardiac end points (15 vs 30) including non-fatal and fatal infarction, sudden death and total mortality in the intervention group compared to control group during a followup of two years. In the intervention group A, patients doing adequate exercise had greater decrease in body weight and better modulation of risk factors compared to persons doing less exercise and having no decrease in body weight. Total cardiac events were less common in this subset of patients doing the exercise and having dietary changes and weight loss compared to rest of group A patients (8 vs 15 cases). However, the number of events were insufficient to make a statistical conclusion.

The Framingham study (3) and North Karelia project(4) demonstrated that decreased consumption of saturated fat and cholesterol, increased physical activity and smoking cessation were associated with 1 - 2.5% decrease in CHD mortality every year. However in none of these studies, patients were provided a exercise programme and comprehensive changes in the diet. Secondly both the studies were uncontrolled. A great body of evidence has demonstrated that dietary changes, exercise and weight reduction can independently modulate risk factors of CHD (6,9). Several long term, randomised and controlled intervention studies have provided evidence that dietary changes (10) and exercise (5) can independently decrease CHD and have a non-significant beneficial influence on total mortality. These studies support decrease in CHD mortality in some of the western countries may be due to diet and lifestyle changes in these countries. This experiment has provided scientific proof that the west has won and the east is losing because of dietary and lifestyle changes. More studies in a larger number of patients and with long-term follow-up would be necessary to further provide scientific proof for our conclusions.

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Frontiers in lipid research: impact on lipid metabolism

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Introduction

Dietary fat is one of the most influential components affecting cholesterol metabolism. Since the regression equations of Keys *et al.* (1) and Hegsted *et al.* (2), we have learned much on the different impacts of different dietary fatty acids on cholesterolaemia. Thus, the concept of the polyunsaturated/saturated fatty acids ratio, namely P/S ratio, has now been widely acknowledged as important and crucial means to the prevention or improvement of atherosclerosis.

Recent extensive studies on the re-evaluation of the effect of individual fatty acids on plasma cholesterol level are gradually disclosing a complex situation of the fatty acid-cholesterol relationships.

In this paper, the recent knowledge on the most attractive field of lipid research, "impact of dietary fat on cholesterol metabolism" is briefly summarised.

Effect of different fatty acids

(a) Monounsaturated fatty acids

Grundy and his colleagues showed that oleic acid is rather hypocholesterolaemic than neutral toward plasma cholesterol level as has been pointed out in the regression equations (3). His study provided an additional benefit that oleic acid does not reduce HDL-cholesterol as often encountered during consumption of a relatively large amount of linoleic acid. However the effect of oleic acid can not always be seen, and in some cases it does not demonstrate a beneficial effect and rather increases plasma cholesterol level (4). Regarding the hypocholesterolaemic mechanism of oleic acid, the up-regulation of LDL-receptor of the liver has been inferred as in the case of linoleic acid (5). Anyhow, it has been known that populations who eat olive oil daily are less atherogenic. In addition, since oleic acid is the most prevalent fatty acid in diets, its consumption is not difficult in a practical sense.

(b) Stearic acid

It has also been repeatedly shown that stearic acid is hypocholesterolemic, in contrast to other long-chain saturated fatty acids (6). This fatty acid has been acknowledged as neutral or less cholesterolaemic than other saturated fatty acids in the predictive equations of Keys and Hegsted. The beneficial effect of stearic acid is considered to be exerted after it is desaturated to oleic acid. Although the report is available that stearic

acid is absorbed reasonably, it is uncertain whether stearic acid can commonly exert a hypocholesterolaemic effect under various dietary protocols. If stearic acid is in fact effective in lowering plasma cholesterol, then it is interesting to know whether highly hardened plant oils are also effective or not.

(c) Palmitic, myristic and lauric acids

Some saturated fats do not follow the regression equations, and they are not hypercholesterolaemic as expected. Examples are palm oil and cocoa butter. More recently Hayes and his colleagues have performed a series of interesting studies on the impacts of individual saturated fatty acids on plasma cholesterol level (7, 8). Their studies clearly showed that myristic acid is more hypercholesterolaemic than palmitic acid. Palmitic acid was virtually neutral in monkeys and hamsters under the situation in which the dietary linoleic acid supply is above the "threshold" level, namely the minimum level required for preventing the rise of plasma cholesterol. Although this observation has not been confirmed in humans, the mental switchover of our common sense that the saturated fatty acids are all hypercholesterolaemic should be necessary.

(d) Polyunsaturated fatty acids

It is also important to know the effects of different polyunsaturated fatty acids. In the regression equations by Keys and Hegsted, polyunsaturated fatty acid (PUFA) is exclusively linoleic acid, and essentially no attention has been paid to other types of PUFAs. The metabolites of linoleic acid such as arachidonic acid and in particular α-linolenic acid (9) appear to be more effective in lowering plasma cholesterol compared with the parent molecule. In addition to the strong hypocholesterolemic potential, α-linolenic acid is readily elongated to dihomo-γ-linolenic acid and serves as a substrate for 1-series prostaglandins. For example, PGE_1 has various desirable physiological functions resembling PGI_2, and exerts a beneficial effect on arterial cholesterol metabolism.

PUFAs of n-3 family have now been receiving much attention in relation to their diverse functions on lipid metabolism (10). α-linolenic acid and eicosapentaenoic acid are usually an effective regulator of plasma triglyceride rather than cholesterol through the reduction of hepatic production and secretion of both lipid and protein portions of very-low-density lipoproteins. However, they have a more specific influence on fatty acid metabolism and hence, eicosanoid production. Unfortunately, the supply of n-3 PUFAs is limited.

In this context, it is essential to consume n-6 and n-3 PUFAs at an appropriate ratio. No definite conclusion is available yet, but the n-6/n-3 ratio of 3 to 5 can be recommended in respect to plasma cholesterol level and hence, the prevention of atherosclerosis (11).

Our current study with interesterified fats with the same P/S ratio but differing in the source of saturated fatty acids, lauric, myristic, palmitic and stearic acids, showed that when the supply of PUFAs is adequate in respect to both quantity and quality, there was no distinct difference in the impact on plasma cholesterol level for these saturated fatty acids. However, the effect of palm oil on plasma cholesterol of rats was not modified by randomisation of fatty acids (12).

(e) Specific polyunsaturated fatty acids

Almost all of plant PUFAs have double bonds in the fixed positions, namely they have a repeating unit of

the methylene-interrupted structure. In the plant kingdom, however, there are several specific PUFAs which have double bonds not obey this general rule. In addition, some unsaturated fatty acids contain *trans*-double bond in contrast to the natural *cis*-double bond.

One such PUFA is columbinic acid, 5t,9c,12c-18:3 in columbine seed oil. This fatty acid has a potential as essential fatty acid like linoleic acid, but may not be converted to eicosanoids due to the presence of *trans*-double bond in its molecule (13). Since an excessive intake of linoleic acid may cause a number of serious metabolic disorders that may in part be caused by excessive production of specific prostaglandin(s) of the 2-series, such PUFA as columbinic acid that does not serve as the precursor of eicosanoids but has an essential fatty acid activity appear useful, in particular if they possess a hypocholesterolaemic activity.

Examples of the other types of specific PUFAs are those from the Oriental medicine plants; 5c,9c,12c-18:3 in Korean pine seed oil and 7c,11c,14c,17c-20:4 in Chinese biota seed oil. PUFA in pine seed oil has been shown to have a considerably greater hypocholesterolemic and hypotensive activities compared with linoleic acid (Figure 1), and in contrast to α-linolenic acid it does not interfere with desaturation of linoleic acid to arachidonic acid.

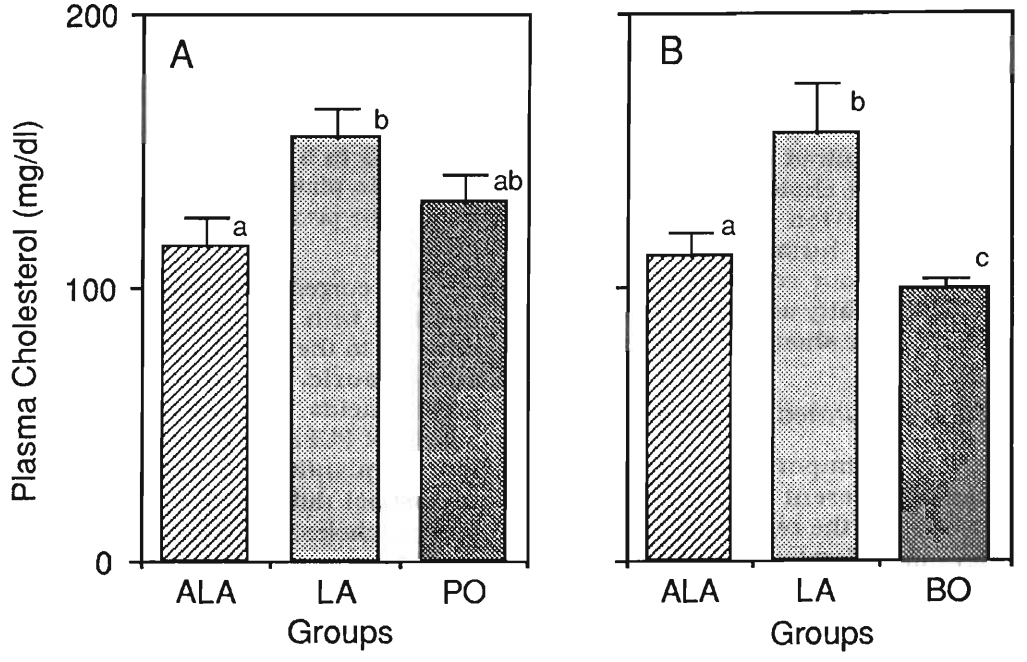

Fig. 1 Effect of pine seed oil (A) and biota seed oil (B) on plasma cholesterol concentration in rats.
Effect of dietary pine seed oil (PO) or biota seed oil (BO) was compared with a fat rich in α-linolenic acid (ALA) or linoleic acid (LA). EAch diet contained 0.5% cholesterol and 0.125% sodium taurocholate. Values are means ± SEM of 6 rats.

PUFA in biota seed oil appears to have essential fatty acid potential comparable with α-linolenic acid as judged from its ability to reduce n-9 eicosatrienoic acid in essential fatty acid-deficient rats. Biota seed oil have a significant hypolipidemic potential and a potent inhibitor of linoleic acid metabolism even compared with a well-known competitor, α-linolenic acid, Thus, these unfamiliar fatty acids can be used for a specific purpose as a metabolic regulator.

There is an ample possibility that plant lipids contain other types of PUFAs having specific modulator functions, and in this sense plant lipids is a treasure-house of physiologically functional factors.

Effects of glyceride structure

In a series of studies mentioned above, the effects have been examined without paying attention to the glyceride structure of dietary fats. When one watches the mode of triglyceride digestion and absorption, namely the preferential absorption of fatty acids as 2-monoglyceride, it seems reasonable that fatty acids esterified to the 2-position of the glyceride molecule may have a specific function which is different from those esterified to the 1- and/or 3-positions. This concept is reasonable when one considers the structure of human milk fat. In fact, it has long been known that linoleic acid in the 2-position is more effective in lowering plasma cholesterol compared with that in the 1- and 3-positions.

When we fed to rats structured lipids composed of linoleic acid and medium-chain fatty acids in the same molecule, but differing in their distribution, absorption of linoleic acid esterified to the 2-position was more efficient than that esterified to the 1- and 3-positions (14) (Figure 2).

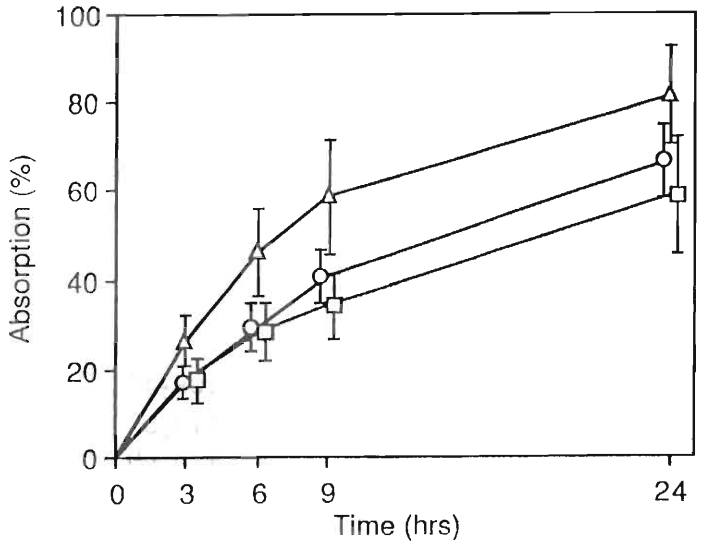

Fig. 2 Absorption of linoleic acid into thoracic duct lymph of rats upon intragastric administration of fat emulsions containing sodium taurocholate and albumin (14).
○, □ or Δ shows linoleic acid absorption in rats given trilinolein (18:2/18:2/18:2), 2-decanoyl-1, 3-dilinoleoyl-glycerol (18:2/10:0/18:2) or 2-linoleoyl-1, 3-didecanoyl- glycerol (10:0/18:2/10:0). Values are means ± SEM of 5 or 6 rats

Since the idea of the structured lipids has recently been introduced and it is now possible to prepare the glycerides having specific fatty acids at arbitrary positions, search into the fats having most effective hypocholesterolaemic potential warrants future study. The most typical structured lipid is phospholipids.

Non-fatty acid components

In addition to fatty acid components, lipids, especially plant lipids, contain various types of metabolic regulator. The most common components are tocopherols and carotenoids. Tocopherol is essential for the prevention of lipid peroxidation. It is also known that tocopherols regulate production of eicosanoids. Plant ß-carotene is the most important source of vitamin A even in the developed countries and it contributes approximately two-thirds of total vitamin A consumption, and almost all in nutritionally- deficient populations.

Plant sterols have been used as a safe antihypercholesterolaemic agent, since their point of action is in the intestine and their adsorbability is markedly low compared with cholesterol. We have shown that plant stanols, hydrogenated sterols, have a significantly greater hypocholesterolaemic activity than plant sterols (15).

Some plant lipids contain specific compounds such as gossypol in cotton seed oil, sesamin in sesame oil, oryzanol in rice bran oil, and tocotrienols in palm oil and coconut oil. Recent studies show that sesamin effectively reduce cholesterol absorption in the intestine and cholesterol synthesis in the liver, and hence, plasma and liver cholesterol levels (16) (Table 1).

TABLE 1

Effect of sesamin on concentrations of serum and liver cholesterol (16)

Exp. No. and Group	No. of rats	Cholesterol Concentration	
		Serum (mg/dl)	Liver (mg/g)
Exp. 1			
Purified diet	6	108 ± 4^{a}	2.54 ± 0.13^{a}
Diet + sesamin	6	110 ± 5^{a}	1.95 ± 0.06^{b}
Diet + cholesterol	6	136 ± 8^{b}	20.8 ± 2.2^{c}
Diet + cholesterol and sesamin	7	102 ± 5^{a}	9.13 ± 1.02^{d}
Exp. 2			
Commercial chow	7	69.1 ± 5.2^{a}	2.86 ± 0.19^{a}
Chow + sesamin	8	55.5 ± 3.0^{b}	1.82 ± 0.04^{b}

Values are means ± SEM. Rats initially weighing an average of 139 g were fed experimental diets for 4 weeks. Values with different letters are significantly different in each experimental ($P < 0.05$). Both sesamin and cholesterol were added to the diet at 0.5% level.

Tocotrienols also have diverse functions, and they are hypocholesterolaemic and hypotensive. The more detailed study on these specific compounds is required.

Conclusion

In summarising, the current information therefore stresses the complexity of the interaction between dietary fats and cholesterol metabolism as has ever been acknowledged. Re-evaluation of the influence of individual fatty acids on cholesterol metabolism indicated a need for mental switchover of our concept based on the classic regression equations. In addition, the importance of the new type of polyunsaturated fatty acids, glyceride structure and non-fatty acid components of dietary fats has also been stressed.

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Dietary fats and cardiac arrhythmia in primates

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Introduction

Sudden Cardiac Death often results from sustained ventricular fibrillation or malignant cardiac arrhythmia (1). The vulnerability of the heart to develop cardiac arrhythmia increases with age and stress (2). Ischaemia frequently triggers serious arrhythmias with a high incidence of mortality (3). Recent experimental studies in our laboratory with the small non-human primate marmoset monkey (Callithrix jacchus) have confirmed earlier findings obtained from a laboratory rodent model of cardiac arrhythmia, that dietary saturated fats promote but dietary polyunsaturated fatty acids (PUFA's) protect against the development of cardiac arrhythmia under ischaemic conditions (4,5). In particular, after prolonged feeding of a PUFA enriched diet both the heart rate and blood pressure are lowered, while the left ventricular ejection fraction (LVEF) and the electrical threshold for the induction of ventricular fibrillation (VFT) are both increased (6,7). All these changes in heart function are associated with a reduced risk of developing malignant cardiac arrhythmias and Sudden Cardiac Death (1,3,8).

The fatty acid composition of cardiac membrane phospholipids is also profoundly altered by changes in dietary lipid (fatty acid) intake (9, 10), and the studies reported here were designed to investigate the possible role of membrane fatty acids in the development of cardiac arrhythmia in the mature marmoset monkey. We have shown that the dietary induced changes in membrane PUFA's can be related to their role in the biosynthesis of myocardial prostacyclin (OGI_2) and thromboxane (TXA_2) and that PUFA-enriched diets reduce the production of arrhythmogenic TXA_2 more than that of the anti-arrhythmic eicosanoid PGI_2 (10). It is proposed that this shift in the balance of pro-and anti-arrhythmic eicosanoids is central to the beneficial effects of PUFA enriched diets on the vulnerability of the heart to respond to ischaemic stress.

Materials and Methods

Eighteen adult male marmosets about one year old were obtained from this Division's primate breeding colony (11). They were assigned in groups of six to three different dietary regimes each containing a 6% by weight supplement of either saturated animal fat (SF), sunflower seed oil (SSO) or fish oil (FO). The composition of these diets and the 24 month long feeding regime have been described in detail in several recent publications from this laboratory (10,12), as have the procedures for measuring both the left ventricular ejection fraction (LVEF) and the electrical threshold for the induction of

ventricular fibrillation (VFT) by programmed electrical stimulation (6,13).

Chloroform-methanol lipid extracts of marmoset cardiac muscle were obtained by the method of Bligh and Dyer (14), and individual phospholipids separated by thin layer chromatography as described previously (9,10). Fatty acid methyl esters (FAME's) were prepared by heating the phospholipids with methanolic boron trifluoride and analysed by gas chromatography as described in several previous publications from this laboratory (15,16). The stable metabolites of myocardial prostacyclin (PGI_2) and thromboxane A_2 (TXA_2), that is 6-keto PGI_{1a} and TXB_2 were determined by the ratio immunoassay procedures we have used in previous experiments (10).

Results

The effect of dietary lipid supplements upon cardiac function is described in Table 1. By comparison with the results obtained after feeding the SF diet, both the SSO and FO diets rich in PUFA's have major beneficial effects upon the heart rate (HR), blood pressure (BP), cardiac output (CO) and the mechanical performance (LVEF; peak filling rate PFR and end diastolic volume EDV) of the marmoset heart.

TABLE 1

Effect of dietary lipids on cardiovascular function in the adult marmoset

Function	SF	SSO	FO
Heart rate (beats min^{-1})	259	250	226
Systolic bp. (mmHg)	94	84	84
Diastolic bp. (mmHg)	68	58	60
Cardiac output ($ml.min^{-1}\ g^{-1}$)	24	32	30
LVEF (% filled vol.)	46	57	55
PFR ($ml.min^{-1}\ g^{-1} \times 10$)	14	20	17
EDV ($ml.min^{-1}\ g^{-1} \times 10^2$)	21	24	25
VFT (milli amps) : normoxic	8.3	15.1	15.0
VFT (milli amps) : ischaemic	6.8	13.3	13.4
VF (%) : normoxic	43	13	8
VF (%) : ischaemic	45	13	NIL

All values are the means from n-6 animals per dietary group. The diets SF, SSO and FO are described in the text and the previous publications cited in the references to this paper. LVEF is left ventricular ejection fraction; PFR is the peak filling rate and EDV is end diastolic volume; VFT is the electrical threshold for sustained vnetricular fibrillation. VF is the proportion (%) of episodes of sustained ventricular fibrillation which required defibrillation.

In addition, the electrical threshold at which sustained ventricular fibrillation (VFT) could be induced by programmed stimulation is greatly enhanced following long-term PUFA enriched diets, when examined under both normoxic and ischaemic conditions. The proportion (%) of animals developing episodes of sustained ventricular fibrillation (VF) is also greatly altered by change in habitual dietary fatty acid intake. There was a significant reduction in VF after both PUFA enriched diets under normoxic condition (by >70% after SSO and >80% after FO). The effect was even more striking under ischaemic conditions where no VF was observed in any animal which had received the FO dietary supplement.

Changes in the major PUFA's of cardiac membrane phospholipids are shown in Table 2. By comparison with the profile of PUFA's found after feeding the saturated fat (SF) enriched diet, after the SSO supplement there is generally a rise in the major ω-6 PUPA's (18:2 and 20:4) although the rise is not identical in all three phospholipids (phosphatidyl choline, PC; phosphatidyl ethanolamine PE; phosphatidyl inositol, PI) that were examined. Equally, less long-chain omega-3 PUFA's are found in all three phospholipids after supplementing the diet with SSO which is rich in linoleic acid (18:2 ω-6). Consequently the ω-6/ω-3 ratio in all these three cardiac phospholipids is much greater after the SSO diet than after the FO diet.

TABLE 2

Effect of dietary lipids on the major PUFA's of several cardiac phospholipids of the adult marmoset

	PUFA's	SF	SSO	FO
Phosphatidyl Choline	18:2ω6	15.0	37.6	4.9
	20:4ω6	4.8	5.5	7.8
	20:5ω3	-	-	8.4
	22:5ω3	1.1	0.6	0.6
	22:6ω3	3.4	1.0	17.0
	$\Sigma\omega$6/ω3	4.4	26.9	0.5
Phosphatidyl Ethanolamine	18:2ω6	15.7	20.0	12.0
	20:4ω6	16.9	20.3	11.1
	20:5ω3	-	-	6.1
	22:5ω3	2.8	1.8	0.1
	22:6ω3	5.6	4.5	26.3
	$\Sigma\omega$6/ω3	3.9	6.4	0.7
Phosphatidyl Inositol	18:2ω6	7.5	20.5	5.6
	20:4ω6	22.3	18.4	16.4
	20:5ω3	-	-	8.6
	22:5ω3	1.2	0.1	1.1
	22:6ω3	1.1	0.1	9.0
	$\Sigma\omega$6/ω3	12.9	19.4	1.2

Values are relative % total fatty acids and are the means of duplicate determinations from 6 animals per dietary group.

A different effect is seen after feeding the fish oil (FO) supplemented diet which contains an appreciable amount of the long-chain omega-3 PUFA's eicosapentaenoic acid (EPA; 20:5 ω3) and docosahexaenoic acid (DHA, 22:6 ω3) as well as considerable saturated and monounsaturated fatty acids (10). While FO feeding always lowers the proportion of 18:2 ω6 in cardiac phospholipids, the effect of FO on arachidonic acid (AA; 20:4 ω6) is not uniform. In PC it is greater than after SF or SSO, while in PE and PI it is less. However, considerable EPA and DHA are now present and the result is a major reduction in the total ω-6/ω-3 ratio of all three cardiac phospholipids. The effect of these changes in substrate or inhibitor levels of fatty acids on the biosynthesis of the myocardial eicosanoids prostacyclin (PGI_2) and thromboxane (TXA_2) is shown in Table 3.

Clearly although there is reduction in the basal level of eicosanoid production *in vitro* after feeding both PUFA enriched diets, the reduction is greatest following FO dietary supplementation. In addition, the reduction of TXA_2 is proportionally greater than that in PGI_2, consequently the ratio of PGI_2 to TXA_2 is greater after FO supplementation than it is after feeding SSO enriched diets. However, when excess substrate in the form of added arachidonic acid (AA) is made available to the system some differences are seen. PGI_2 production is still reduced, but the difference between SSO and FO is no longer apparent. Similarly the reduction in TXA_2 production after PUFA supplementation is still found, but the effect after FO is again greater than that after SSO. Consequently the dietary induced shift in PGI_2 to TXA_2 balance is now only apparent after FO supplementation and not after feeding the SSO diet.

Discussion

Just as we have previously demonstrated in a rodent model of ischaemic cardiac arrhythmia (4,5), the long-term feeding of PUFA-enriched diets was shown to be beneficial for many

TABLE 3

Effect of dietary lipids on myocardial eicosanoid synthesis in the adult marmoset

	Eicosanoid	SF	SSO	FO
Basal	PGI_2	167	114	88
	TXA_2	69	24	12
	$\Sigma PGI_2/TXA_2$	2.4	4.8	7.3
+ AA	PGI_2	153	128	127
	TXA_2	128	96	59
	$\Sigma PGI_2/TXA_2$	1.2	1.3	2.1

Values are pg. mg^{-1} dry heart wgt; adapted from Abeywardena *et al.* 1991, cited as reference 10.

aspects of cardiovascular function in the mature male marmoset. In particular, two important risk factors in the development of ischaemic arrhythmia, namely the left ventricular ejection fraction (LVEF) and the ventricular fibrillation threshold (VFT) were both significantly improved after PUFA enriched diets in comparison to the values obtained after feeding a saturated fat (SF) dietary supplement.

These improvements in cardiac function occurred in parallel with changes in the PUFA profiles of several cardiac membrane phospholipids. In particular the changes in major *w*-6 and *w*-3 PUFA's in PC, PE and PI result in wide differences in the relative proportions of arachidonic acid (AA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), each of which has a different role in the biosynthesis of series-2 and series-3 eicosanoids (10). When measured directly *in vitro* it is apparent that the relative biosynthetic capacity of the myocardium to generate prostacyclin (PGI_2) and thromboxane (TXA_2) is reduced by both PUFA enriched diets. However the effect of FO is greater than that of SSO, and is not abolished by the provision of additional AA substrate for series-2 eicosanoid synthesis. Thus, it is reasonable to suggest that while both PUFA enriched diets result in improved PGI_2 to TXA_2 ratios, and thus reduced vulnerability to the arrhythmogenic properties of thromboxane, the mechanisms by which this is achieved differ for the PUFA's of the *w*-6 and *w*-3 series. There is the strong possibility that the omega-3 PUFA's of FO have a particular inhibitory effect upon the synthesis of TXA_2 which is not shared by linoleic acid, the major *w*6 PUFA found in sunflower seed oil.

Further studies with edible oils of different composition or mixtures of several edible oils may shed further light on the effect of different PUFA's on eicosanoid production, cardiac membrane fatty acid composition and the mechanical performance and electrical stability of the heart (17).

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Dietary fatty aicds and the regulation of the plasma lipoprotein profile

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Abstract

A series of metabolic studies in monkeys and hamsters, and reevaluation of published human data, indicate that dietary saturated fatty acids are not equal in terms of their metabolic impact on cholesterol metabolism. Myristic acid (14:0) appears to exert the major cholesterol-raising effect by decreasing LDL receptor activity and by increasing the direct production of LDL (from sources other than VLDL-catabolism). Palmitic acid (16:0) does not depress LDL receptor activity and appears to have a neutral effect on plasma cholesterol in most cases (when plasma cholesterol < 200 mg/dL) or until the LDL receptor is down-regulated for other reasons, as with high cholesterol intake or obesity. In such cases, the down-regulated LDL receptors coupled with an increased VLDL production (induced by dietary 16:0 and 18:1) can divert VLDL remnants from normal clearance into LDL to expand the LDL pool. Furthermore, the cholesterolaemic impact of any saturated fatty acid appears to be countered (up to a saturable "threshold" level) by dietary linoleic acid (18:2), which up-regulates the LDL receptor. Once above this "threshold" of 18:2, the major fatty acids (16:0, 18:0, 18:1, 18:2, 18:3) appear to exert an equal impact on the circulating cholesterol concentration.

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Tocotrienols, soluble dietary fibre and blood cholesterol

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Introduction

Elevated blood cholesterol concentration, in particular, the concentration of low-density lipoprotein cholesterol, has been shown to be a major risk factor in the development of atherosclerosis and cardiovascular diseases. Elevated blood cholesterol is linked to increased risk of cardiovascular disease (1-3) and proponents of cholesterol reduction claim a fall in serum cholesterol of 1% is associated with at least a 2% fall in coronary heart disease (4). Blood cholesterol concentration can be reduced by controlling the composition and quantity of dietary fat and by including food components (e.g. soluble dietary fibre, tocotrienols) that possess hypocholesterolaemic properties.

The only forms of dietary fibre with the ability to lower blood cholesterol are the water-soluble fractions. Guar gum (5), pectins (6), xanthan gum (7) and locust bean (8) have been shown to be effective in lowering blood cholesterol in animal experiments and human trials. Oat bran also lowers plasma cholesterol (9) and this appears to be due to a high concentration of soluble ß-glucans (10,11). The hypocholesterolaemic effect of soluble dietary fibres is due to either/or a combination of two or more possible mechanisms. Firstly, soluble fibre may increase the viscosity of the digesta, increasing the thickness of the unstirred layer hence reducing the uptake of cholesterol and bile acids (12). Secondly, soluble dietary fibre is an excellent substrate for microbial fermentation in the caecum and large intestine and the resultant volatile fatty acids may suppress hepatic cholesterol synthesis (13). Thirdly, the presence of soluble fibre may cause tropic effects on the enzymes and the structure of the gastrointestinal tract (14,15).

Tocotrienols, unsaturated analogues of tocopherols, are not widely found in nature, however, palm oil and its fractions, and barley contain high concentrations of tocotrienols. Palm oil is especially rich in α-tocotrienol (16). Recently, Qureshi *et al.* (17) isolated tocotrienols from barley flour and showed that they inhibited the activity of 3-hydroxy-3-methylglutaryl coenzyme A reductase in chickens. A number of human trials (18-20) have since shown that capsulated vitamin E concentrate from palm oil (Palmvitee), which is rich in tocotrienols, is effective in reducing blood cholesterol.

Soluble dietary fibre

The concept that soluble fibre

inhibits cholesterol absorption from the small intestine because it increases the viscosity of digesta is not supported by the data of Evans *et al.* (21). This study involved three galactomannans with different proportion of D-galactosyl side groups per D-mannose residue and the magnitude of the cholesterol-lowering effects was in the opposite order to their viscosity. The most viscous (guar gum) had less effect on plasma cholesterol than the least viscous (fenugreek gum). These results are supported by the finding that feeding methyl cellulose of different grades of viscosity did not influence plasma cholesterol concentrations, but did influence plasma glucose (22).

In contrast to earlier suggestions (13,23), recent results (21,24) are also inconsistent with the view that volatile fatty acids, from fermentation in the large bowel, inhibit hepatic cholesterol synthesis. Although Evans *et al.* (21) found that galactomannans reduced the rate hepatic synthesis of cholesterol, the galactomannan with the greatest cholesterol-lowering activity had the least effect on caecal pH, the size of the caecum and mass of caecal contents. In a study to suppress microbial activity, and hence volatile fatty acid production, using antibiotics in the drinking water of rats fed guar gum; synthesis of cholesterol was not affected by antibiotic, whereas guar gum caused a significant decrease in blood cholesterol which was independent of the presence of antibiotic (24). Increased volatile fatty acid production arising from the ingestion of soluble dietary fibre, therefore, may not be a primary cause for the reduction in blood cholesterol and rate of cholesterol synthesis.

Intestinal absorption and binding of bile acids or cholesterol by soluble dietary fibres also does not satisfactory explain their hypocholesterolaemic effect. In a gut perfusion study, fenugreek gum had no effect on intestinal absorption of taurocholate (21). Cholesterol-lowering by pectin is accompanied by increased faecal excretion of bile acids (25), however, the degree of hydrophobicity of pectins would strongly influence their capacity to absorb bile acids. When low- or high-methoxyl pectins were fed to human subjects there were no differences in plasma cholesterol or faecal steroid excretion (26). Moreover, a gut perfusion study showed that pectins do not inhibit reabsorption of bile acids from the terminal ileum (27). Thus the mechanism by which soluble fibres reduce blood cholesterol remains unclear.

Dietary tocotrienols

The observation of Qureshi *et al.* (17) that tocotrienols from barley flour inhibit the activity of 3-hydroxy-3-methylglutaryl coenzyme A reductase has stimulated a number of research groups to investigate the effect of tocotrienols on human blood lipids. Tocotrienols are typically given as capsulated palm oil-vitamin E concentrate (Palmvitee). When twenty-two volunteers took one Palmvitee capsule (18mg tocopherol, 42 mg tocotrienol, 240 mg palm olein) per day for 30 days, both serum total cholesterol and low-density lipoprotein cholesterol concentrations were lowered (0.9% to 37.0%) in all volunteers when compared with their respective starting values (20). Dietary supplementation of Palmvitee capsules to hypercholesterolaemic subjects caused serum total cholesterol to decrease by 10% to 15% after 14 and 28 d, respectively, as compared to baseline values (19). However, when a α-tocotrienol preparation isolated from palm oil was fed, a significant fall in blood cholesterol was observed in subjects that showed little response to Palmvitee administration (19). The considerable individual variation in the response to Palmvitee capsules can be attributed to inherent variation in

biochemical pathways controlling blood cholesterol concentrations within the human population.

Since Palmvitee contains tocopherol, tocotrienol and palm olein, it is not possible to identify which component is responsible for the observed hypocholesterolaemic effect of Palmvitee. Tocopherol supplementation has been shown not to effect human serum cholesterol (28,29). Except for one small study (19), pure tocotrienols have not been fed to humans. However, the addition of a tocotrienol-rich fraction or purified α-, α- or ∂- tocotrienol from palm oil at levels of 20 ppm to chick diets led to a significant inhibition (38-54%) of hepatic activity of 3-hydroxy-3-methylglutaryl coenzyme A reductase and a concomitant decline in serum concentration of cholesterol (17-28%) and low-density lipoprotein cholesterol (27-46%)(30). These results indicate that α- and ∂-tocotrienols are more potent cholesterol inhibitors than α-tocotrienol in the avian system.

Dietary interactions

Soluble fibres increase faecal bile acid excretion and hence influence cholesterol homeostasis by using hepatic cholesterol to replenish bile acids. On this basis, Hood and Sidhu (31), have investigated the effect in Japanese quail of feeding soluble dietary fibre with a tocotrienol-rich fraction (TRF) from palm oil to ascertain if these two components produce a synergistic effect on blood cholesterol. The diets contained either 5% guar gum or 5% α-cellulose and half the birds had 50 ppm of the TRF (50% tocotrienols) added to their diets. Total plasma cholesterol was lower in the quail fed guar gum when compared to birds fed α-cellulose. When the TRF was included in the diet containing guar gum a significant ($P<0.05$) further reduction was observed in total plasma cholesterol (Table 1). The TRF was not effective when α-cellulose, a non-fermentable fibre, replaced guar gum. Although differences were observed in blood cholesterol among the four treatment groups, no significant changes were observed in *in vitro* rates of cholesterol synthesis. In a subsequent experiment, where varying concentrations of TRF from palm oil were included in the diet of Japanese quail, tocotrienols did not influence blood cholesterol concentrations (unpublished data). In contrast, when Japanese quail were given TRF (5 mg/day) directly by mouth, blood cholesterol concentrations were observed to fall by 19% from 6.14 to 4.98 mmol/L. These preliminary observations suggest that tocotrienols may not be as effective when the pure compounds are mixed into a diet as compared to when they are given orally.

TABLE 1

Effect of added tocotrienol-rich fraction (TRF) (50 ppm) from palm oil on cholesterol status of nine-week-old Japanese quail fed 5% guar gum

	TRF	+ TRF
Live wt (g)	199 ± 6	201 ± 10
Liver lipid (%)	6.0 ± 0.5	4.8 ± 0.3
Liver cholesterol (mg/liver)	7.4 ± 1.1	6.5 ± 0.5
Total plasma cholesterol (mmol/L)	4.44 ± 0.33	3.59 ± 0.20[a]
Cholesterol synthesis[b]	538 ± 26	499 ± 20

[a] Significantly different, $P<0.5$.

[b] Nanomoles of mevalonate converted to cholesterol per liver per hr.

Although there is clear evidence of the effectiveness of soluble dietary fibre in lowering blood cholesterol, the biochemical mechanisms involved have yet to be satisfactorily explained. Tocotrienols may also prove to be important in the control of hypercholesterolaemia. However, further studies are required to define their role more clearly.

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New developments in understanding atherogenesis

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More than a decade ago, Brown and Goldstein made the pioneering observations that chemically modified low-density lipoprotein can load macrophages with huge quantities of lipid, so that they become 'foamy' in appearance, like the cells characteristic of the initiation of atherogenesis. The modification first studied was acetylation, but subsequently many investigators have sought more physiological mechanisms by which similar modification might occur. The hypothesis that free radicals modify lipoproteins in this manner during the development of atherosclerosis is now under intense scrutiny. Free radicals, being fragments of molecules which contain one or more unpaired electrons, can be generated as byproducts of many normal physiological processes, such as the mitochondrial and endoplasmic reticulum electron transport chains. It is proposed that such modification is necessary to generate high-uptake forms of lipoproteins: these are rapidly internalised, by endocytosis, but poorly metabolised so that they can deposit gross quantities of lipids in cells such as macrophages, giving rise to the foam cells' characteristic of the disease. We will discuss two components of this process: the failure of complete catabolism of the apoprotein of modified lipoproteins, and the accumulation of cholesterol and particularly its esters.

This presentation will first discuss new observations from our laboratory on the mechanisms of radical damage to proteins, including apoproteins of lipoproteins. We have characterised two novel reactive but long-lived moieties generated on radical damaged proteins. One is a protein hydroperoxide, and can consume critical cellular reductants such as ascorbate and glutathione, while also being reactive with metals. While lipid hydroperoxides have been studied intensively for many years, and are known to act as depots of potentially active radicals, protein hydroperoxides have in contrast been neglected. Three papers more than 30 years ago demonstrated their production during exposure of proteins to radicals generated by ionizing radiation, but since then they have totally disappeared from the scientific literature. We have rediscovered, and further defined these moieties, in collaboration with Dr. Jan Gebicki (Macquarie University, Sydney). Hydroxyl radicals are active in their generation, and they can occur in many radical-producing circumstances. They can be reduced by borohydride, and some of the moieties are clearly associated with the protein backbone, as judged by gel filtration and other techniques.

The other novel species produced on protein by radical attack is a reduc-

ing moiety, present particularly on aromatic amino acids, which can act on the transition metals iron and copper, whether free or bound to certain metalloproteins such as cytochrome C. This entity is produced particularly by irradiation under anoxic conditions, when electrons and hydroxyl radicals are generated. But the reducing moiety also occurs during exposure of proteins to Fenton systems, comprising hydrogen peroxide and transition metal; or to autoxidising sugars. Thus the reaction may be quite widespread. The importance of these reducing moieties is probably in their possible influence on the redox balance of transition metals on the protein surface. Since metals are mostly bound to macromolecules such as proteins, the metal atoms concerned with radical reactions and interconversions are often present there rather than in 'free solution', complexed to ions such as citrate. Many radical reactions tend to consume the reduced metal, whose concentration becomes limiting. Reductants, particularly if present on the same molecular surface may then be very important in determining the future progression of the radical reaction.

Studies such as these permit much more critical and precise assessment of oxidative events in lipoproteins and in atherosclerotic plaque. I will summarise work from Dr. Wendy Jessup from our Institute, and other colleagues indicating the mechanisms by which macrophages oxidise low density lipoproteins, and discuss the roles of radicals generated in the respiratory burst, from lipoxygenase activity, and in the nitric oxide pathway. The roles of the respiratory burst and of lipoxygenases may be more crucial. Other respiratory systems may also contribute. We will point out a major difficulty with studies on lipoxygenase, besides the universal problem of selectivity of inhibitory action of studied compounds: this is that lipoxygenase inhibitors tend to be powerful antioxidants, and antioxidants are amongst the critical defences against lipoprotein oxidations. Thus lipoxygenase inhibitors often restrict lipoprotein oxidation by cells quite independently of their action on lipoxygenases.

Other work in our lab has shown that the intracellular handling of oxidised low density lipoprotein is abnormal. While uptake and overall catabolism of the apoprotein is faster than for normal LDL, the intracellular pool is much larger than with normal, and its intracellular half-life is prolonged, indicating that a component of the protein is poorly degraded. This may be related to the concomitant accumulation of lipids.

We will then consider endogenous antioxidant protection mechanisms, and outline studies in collaboration with Roland Stocker of our institute on the antioxidant roles of tocotrienols and other work of Dr. Stocker's on ubiquinols. Tocotrienols, an important component of palm oil, have been compared in their antioxidant activity with tocopherols, and in several different systems are comparably effective. During studies in collaboration with Dr. Ross Hood, (CSIRO, Sydney), we have found that dietary tocotrienols can enter the plasma of rats, and we are presently seeking human samples in which to make a comparable demonstration. Plasma containing lipoproteins which have gained tocotrienol will be used in imminent studies to determine the role of the tocotrienols in the antioxidant chain in low density lipoproteins.

Dr Stoker's studies have also revealed an important antioxidant role in low density lipoprotein (LDL) for ubiquinol, previously unappreciated. During attack of several radical generating systems, including triggered neutrophils, upon human LDL, ubiquinols is the first endogenous

antioxidant to be consumed, before tocopherol and the carotenoid compounds. This observation contrasts with the apparently slighter importance of ubiquinol in bilayer biological membranes, and indicates the potential for further research in this area, and the possibility of further optimisation of antioxidant state in nutrition.

A currently central question in this theory of atherogenesis is whether specifically *radical-modified* lipoproteins and lipids, can be detected in atherogenic sites. The published data are mainly equivocal, because they do not distinguish lipoproteins from other proteins sufficiently. However, there are indications of damaged protein, possibly modified amino acids, and oxidised lipids in plaque. We will present analyses of the antioxidant status of plaque, and its lipid composition (in collaboration with Dr. Bill Huang). These studies are presently being extended to test precisely whether oxidised apoprotein B of LDL occurs in plaque. While it is known the fragments of apoB can be isolated from plaque, it is not yet clear whether they are oxidative or proteolytic fragments, and thus many central questions within the hypothesis remain to be answered adequately.

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Dietary fats and cardiovascular disease: effect of teaseed oil

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Dietary lipids appear to be a very important environmental factor in the etiology of cardiovascular diseases. Either the amount or the varieties of dietary fats might impose different effects on blood lipids. Intake of large amount of dietary fats, especially the saturated fatty acids will cause increase of plasma cholesterol level, whereas polyunsaturates decrease it. The effect of monounsaturated fatty acid on blood cholesterol is considered to be neutral.

However, some epidemiological studies revealed that in populations living in the Mediterranean region where olive oil is consumed, CHD rates are relatively low. There is significant negative relationship between the calories of dietary monoenoic acid and incidence of coronary heart disease. Results of the nutritional survey in 49 counties in China in 1983 found a significant negative correlation between erythrocyte phospholipid oleic acid content and the cumulative mortality of cardiovascular diseases. Many animal and human experiments also showed a lowering effect of monounsaturates on blood lipids level.

The purpose of this study was to examine the effect of oleic acid on the blood lipids, platelet aggregation and plasma prostanoid production of rabbits when fed with cholesterol. We used teaseed oil instead of olive oil or high-oleic safflower oil, which most western investigators used. Teaseed oil is one of special oil product in our country. This oil is of high quality, easily grown in valley, hillside and mountainous areas, and so does not compete with grains for land area. This is very important in China and also in other developing countries where arable land area is limited and a huge population to be fed. Teaseed contains about 76% oleic acid.

Twenty-two female New Zealand rabbits weighing 2-3 kg were housed individually in cages by feeding stock diet for 4 days. Then baseline fasting serum total cholesterol (TC) levels were determined. Based on the TC level, animals were divided into 3 groups. Three kinds of test oils: teaseed, coconut or high-linoleic safflower were given by stomach tube in a dose of 5 ml per day per animal along with stock diet. Cholesterol was added to each kind of oil up to a concentration of 10% (w/v). Venous blood were drawn from rabbits' ear at the 4th and 8th week. Animals were killed at the end of 8th week. Blood were collected from carotid by inserting a polyethylene tube in this artery. Serum TC, TG, HDL-C, platelet aggregation, plasma thrombox-

ane A_2 (TXA_2) and prostacyclin I_2 (PGI_2) (measured as their metabolites, TXB_2 and 6-keto-$PGF_{1\alpha}$ respectively) were determined. LDL-C was calculated according to Friedewald formula.

Experimental results showed that serum TC, LDL-C were significantly lowered in teaseed oil group than that in coconut oil group after on the diets for 4 week and 8 weeks, but no significant difference was observed between teaseed group and safflower group. HDL-C levels were similar in the three groups, and HDL-C/TC ratio was much higher in teaseed oil group than the other two groups (both $P<0.05$). Using ADP as the antagonist only, platelet aggregation was reduced in teaseed oil group, but the difference was significant only when compared with safflower oil group ($P<0.05$), and not to coconut oil group. Plasma TXB_2 levels were reduced both in teaseed and safflower oil groups when compared with coconut oil group (both $P<0.05$). Plasma $PGF_{1\alpha}$ was also reduced in these two groups, and the difference was significant between coconut and safflower oil, not significant between coconut and teaseed oil groups. The PGF/TXB ratio in teaseed group was the highest, but statistical significance was not found between groups.

All the results mentioned above showed a tendency of teaseed oil in alleviating the CVD risk by reducing blood total cholesterol, LDL-C, platelet aggregation and by raising the HDL-C/TC and PGF/TXB ratio. Teaseed and rapeseed oils are common edible oils in South China. Owing to their high content of monoenes, it might be considered that a high consumption of these two kinds of oils may be beneficial, contributing to the low CVD mortality in South rather than in North China as Chen *et al.*'s report published in "Diet, Life-style, Mortality in China", 1990.

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Clinical study on the relation of electrolytes and coronary artery disease

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Introduction

It has been reported all these years that there exists a close relationship between ischaemic heart disease and electrolytes such as sodium (Na), potassium (K), calcium (Ca) and magnesium (Mg) (1,2). However there were few detailed reports about this matter in human subjects who underwent coronary angiography (CAG). Coronary spasm is observed in Japanese patients who showed mild coronary sclerosis (3). It was with this view in mind that the author undertook this study, taking into account the patients' coronary spasm, the relationship between electrolytes and patients with acute myocardial infarction (AMI) and patients with angina pectoris (AP).

Materials and Methods

Subjects

926 subjects who had not been administered diuretics or digitals before admission, were admitted and underwent CAG. Group I consisted of 326 subjects with AMI, who prior to the occurrence of AMI suffered from AP. Group II subjects showed no signs of AP prior to the occurrence of AMI (4,5). 416 subjects with AP were divided into effort angina (Group III) and vasospastic angina (Group IV). 184 subjects showed no abnormality in their coronary angiography. This last group was used as our control group (Group V).

Methods

CAG findings were studied in compliance with the standards of the American Heart Association (6), and divided into five groups; C-1: normal, C-2: slight stenosis cases (less than 50%), C-3: 50% and over and less than 75% stenosis in one artery, and C-5: those with advanced stenosis in multiple arteries. Blood and urine during a 24 hour period, were collected in order to measure Na, K, Ca and Mg. Na and K were measured by flame photometry and Ca and Mg were measured using atomic absorption spectrophotometry. Also serum total protein and 24-hour's urinary excretions of creatinine and creatinine clearance were measured. Provocative testing for coronary spasm using acetylcholine (7) was undertaken in 82 cases of AMI who showed spastic findings at the time of CAG in chronic stage or suggested vasospastic AP clinically, and all the cases of Group IV. The Mg tolerance test (8) was undertaken by those who showed lower value than 1.6 mEq/L. MgO_2 was administered to those who showed Mg deficiency. Rates of angina attack and

change of percentage of PVC's frequency were observed before and after administration of MgO_2 using Holter monitoring.

Results

1. The ratio of those classified into C-1, C-2 or C-3 group was significantly larger in Group II than in Group I ($p<0.01$), and was significantly larger in Group IV than in Group III ($p<0.01$). The ratio of those classified into C-4 group was significantly smaller in Group I than Group II ($p<0.01$) and was significantly smaller in Group IV than in Group III ($p<0.01$). The ratio of those classified into C-5 group was significantly larger in Group I than in Group II ($p<0.01$), and was significantly larger in Group III than in Group IV ($p<0.01$). Moreover, the ratio was significantly larger in Group I than in Group III ($p<0.01$) and was significantly larger in Group II than in Group IV ($p<0.01$).

2. There were no significant differences in serum and urinary excretion of Na and Ca among the five groups. But the values of serum and urinary Ca tended to be lower in Group I and Group III than in Group V ($p<0.1$).

3. The values of serum and urinary K were significantly lower in patients of Group I and Group II than Group III, Group IV or Group V ($p<0.05$).

4. The values of both serum and urinary Mg were significantly lower in Group II than in Group I ($p<0.01$) and was significantly lower in Group IV than in Group III ($p<0.01$). The value tended to be lower in Group I, Group II, Group III or Group IV than in Group V ($p<0.1$).

5. The ratio of urinary Na to K was significantly larger in Group I and Group II than Group III, Group IV or Group V ($p<0.01$).

6. The ratio of urinary Ca to Mg was significantly larger in Group II than in Group I ($p<0.01$), and significantly larger in Group I, Group II, Group III or Group IV than in Group V ($p<0.05$).

7. The quantity of excretion of Mg during the Mg tolerance test was significantly lower in Group II than in Group I ($p<0.01$), and significantly lower in Group IV than in Group III ($p<0.01$).

8. There were no significant differences in serum total protein, urinary excretion of creatinine and the value of creatinine clearance among the five groups.

9. There was significant decrease in the rate of frequency of angina attacks ($p<0.01$) and percentage of PVC's frequency ($p<0.01$) after administration of MgO_2 in Group III and Group IV, respectively.

Discussion

There were many reports, both epidemiological and experimental, which related electrolytes to ischaemic heart disease. The renal function of the subjects of this study were within normal range and had no differences in the level of creatinine clearance. Moreover neither diuretics nor digitalis which affect the electrolytic metabolic process was administered. So, it can be considered that the results of this study, to a large extent, revealed the actual pathological relationship between coronary artery disease and electrolytes. In fact, judging from the results of acetylcholine provocative testing, Group II was closely related to coronary spasm. The pathologic condition of Group IV with respect to the electrolytes and the clinical characteristics of heart attack which occurred at night or early morning in bed suggested that Group IV might be similar to Group II. The values of K in Group I and Group II were lower, and this may have been caused by AMI

attack. The value of Ca tended to be lower in Group I and Group III. As the sclerotic change in CAG findings were drastic in Group I and Group III, Ca may be involved in the advancement of the sclerotic changes in coronary arteries. The value of Mg in Group II was low and the ratio of Ca to Mg[9] was large, and this indicates that Ca and Mg have an effect on the occurrence of AMI. Mg is thought to be a natural Ca^{++} channel blocker which prevents the entry of Ca^{++} through the cell membrane. So, Mg deficiency in Group II tends to bring about the occurrence of spasms by increasing much Ca^{++} in the cell. The sclerotic change in CAG findings was drastic and Mg was low. Furthermore the ratio of Ca to Mg was large, in both AMI and AP than in the control group. This suggests that Ca and Mg have a close involvement with the progression of sclerotic change of the coronary artery as well as to coronary spasms. Moreover, the author reported that electrolytes were closely related to cardiac sudden death due to AMI (10). Thus, electrolytes, particularly Ka and Mg are closely involved in the development of coronary artery sclerosis or coronary spasm. But further examination is needed to assess the relationship between the mechanism of coronary artery sclerosis or coronary spasm and electrolytes.

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Dietary protein and serum cholesterol

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Introduction

It has been well established that the nature of the protein source in the diet of rabbits is an important determinant of the concentration of cholesterol in the blood serum (1,2). Certain protein sources, such as extracted whole egg, casein and beef protein concentrate produce rather high concentrations of serum cholesterol, whereas other sources of protein, such as wheat gluten, peanut meal and soybean protein are able to maintain low levels of serum cholesterol. The induction of hyper-cholesterolaemia in rabbits fed diets containing casein is associated with the development of arterial lesions. In contrast, dietary soybean protein not only produces low levels of serum cholesterol but it also prevents atherogenesis (1).

For the rabbit model the mechanism underlying the cholesterol lowering activity of soybean protein, when compared to casein, can be described as follows (3). Soyabean protein decreases the absorption of intestinal cholesterol, which is of endogenous and/or exogenous origin, and probably also reduces the re-absorption of bile acids. This results in the observed increase in faecal excretion of neutral steroids (cholesterol and its bacterial metabolites) and bile acids. Thus, soyabean protein causes a diminished feed-back inhibition of the hepatic conversion of cholesterol into bile acids, and more cholesterol will be channeled into the bile acid synthetic pathway.

The increased loss of neutral steroids and bile acids in rabbits fed soyabean protein is responsible for the fall in serum cholesterol. However, in order to prevent the body from depletion of cholesterol, *de novo* synthesis has to be activated. A new steady state will be reached, at which hepatic cholesterol synthesis is increased and faecal excretion of bile acids is also increased. Thus, cholesterol turnover is enhanced.

Diets enriched with soyabean protein

In 1977 Sirtori *et al.* (4) reported the hypocholesterolaemic activity of the soyabean protein diet in type II hypercholesterolaemic patients. The soyabean protein diet contained 13% of energy as soyabean protein, 6% as other vegetable protein and 1.5% as animal protein. When compared to a diet containing 8% of energy as vegetable protein and 13% as animal protein, the soyabean protein diet reduced serum total cholesterol by 10 to 20% after three weeks (Table 1). Further studies from other laboratories

(5,6) have confirmed the cholesterol-lowering activity of high soy protein diets. The soybean protein diet specifically lowers cholesterol in the low-density lipoproteins (LDL) whereas that in the high-density lipoproteins (HDL) is left unchanged or somewhat increased.

Liquid formula diets

Grundy and Abrams (7) compared liquid diets containing either soyabean protein or casein. The diets contained 30% of calories as lard, 55% as glucose and 15% as protein. Cholesterol intake was about 200 mg/day. With these diets there was no effect of the type of

TABLE 1

Effect of diets rich in either soybean protein or mixed animal proteins on serum cholesterol concentrations in Type II hypercholesterolaemic patients.

Dietary protein	Serum cholesterol (mmol/L)	
	Before cross-over	After cross-over
Animal protein ⟶ Soy	8.7	6.7
Soy ⟶ Animal protein	8.6	7.2

Means for 10 patients per group. The patients consumed one type of diet for three weeks followed by the other diet for another three weeks. After Sirtori *et al.* (4).

TABLE 2

Effect of dietary soybean protein versus casein on serum cholesterol concentrations in subjects given liquid formula diets

Serum cholesterol (mmol/L)	Dietary protein	Low-cholesterol diets	High-cholesterol diets
Total	Casein	3.24	3.57
	Soy	3.29	3.43
LDL	Casein	1.66	2.15
	Soy	1.66	1.80
HDL	Casein	1.18	1.24
	Soy	1.23	1.44

Means for 10-11 subjects per diet. After Meinertz *et al.* (8,9)

dietary protein on serum total cholesterol concentrations in patients. Meiertz *et al.* (8) had similar results with liquid formula diets providing about 40 mg of cholesterol/day. However, when diets providing about 500 mg cholesterol/day were used (9), soyabean protein significantly reduced LDL-cholesterol and increased HLD-cholesterol when compared with casein (Table 2).

Diets based on regular foodstuffs

Controlled studies with healthy volunteers (19,11) have demonstrated that casein, when compared to soy protein isolate, does not significantly affect the level of serum total cholesterol. In these studies diets were used in which 60 or 65% of the protein in the diet consisted of either casein or soy protein. The diets were essentially identical with respect to the contents of cholesterol and fat, and the polyunsaturated:saturated fatty acid (P/S) ratio (10,11). Although there was no differential effect on serum total cholesterol, the diet containing soy protein isolate produced a shift in cholesterol from the LDL to the high density lipoproteins (HDL), resulting in a 7 (11) to 14% (10) increase in the HDL/LDL-cholesterol ratio. This effect of soy protein versus casein may be favorable with regard to the risk for atherosclerotic disease.

Various studies have been published in the last few years in which the type of protein was the only dietary variable (12-16). These studies reported either a small effect or no effect at all of mixed animal proteins or casein over soy protein on plasma cholesterol in healthy subjects, and a slightly larger effect in hypercholesterolaemic patients.

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Basal metabolic rates in chronic energy deficiency

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Introduction

It is universally assumed that the physiology and metabolic responses of the human body to chronic energy deficiency are similar to and can be explained on the basis of the changes that occur during acute energy restriction. As a result, there is considerable interest to look for physiological changes suggestive of an increase in metabolic efficiency of the active tissues even in chronically energy deficient subjects. A reduction in O_2 consumption per unit active tissue has been considered as being indicative of enhanced metabolic efficiency and as sign of the existence of metabolic adaptation. A decrease in BMR per kg fat free mass (FFM) in turn implies that the increase in metabolic efficiency is demonstrable in the other components of energy expenditure, particularly a decrease in the energy cost of physical activity of the individual.

BMR expressed either in absolute terms or expressed per unit body surface area (BSA) have always been found to be lower in chronically undernourished subjects. This is true of German prisoners of war, victims of severe malnutrition in ghettos, chronically malnourished adults studied during the war and malnourished or starved individuals seen during natural disasters like famine. However, when the BMR is expressed per unit of active tissue mass, in the same individuals, it is often difficult to demonstrate a significant decrease in metabolic rates thereby leading to the conclusion that it is in fact difficult to show clear cut evidence of an adaptive response in the BMR of chronically energy deficient, undernourished adults.

BMR in CED subjects

BMR measurements made in apparently healthy undernourished labourers showed a reduction in metabolic activity of the active tissue mass which perhaps could be interpreted as indicating an enhanced metabolic efficiency, although the major share of the fall in BMR was attributed to a decrease in total mass of lean tissues (1). Recalculation of data from earlier reports from India also showed that the BMR expressed per unit active tissue was considerably lower in adult undernourished males. A large number of measurements made recently, over the last decade, in chronically energy deficient (CED) subjects do not seem to confirm the existence of an enhanced metabolic efficiency as indicated by a reduced O_2 consumption per unit FFM. On the contrary, it now appears that BMR expressed per kg FFM is signifcantly higher in a large number of CED subjects measured by us as compared to well-nourished individuals (2). Comparable BMR

measurements made elsewhere in the country were also unable to provide supportive evidence for enhanced metabolic efficiency in CED individuals from poor socio-economic groups on lower than recommended levels of energy intake. The changes in BMRs seen in these groups seems to reflect the trends seen in the food intake surveys conducted during the same two decades which have also indicated a remarkable increase in the mean energy intakes of individuals and households. However, when BMR measurements made by us in the CED subjects is adjusted for differences in body weight and FFM by means of an analysis of covariance (ANACOVA), CED subjects, both urban and rural, demonstrate a significantly lower BMR for the adjusted FFM suggesting the presence of an apparent metabolic economy in these individuals (2).

The evidence that mechanisms of improved efficiency of energy utilisation are operative in free living populations on low energy intakes with similar but compromised anthropometry thus appears tenous and contradictory. If enhanced metabolic efficiency is indeed present in CED, than a reduction in BMR per kg FFM may not necessarily reflect its existence. If individuals who have anthropometric or functional characteristics suggestive of long term CED manifest a reduction in BMR per kg FFM, either BMR per kg FFM is not an index of metabolic efficiency as is universally believed or metabolic efficiency is not a constant and characteristic feature of CED. Changes in BMR per unit active tissue mass are perhaps not a *sine qua non* for metabolic efficiency.

BMR and body composition

One possible way in which these apparently contradictory data may be reconciled will be to seek an explanation on the basis of variable changes in body composition. Body compositional changes of adults with chronic undernutrition reveal a gradation of changes related to the severity of the deficiency (3). Muscle mass seemed to decrease linearly with increasing severity of undernutrition, while visceral mass showed little change. Protein turnover studies using ^{15}N glycine by our group also showed the existence of a greater visceral pool and a reduced muscle mass (4). The visceral component of FFM utilize nearly 45 percent of total O_2 consumption at rest while skeletal muscle which comprises up to 50 percent of body weight contributes only 18 percent to BMR. If the FFM had a significantly greater proportion of the metabolically active visceral mass and a reduced quantum of relatively less active muscle mass, BMR expressed per kg FFM would be apparently high. This may indeed be the case with mild to moderate energy deficiency since muscle mass is likely to be reduced while visceral mass is spared. As undernutrition progresses, mobilisation of tissue from the visceral mass also occurs and in severe forms of undernutrition the BMR per kg FFM is reduced. An elegant series of studies using animal models have also demonstrated that animals with similar body weights produced by different nutritional regimens show differences is BMR corrected for metabolic body size when the visceral mass: body weight ratio changes (5). Metabolically active tissues account for a significant proportion of BMR which is far in excess of the proportional weights of these tissues. Thus the BMR seems to be dictated by the heterogeneity of active protoplasmic tissues in the body; the relative proportions of contributing active tissues varying in different individuals and nutritional states.

Conclusion

It is likely therefore that variations in body composition, in particular

the relative contributions of visceral and muscle mass may account for changes in BMR expressed per unit active tissue or FFM. If the range of body composition changes seen in CED influence the parameter BMR per kg FFM, undoubtedly then, changes in this index cannot reflect a true change in metabolic efficiency of the active tissues of the body. It would thus appear that an increase in metabolic efficiency in the BMR component of energy expenditure which can be considered as being a beneficial, adaptive response to energy inadequacy, is itself of doubtful existence.

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Basal metabolic rate in tropical peoples – A reappraisal

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Introduction

In 1896, almost a century ago, not far from where we are assembled today, namely Indonesia, the great Dutch nutritionist, Eijkman (1) measured the basal metabolic rate (BMR) of German and native Malays living in Indonesia. He reported no significant difference in the metabolic rate between the two groups. Although these measurements may be regarded as the earliest reports of BMR in two contrasting communities, the paper that provoked the greatest controversy was that by Almeida (2) from Brazil, who claimed that the BMR of native Brazilians was 16-20% below American standards. In the same year (1921) a similar report of a lower BMR in people living in Cuba emerged (3). Since these early observations, physiologists and nutritionists have been interested in confirming or refuting these putative reports of a lower BMR in tropical peoples. In fact for more than half a century, Indian scientists (4-6) have repeatedly claimed a lower BMR in subjects living in India.

BMR represents the largest component of energy expenditure. It has also come to play a significant role in the estimation of energy requirements in humans. The recent FAO/WHO/UNU report on energy and protein requirements (7), proposed the use of energy expenditure rather than intake as the basis for estimating energy needs in man. The report also suggested that various components of energy expenditure be expressed as multiples of basal metabolic rate (BMR). This new approach in estimating energy requirements emphasises the need to estimate accurately BMR in peoples living under various climatic and environmental conditions. Under- or overestimation of BMR would significantly affect the overall estimation of energy requirements.

A review of the literature presented predictive equations for both sexes for the following age: 0-3, 3-10, 10-18, 18-30, 30-60 and >60 years (8) and the analysis also formed the basis for the equations used by the FAO/WHO/UNU report (7). Although the data base was comprised of almost 11000 BMR measurements, most of the values were obtained from European and North American subjects. An interesting feature that emerged from their analysis was that the BMR of Asiatic Indians was overestimated by 10-11 per cent by their equations. This issue was further highlighted by the FAO/WHO/UNU report (7). At the time of their analysis there was insufficient

data to ascertain whether the effect noted in Indians was unique or whether it reflected a general pattern of metabolism present in tropical people.

Before any generalisations may be made about the BMR in other tropical peoples, it is necessary to analyse systematically the BMR in people living under varying tropical environments. With this objective in mind, this paper is a reappraisal of BMR studies conducted in the tropics and demonstrates that the BMR of people living in the tropics is significantly lower than that predicted by the Schofield equations. Data not previously evaluated by FAO/WHO/UNU report (7) are also presented, thus representing the most comprehensive analysis of BMR in tropical peoples ever undertaken.

Materials and Methods

Data collection

After careful screening of the literature, data was accepted for statistical analysis only if they met the following criteria:

(1) BMR was conducted in normal, healthy subjects.

(2) BMR was measured under standard conditions, i.e. post-absorptive, relaxed state.

(3) General descriptions of the equipment used for the study were available.

(4) Measurements such as weight, height, age, sex were reported.

Several papers were excluded from the analysis as one or more of the criteria were not met.

Statistical methods

Linear equations relating BMR to body weight were derived by regression analysis. The range of body weight over which our equations differed significantly from those of Schofield *et al.* (8) were determined by the method proposed by Rees and Henry (9) and Henry and Rees (10).

Results

Applying the strict criteria listed above, 2822 new BMR measurements were obtained from both sexes and a range of ages. Table 1 summarises the number of subjects in each age group. Linear regression equations of BMR on body weight were obtained and compared with those published (8).

TABLE 1

Summary of number of subjects in each age group

	Age group (yrs)				
	3-10	10-18	18-30	30-60	Total
Males	196	409	1174	274	2053
Females	88	233	350	98	769
Total	284	642	1524	372	2822

Table 2a shows the regression for BMR related to body weight at each age band in the present analysis as compared to Schofield (Table 2b). Figures 1a - 4b present the graphical relationship of BMR to body weight. Visual inspection of the graphs for males and females in the age group 3-10 years (Figures 1a & b) show that our regression lines lie close to those of Schofield (8) implying a close agreement in this age group. Other age groups show marked deviations (Figures 2a - 4b).

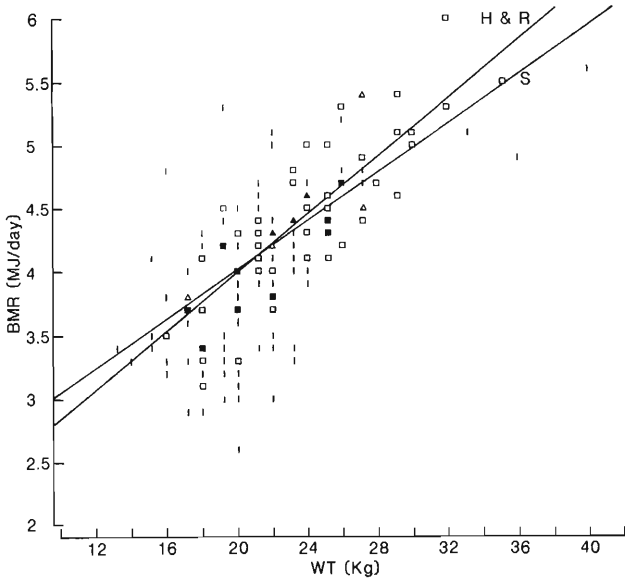

FIG. 1a: Regression of BMR against bodyweight in 196 males aged 3-10 years. S, Schofield equation, H&R, Henry & Rees equation.

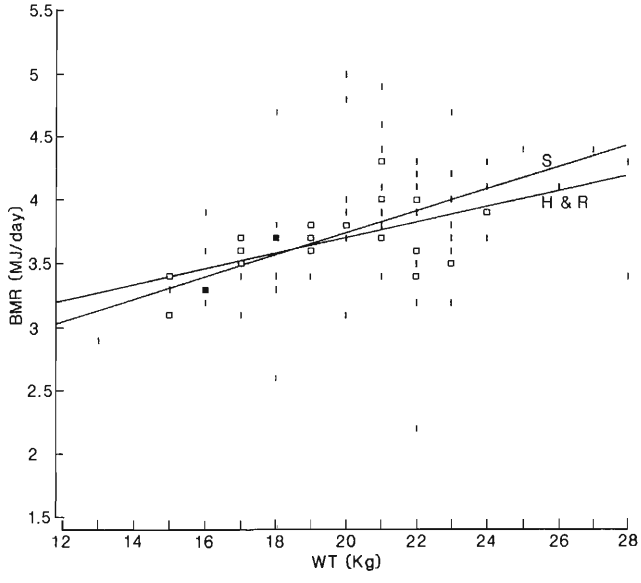

FIG. 1b Regression of BMR against bodyweight in 88 females aged 3-10 years. S, Schofield equation, H&R, Henry & Rees equation.

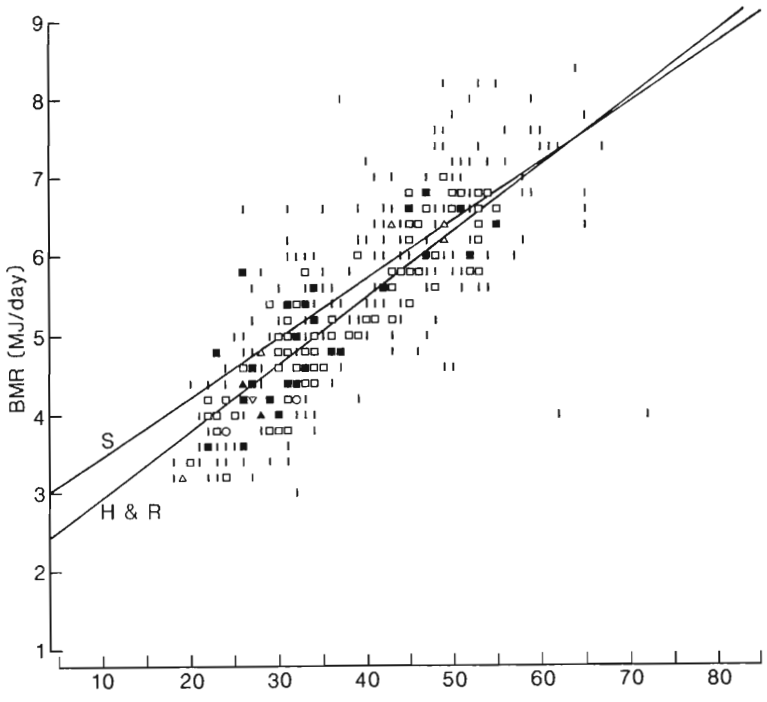

FIG. 2a: Regression of BMR against bodyweight in 409 males aged 10-18 years. S, Schofield equation, H&R, Henry & Rees equation.

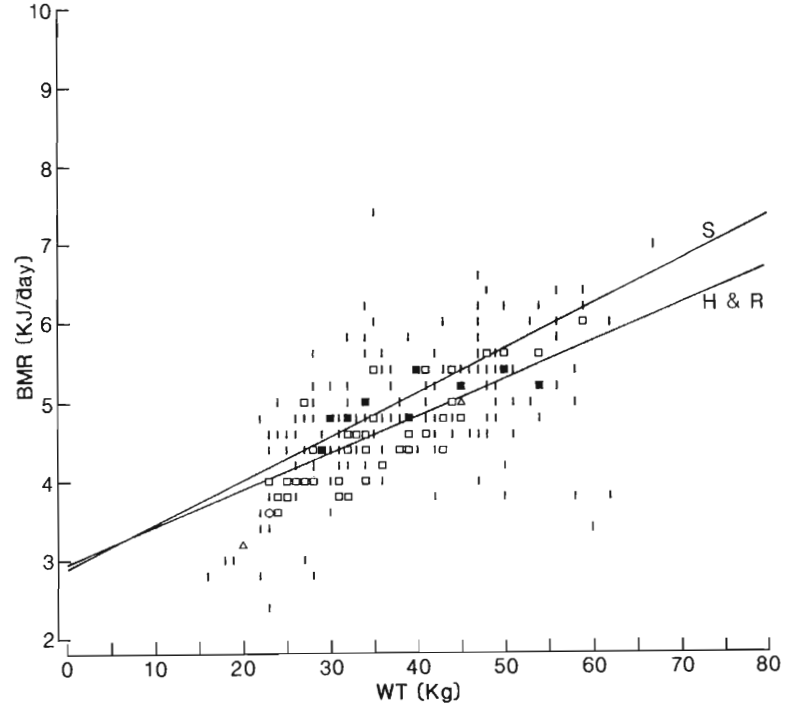

FIG. 2b: Regression of BMR against bodyweight in 233 females aged 10-18 years. S, Schofield equation, H&R, Henry & Rees equation.

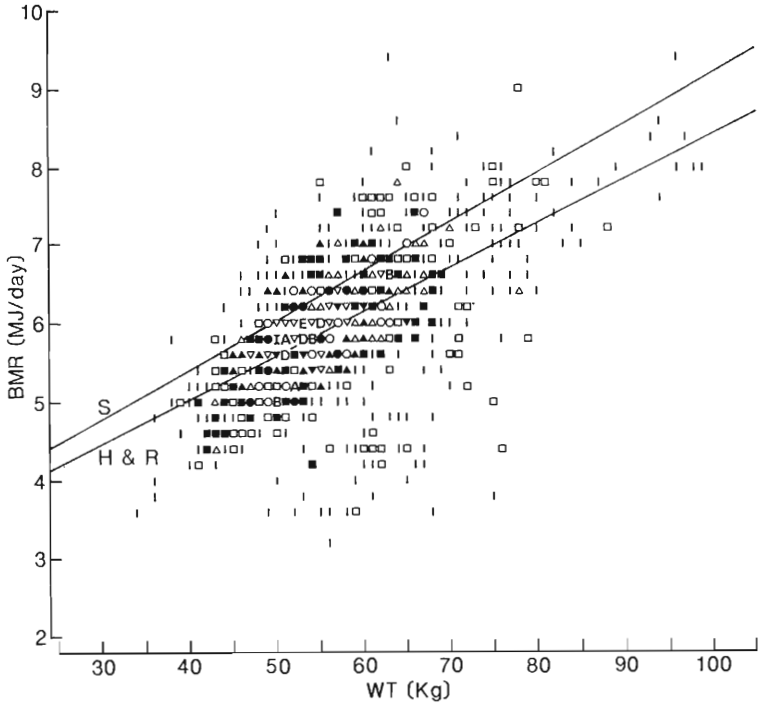

FIG. 3a: Regression of BMR against bodyweight in 1174 males aged 18-30 years. S, Schofield equation, H&R, Henry & Rees equation.

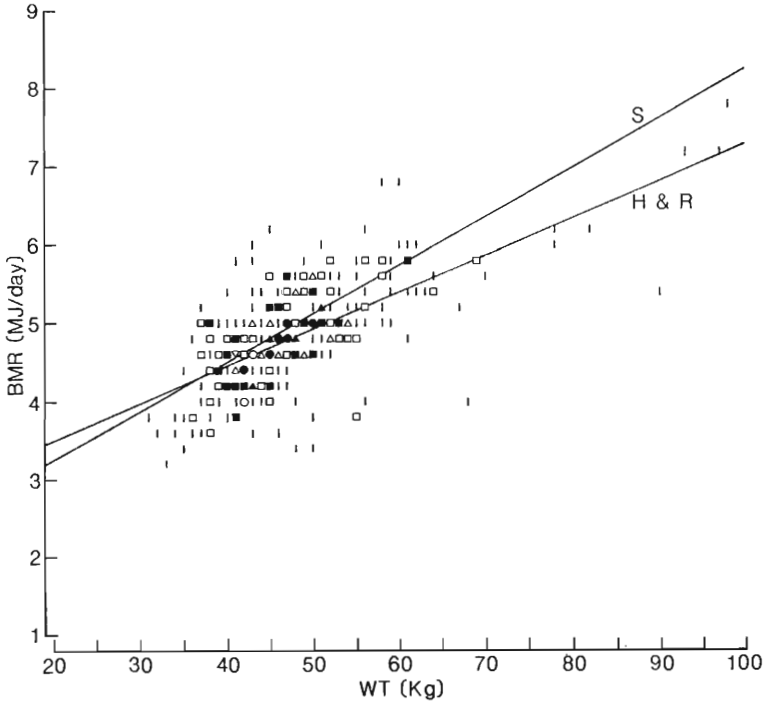

FIG. 3b: Regression of BMR against bodyweight in 350 females aged 18-30 years. S, Schofield equation, H&R, Henry & Rees equation.

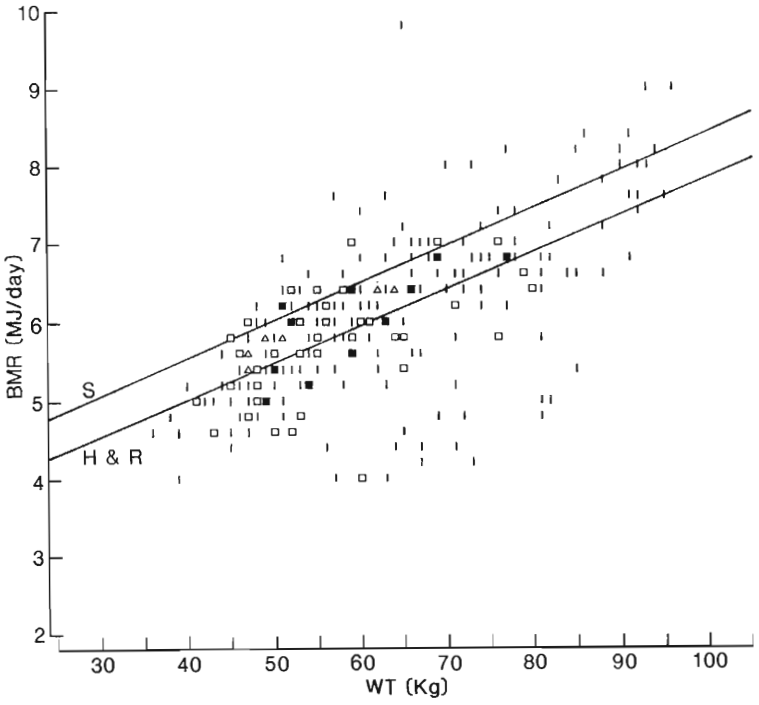

FIG. 4a: Regression of BMR against bodyweight in 274 males aged 30-60 years. S, Schofield equation, H&R, Henry & Rees equation.

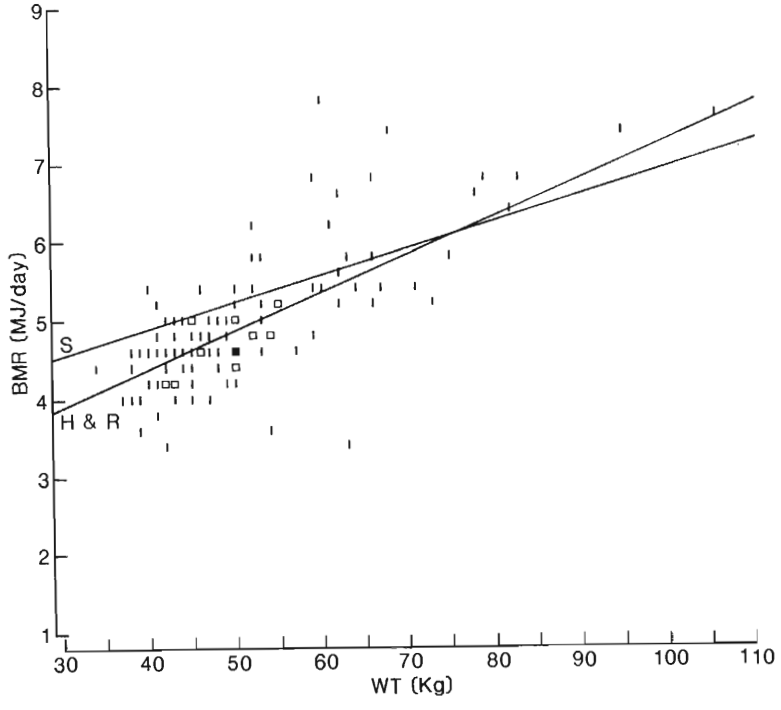

FIG. 4b: Regression of BMR against bodyweight in 98 females aged 30-60 years. S, Schofield equation, H&R, Henry & Rees equation.

TABLE 2a

Equations derived for BMR related to body weight in present analysis (BMR MJ/d, weight in kg)

		n	R	s.e.
Age 3-10 years				
Males	BMR = 0.113W + 1.689	196	0.75	0.4422
Females	BMR = 0.063W + 2.466	88	0.41	0.4421
Age 10-18 years				
Males	BMR = 0.084W + 2.122	409	0.80	0.6995
Females	BMR = 0.047W + 2.951	233	0.63	0.6246
Age 18-30 years				
Males	BMR = 0.056W + 2.800	1174	0.59	0.7091
Females	BMR = 0.048W + 2.562	350	0.67	0.4812
Age 30-60 years				
Males	BMR = 0.046W + 3.160	274	0.66	0.7039
Females	BMR = 0.048W + 2.448	103	0.74	0.5056

TABLE 2b

Schofield equations for same age groups (BMR MJ/d, weight in kg)

		n	R	s.e.
Age 3-10 years				
Males	BMR = 0.095W + 2.110	338	0.83	0.2803
Females	BMR = 0.085W + 2.033	413	0.81	0.2924
Age 10-18 years				
Males	BMR = 0.074W + 2.754	734	0.93	0.4404
Females	BMR = 0.056W + 2.898	575	0.80	0.4661
Age 18-30 years				
Males	BMR = 0.063W + 2.896	2879	0.65	0.6407
Females	BMR = 0.062W + 2.036	829	0.73	0.4965
Age 30-60 years				
Males	BMR = 0.048W + 3.653	646	0.60	0.699
Females	BMR = 0.034W + 3.538	372	0.68	0.465

We have calculated for each data point the percentage by which the Schofield equations overestimate or underestimate the BMR actually measured in tropical peoples. The percentages are averaged for each age/sex category in Table 3 and for each ethnicity in Table 4. Table 5 shows the 'normal' range of body weight for the various categories and also the percentage of each normal range over which our equations differ significantly from Schofield's equations (8).

TABLE 3

The percentages by which Schofield equations over-estimate (+) or under-estimate (-) the actual BMR in different ethnic groups

1 Males, all ethnicities

Age group	Mean %	Sample Size
3 - 10	+ 1.9	196
10 - 18	+ 7.1	409
18 - 30	+ 10.3	1174
30 - 60	+ 11.2	274
3 - 60	+ 9.0	2053

2 Females, all ethnicities

Age group	Mean %	Sample Size
3 - 10	+ 1.5	88
10 - 18	+ 7.6	233
18 - 30	+ 3.8	350
30 - 60	+ 9.7	98
3 - 60	+ 5.4	769

3 All ethnicities, all ages, both sexes

Mean %	Sample Size
+ 8.0	2822

TABLE 4

The percentage by which Schofield equations overestimate (+) or under-estimate (-) BMR in different ethnic groups by sex, all ages 3-60 years.

	Males		Females	
Ethnicity* %	Mean %	Sample Size	Mean	Sample Size
Filipinos	+ 9.5	172	+ 1.1	31
Indian	+12.8	50	+12.9	7
Japanese	+ 5.8	202	+ 4.6	152
South American	+ 9.4	941	+ 4.8	227
Chinese	+ 7.6	274	+ 3.8	190
Malay	+ 9.3	62	no data	
Javanese	+ 5.0	86	no data	
Mayan	+ 1.5	76	no data	
Ceylonese	+22.4	125	+12.5	100
African	+ 6.5	20	no data	
Hawaiian	+ 7.2	19	+ 4.5	62
Samoan	+ 3.3	21	no data	
All	+ 9.0	2053	+ 5.4	769

* A complete list of papers used for the analysis may be obtained by contacting Dr Jeya Henry)

TABLE 5

5% significance region for weight within normal range

		(1) *`Normal' bodyweight, W(Kg) range for present data	(2) 5% significance region for W within normal range	(2)/(1) x 100%
Males	3 - 10	15 - 36	0	0
	10 - 18	20 - 66	20 - 50	65
	18 - 30	41 - 77	41 - 77	100
	30 - 60	39 - 92	39 - 92	100
Females	3 - 10	15 - 27	0	0
	10 - 18	20 - 65	27 - 65	84
	18 - 30	33 - 66	43 - 66	70
	30 - 60	33 - 77	33 - 64	70

* `Normal' have indicates with means $\pm$ 2 standard deviations of log W, i e. assuming W is lognormally distributed.

Discussion

Our analysis indicated that, in the range of tropical peoples surveyed, actual BMR is on average 8 per cent (Table 3) below that predicted by the FAO/WHO/UNU equations (7). The percentage is higher for males (9 per cent) than for females (5.4 per cent) and higher generally for older individuals. The pattern of overestimation is the same for all ethnicities but to varying degrees (1 per cent up to 22 per cent; see Table 4)

The percentages of the normal weight range over which our new predictive equations differ significantly from Schofield's vary between 65 and 100 per cent for all age groups except for the 3-10 year olds where no significant differences were found (Table 5). It thus appears that the reported lower BMR in Asiatic Indians is not unique but reflects a phenomenon also found in other tropical peoples. Explanation for this lower BMR in tropical peoples is not simple. Using a set of BMR measurements made on subjects living in Malaysia (11), we have compared the predictive power of the two equations (8, 10). The results are shown in Table 6.

Whilst the present equations come closer to the observed values, the observed BMR values are considerably lower in comparison to the widely used Schofield equation. It is likely that it is due to a combination of factors - climate, diet, ethnic background and body configuration, i.e. allometry (12,13). It is unlikely that the lower BMR observed in our analysis is due to the inclusion of malnourished subjects as they were all drawn from a 'normal' healthy population.

Several explanations have been proposed for the lower BMR in tropical peoples. For example Durnin (14) commented 'varying racial abilities in producing differing degrees of muscular relaxation or perhaps more importantly the minor degrees of muscular relaxation may be induced by environmental temperatures, which may still appear to be comfortable'.

Climatic influence on BMR may also be of some significance. Whilst evidence in the literature for changes in BMR on moving to the tropics from the temperate regions is equivocal, the overall consensus appears to be a fall in BMR in most people who move to the tropics. A likely explanation for this

TABLE 6

BMR values in Malaysian subjects: observed and predicted values (males)

Ethnicity	n	Body wt (kg)	Observed BMR (MJ/d)	Predicted BMR (MJ/d)		% Deviation	
				Schofield	Henry & Rees	Schofield	Henry & Rees
Malay	14	60.2+5.9	5.603+0.54	6.689	6.171	+16.2	+ 9.2
Chinese	14	62.8+5.9	5.543+0.36	6.852	6.317	+19.1	+12.2
Indian	14	62.8+7.6	5.302+0.60	6.852	6.317	+22.6	+16.1
All races	42	61.9±6.7	5.483±0.54	6.796	6.266	+19.3	+12.5

fall in BMR may be due to the temperature-induced changes in thyroid gland activity (15).

Although a complete explanation for these deviations in BMR may not be offered at this stage, the results are consistent and appear genuine. The lower BMR noted in these people may, in part, explain the observation that certain individuals in the tropics are capable of active lives even on low energy intakes. Indeed recent reports from Africa, South America and Malaysia support the views expressed in the paper. It has been reported that the BMR was roughly 10 per cent lower in Gambian men than in Europeans (16) whilst the BMR in mestizo boys was 7 per cent lower than predicted by the Schofield equations (17).

Conclusion

In 1985, James commented on the ethnic differnces in BMR as follows: `clear evidence has been given that in the data used to compute the new equations (Schofield) the Indian values are significantly lower ... there is insufficient information on other Asian groups - Chinese, Indonesians, Malays, Koreans for further comparison'. The present paper has precisely addressed this point and has included groups such as the Chinese, Malays, Javanese, Japanese, Filipinos, Ceylonese, Africans, Hawaiians, Samoans, Mayan and South Americans. They all point to a lower BMR than predicted by Schofield's equations. Therefore there is now sufficient data to suggest that the BMR in all the tropical people reviewed is lower than predicted by the Schofield equations (8).

One practical use of BMR is in the estimation of energy requirements for population groups and subsequently their food needs. The latest FAO/WHO/UNU report Energy and protein requirements (1985)' makes clear for the first time the two main purposes for determining energy requirements. The first is for prescriptive purposes, that is, for making recommendations about the level of consumption that ought to be maintained in a population; the second, for diagnostic purposes, that is, the assessment of the adequacy or inadequacy of the food situation of a population. Several factors are involved in the final estimation of energy requirements. These include (i) body size of the population, (ii) activity patterns of the population and (iii) choice of the physical activity index (18). Whilst some uncertainties and variability may exist in each of these factors, the fundamental measurement for which energy requirement is built up is the basal metabolic rate. The present analysis shows that the BMR in the tropics is lower than that predicted by Schofield's equations and can no longer be dismissed as an artifact. Although caution must be exercised in interpreting the results presented here, especially in the context of food policy, further discussion on energy metabolism in tropical peoples must consider these recorded differences in BMR of total energy expenditure. More detailed field studies of total energy expenditure in the tropics will prove the utility of these predictive equations.

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Strategies to counteract re-adjustments towards lower metabolic rates during obesity management

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Introduction

Aesthetically speaking, fatness may be considered to be both undesirable, as is currently the attitude in the western world, as well as desirable for example, among certain communities in Africa, the Middle East and in Asia. Medically, however, it is a health hazard bypassing all national and cultural boundaries since it is a major mortality risk in affluent societies and an underlying factor in many debilitating conditions including diabetes, coronary heart diseases, hypertension etc. While its prevalence has been increasing steadily over the past 30 years, there has been little advance in the treatment of this disorder. Reducing calorie intake by dieting or with the help of appetite-suppressant drugs remains the method of choice to lose weight. Despite its poor prognosis - due to a high drop-out rate, poor compliance to dietary regimes, and the development of tolerance to anorectic drugs – this approach is likely to continue in the foreseeable future. However, there is growing awareness that energy intake and energy expenditure are closely linked, and that in response to caloric restriction, the accompanying fall in energy expenditure is a major factor that limits weight loss and facilitates the return to the obese condition. This paper reviews briefly the various compartments of energy expenditure that participate in the "adaptation" to low calorie intake. It then analyses the rationale, applicability and effectiveness of various approaches (behavioural, dietary and pharmacological) that could conceivably stimulate metabolic rate and thus counteract such adaptive changes in energy expenditure.

Adjustments in the compartments of energy expenditure in response to low energy intake

As a result of lower food intake, the loss in body mass will entail *obligatory* reductions in (i) the energy cost for basal metabolism, since the basal metabolic rate (BMR) is related to an index of metabolic mass (lean body mass, $W^{0.75}$ or $W^{0.66}$), and (ii) in the amount of energy spent in performing work since from a consideration of simple mechanics, the energy cost of physical activity (i.e. work done on the environment) is related directly to body weight. In addition, there may also be behavioural changes (e.g. reduced activity levels) as well as specific physiological mechanisms operating to spare energy. In support of the latter contention, Miller & Parsonage (1) studying a group of 29 obese women isolated in a country house and kept on a 1500 kcal dietary regime for 3 weeks, found that nearly a third of the

women failed to lose weight, and that resistance to slimming can be associated with a low BMR and low daily energy expenditure (EE). More recent studies indicate that after substantial weight loss, some postobese adults tend to have a lower 24hEE than weightmatched lean controls (2), others a reduced energy requirement for weight maintenance (3), and still others, a subnormal thermogenic response to food or to exercise (4). In our own studies, postobese subjects had a normal BMR but they showed only athird to ahalf of the thermogenic response to food observed in lean controls (5, 6). It is clear that there is a lack of homogeneity in the compartments of EE that may be reduced in the obese and postobese, but the final outcome is the same, that is, subjects with a predisposition to obesity tend to be metabolically more efficient in energy utilisation (7). However, in the face of both genetic and dietary variability, coupled with limitations in methodological and experimental approaches, the accurate analysis of human data on obesity is difficult. This has resulted in controversies concerning the existence and quantitative importance of an increase in wholebody metabolic efficiency in lowenergy adapted humans. However, longterm energy balance measurements and precise body composition analysis in animal models indicate that this adaptive metabolic component during low calorie intake corresponds to 1015% of normal EE, and that it is "carried on" to accelerate the replenishment of fat stores whenever food availability is increased (8,9). In humans, it seems unlikely that this debate concerning "metabolic adaptation" could be resolved in the near future, but it is clear that as a result of weight loss, the accompanying reductions in the various compartments of EE result in an energy requirement that is substantially lower than predieting values for example, as much as 300600 kcal after a weight loss of 2030 kg. Reductions in energy metabolism of this magnitude are not only counterproductive to the efficacy of the dietary regime in achieving the target weight, but they also contribute importantly to the relapse of the obese condition. Hence, approaches that can effectively and safely raise the rate of energy expenditure would be an invaluable help in the management of obesity.

Strategies to counteract diminished energy expenditure on slimming regimes

The idea of stimulating metabolic rate in order to facilitate weight loss is not new, but the physiological basis upon which various approaches were developed has undergone considerable changes over the past decades. The remaining part of this paper analyses these various strategies which include behavioural, dietary, hormonal and pharmacological interventions.

Exercise

Increasing the amount and intensity of physical activity would seem to be an effective way to compensate for the drop in EE in response to low calorie intake since this would involve (i) expending more calories for performance of an increased work load and (ii) minimising the reduction in lean body mass and hence the obligatory fall in BMR. In fact, most clinics and slimming groups try to combine both types of treatment (i.e. dieting and exercise). But the dropout rate is high (10) since the amount and intensity of exercise required to produce a substantial negative energy balance often involving daily aerobic exercise exceeding 60% of maximal aerobic capacity for 12 hours is simply beyond the physical ability of most obese subjects.

Meal frequency

Since the work of Fabry (11) in

man showing an inverse relationship between meal frequency and adiposity, several studies have investigated the notion that isoenergetic low calorie intake diets taken as a large number of small meals (nibbling) may be more energycosting and hence induce greater weight loss than the same diet taken as a small number of large meals (gorging). Calorimetry studies, albeit over only 24h, have been unabled to detect differences in daily EE during nibbling versus gorging, and seem to support the majority of chronic studies (12) that have failed to find any significant relationship between meal frequency and weight loss during dieting.

Hormones

Crude thyroid extracts were used in obesity therapy at the turn of this century, and thyroid hormones are still used nowadays to treat the hypothyroid obese. The vast majority of obese however are euthyroid, and treatment with thyroid hormones has proven to be either ineffective or too dangerous, since an increase in metabolic rate can only be achieved with doses of the hormones which are high enough to expose them to risk of thyrotoxicosis and other complications. It is often suggested that T_3 replacement may play a role in enhancing weight loss during dieting (when both the metabolic rate and T_3 levels fall), but much of the additional weight loss is due to reductions in body protein rather than fat (13). The reports that other hormones examples, glucagon, growth hormone, human chorionic gonadotropin (HCG) and some of the oestrogens were thermogenic in man have never been confirmed (13). Glucagon seemed particularly interesting in view of its antagonism to the energy storage function of insulin, but the exogenous doses of glucagon required to elicit a thermogenic response are far outside the physiological range. Administration of growth hormone, or LDOPA, which stimulates its secretion, fails to alter the body weight of obese patients (14,15). In general, there is little interest today in testing these hormones as thermogenic antiobesity agents mainly because of the lack of physiological basis for their use.

Synthetic drugs

2,4dinitrophenol was the first synthetic drug put to use in the treatment of obesity. By uncoupling oxidative phosphorylation and hence allowing energy to be dissipated as heat, it was effective in reducing body weight among many of the 100,000 or so obese humans treated in between the two world wars. It was discontinued because of serious side effects and even some deaths. Derivatives of dinitrophenol (e.g. dinitrocresol) were also tested (16), but no one was able to separate the uncoupling effects from the serious side effects such as cataracts. Antiinflammatory drugs such as salicylates, aspirin and indomethacin (17,18) also raise metabolic rate acutely, but the effect is too mild to have practical value.

Foods and nutrients

Over the decades there have been frequent claims that one food is more thermogenic than others, with the explanation for such differences attributed to the energy costs of their metabolic fates. However, it is often argued that such differences apply only to artificial meals (single nutrients rather than food), relate to incomplete measurements of the thermic effect of the meal, or that they are so trivial in quantitative terms that they have no impact on longterm EE particularly during weight loss. In fact, recent studies found no difference in 24h EE in response to isocaloric exchange between high fat and high carbohy-

drate diets in both lean and obese humans (19). Similarly, clinical trials have failed to show differences in weight loss when obese patients were put on hypocaloric diets differing in the ratios of fat to carbohydrate, medium-chain to longchain triglycerides, or in the ratio of polyunsaturated to saturated fats (2022). Nonetheless, considerable optimism persists in that even though alterations in dietary composition have no impact on EE once the obese condition is already morbid or during weight loss, they may have a role in the dynamic phase leading to the obese condition. Such investigations are difficult to conduct in humans, but studies in laboratory animals have provided insights into the potential role of manipulating dietary composition on the elevated efficiency favouring fat deposition during obesity relapse (23). The general conclusions are that high fat diets (>40% of energy intake) exacerbate the adaptive fall in EE during body weight recovery. However, within the recommended range of nutrient intake for general good health (adequate protein and <35% fat), neither differences in fat levels, chain length and degree of unsaturation, nor differences in carbohydrate types influence the energetics of fat accumulation during the regain of body weight. It would seem therefore that there is little hope of countering the enhanced efficiency for fat deposition in response to a low energy diet by altering diet composition. It turns out that one has to focus on pharmacological means.

Cigarettes, coffee and alcohol

Coined as the "Drugs of Everydaylife" by Miller (17), caffeine, nicotine and alcohol, which have become part of our food, are well known to possess thermogenic properties. Smoking a packet of cigarettes a day raises the daily metabolic rate by 10% (24), effects that would in part explain the tendency to gain weight upon cessation of smoking. However, the high risks of cardiovascular diseases, cancer and other complications associated with cigarette smoking and alcohol consumption clearly outweigh any beneficial effect that they may have on body weight. In contrast, caffeine is relatively safe in moderate amounts and is usually found in beverages (e.g. coffee), chocolates, cakes, and in numerous pharmaceutical preparations (e.g. for coughs and asthma). In commonlyconsumed doses, caffeine (600 mg/day) has recently been shown to enhance dietinduced thermogenesis in postobese human subjects (6) and to increase their daily energy expenditure by 5%. However this effect is too mild to be therapeutically useful, and in fact a recent doubleblind study (25) indicate a mild and insignificant effect of caffeine compared to placebo on weight loss when administered in conjunction with a low calorie diet.

Sympathomimetics

The thermogenic effects of nicotine and caffeine have long been suspected to be mediated through interference with the activity of the sympathetic nervous system (SNS). It is only over the past ten years however that interest in thermogenic drugs has shifted towards an active search for stimulants which mimic the activity of the SNS (i.e. sympathomimetics). This new approach follows several lines of evidence suggesting that diminished SNS activity (hence reduced heatproducing neurotransmitter noradrenaline, NA) contribute to the diminished EE leading to obesity, as well as to the adaptive fall in EE in response to low calorie intake (26). Drugs that mimic the activity of the SNS and increase the metabolic rate therefore offer considerable therapeutic potential, and provide a rational pharmacological approach in obesity treatment. This had led to the testing (23) of a

wide variety of sympathetic stimulants already in clinical use for other treatments, as well as some βagonists used experimentally for the production of leaner livestock. In addition, several pharmaceutical companies, largely motivated by evidence suggesting that the adrenergic control of thermogenesis involves mechanisms other than conventional α and β adrenoceptors, have been sucessful in putting forward a new generation of atypical βagonists (often termed β_3 agonists). The aim is to target specifically the β_3 adrenoceptors and hence minimising sideeffects associated with β_1 and $\beta_2$adrenoceptor activation.

Those sympathomimetics of interest include ephedrine (enhancer of NA release), clenbuterol and cimaterol ($\beta_2$agonists) and several of those novel $\beta_3$agonists (23). In animals, they have all been shown to possess potent antiobesity properties and to reduce specifically fat and not body protein. At the current state of knowledge, however, information about their safety and efficacy in obese human subjects is limited to only one of these novel $\beta_3$agonists (BRL 26830A) and the "old" sympathomimetic ephedrine. When administered in conjunction with low calorie diets, both types of sympathomimetics have been shown to induce greater weight loss than with placebo, and to be reasonably well tolerated (2729). In fact, it should not be a surprise that with ephedrine, a compound apparently mediating its thermogenic effects by inducing the release of NA from sympathetic nerve terminals (30), the side effects were mild and mostly transient. This is because (i) when administered in conjunction with a low calorie diet, ephedrine may merely reduce the fall in NA turnover rates rather than augmenting it above predieting levels, and also (ii) because of the wellknown rapid development of tolerance *visavis* its effect on the cardiovascular functions. In contrast, tolerance does not develop to its thermogenic effects thereby raising the possibility that ephedrine, by exerting its effects via sympathetically released NA, may be activating the same population of atypical adrenoceptors shown to possess high affinity for the novel βagonists.

It should be borne in mind that so far, these drugs represent only the first generation of sympathomimetics tested primarily for their thermogenic antiobesity properties. There is no doubt that more selective and more efficacious future generations of atypical $\beta_3$agonists will be found. At the same time, one can also look ahead to the possibilities of enhancing the effects of ephedrine on thermogenesis, particularly with compounds that counter the inhibitory modulators of NA release and actions. For example, methylxanthines and aspirin have mild thermogenic effects in their own rights, but they can markedly potentiate the thermogenic effects of ephedrine in obese and postobese human volunteers, and induce greater weight loss than ephedrine alone (5, 25, 29, 31, 32). Such mixtures can be considered to be relatively safe and acceptable given their long history in clinical use and common occurrence for cough and asthma (33). But more interesting is the fact that this approach provides a rational basis to extend the search for safer and more effective novel xanthines and aspirinlike compounds as potentiators of sympathomimeticinduced increase in metabolic rate.

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Some features of the control system for energy balance in humans

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Introduction

The constancy of the body weight and composition in human subjects appears to require a system by which the energy intake and the energy expenditure is controlled by way of feedback from elements that measure body weight or body energy content or both. The nature of these elements are not known and, furthermore, there has been a serious lack of data with respect to the parameters of the feed back loops in free living subjects. Accordingly, very few attempts have been made to describe the quantitative aspects of the control system (1).

New data on the between subjects variation in energy expenditure for fixed physical activity suggest that this variation is almost completely described by (i) within subjects variation in time, (ii) by measurement error and (iii) by variation in organ weights (2). This observation suggests that variation in energy expenditure within and between subjects can be related to body energy content only.

The introduction of the double labelled water method to measure energy expenditure in free living subjects has recently provided data on the effects of overfeeding and subsequently lower energy intake on the body energy content and energy expenditure of free living subjects (3,4).

We have used data from these studies to calculate energy balance in a number of situations on the basis of a model that assumes proportional feed back control of the energy intake and energy expenditure from the body energy content. Due to the nature of the fundamental assumption and imprecision in the data, the results of the calculation must be taken as first approximations only.

Theory

With the assumption of proportional feedback to energy expenditure and energy intake from the body energy content (BEC) the principle of energy conservation:

[rate of change in body energy content] (1)

= [rate of energy intake] – [rate of energy expenditure]

becomes very simple,

$$d[BEC(t)]/dt = [k_3k_4*BEC(t)] \quad [k_1+k_2*BEC(t)] \qquad (2)$$

and the solution to eq. 2 is:

$$\Delta BEC(t) = (k_3k_1)/(k_4+k_2)* (1 \exp [(k_2+k_4)*t]) \qquad (3)$$

where Δ BEC is the change in body energy content from a maintenance state to the body energy content at time, (t). k_3 is the energy intake of the maintenance state and k_1 is the analogous balanced energy expenditure. k_4 is a feed back constant controlling energy intake in order to navigate Δ BEC towards the maintenance value. k_2 is a similar constant controlling energy expenditure.

We utilised the model to simulate a 10year period of random energy intake and calculated the corresponding standard deviation in Δ BEC(t). Furthermore, the system was investigated with respect to the effect of the feedback constants k_2 and k_4 in relation to overfeeding.

Results

Variations in body energy content were calculated by calculating daily Δ BEC as a result of random daily energy intake. Equation 3 was modified to calculate Δ BEC per day.

$$\Delta \text{ BEC}(t) = \Delta \text{ BEC}(t1) + \frac{(k_3 k_1)*(1 - \exp[(k_2+k_4)])}{(k_4+k_2)}$$

Different values of the constant k_2 was investigated and with energy intakes, k_3, that varied randomly from a uniform distribution of intakes between 0 and 20 MJ/day, between 3 and 17 MJ/day and between 5 and 15 MJ/day. k_4 was assumed to be zero and k_1 was fixed at 10 MJ/day. Each calculation was performed 20 times. Figure 1 shows the results with respect to the variation in body energy content as a function of the magnitude of k_2 for various ranges of the intake distribution.

The overfeeding study of Bandini *et al.* (3) provided data to evaluate the

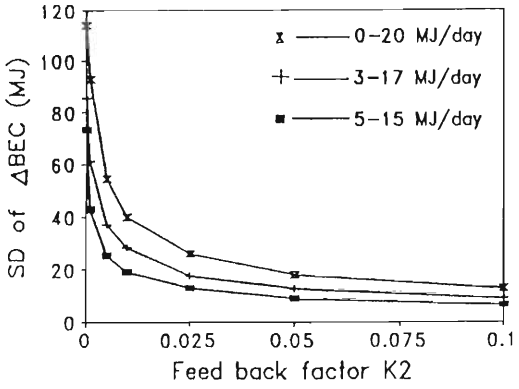

FIG. 1 Variation in body energy content as a function magnitude of k_2 for various ranges of the intake distribution.

model in terms of applicability. Nine subjects were overfed for 14 days and their total daily energy expenditure and excess body energy content were measured. The relation between body weight and body energy content was 22 kJ per gram, and the overall k_2 of the study was 0.014 per day (i.e. k_2 = Δ TDEE / Δ BEC(t)).

Figure 2 shows the results with respect to overfeeding with 6.15 MJ per day during 14 days and the data of Bandini *et al.* (3), are marked by squares. The 4 lines represents the predicted change in Δ BEC(t), calculated by use of equation 3, for different

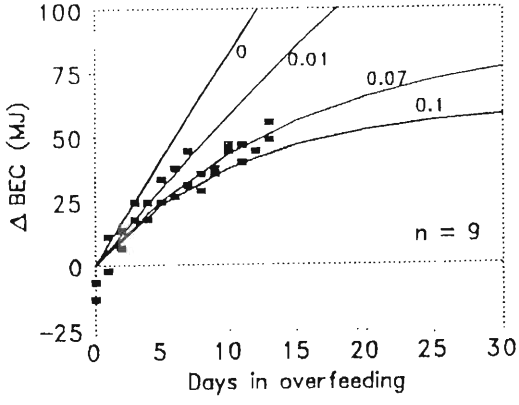

FIG. 2 Overfeeding with 6.15 MJ per day.

The overfeeding study by Roberts *et al.* (4) was followed by a period of spontaneous eating. Daily energy intake and body energy content were measured. The relation between body weight and body energy content was 32 kJ per gram, and the overall k_2 of the study was 0.006 1/day and the calculated k_4 was 0.03 (i.e. k_4 = Δ Energy intake / Δ BEC(t)). Hence, the sum of k_2 and k_4 was assumed to be about 0.04 per day.

Figure 3 shows the result of change in Δ BEC after overfeeding. The bars indicate the mean Δ BEC(t) and the 95% c.i. at 0, 10 and 50 days. The 3 lines represents the predicted change in Δ BEC(t) for different values of k_3+k_4, calculated by the use of equation 3.

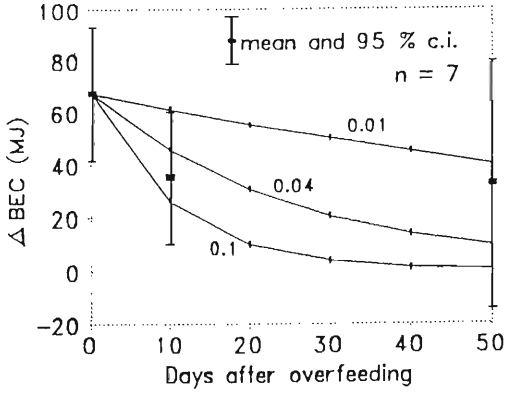

FIG. 3 Change in vBEC after overfeeding.

The stationary Δ BEC during overfeeding was calculated from equation 3 with t = ∞ as:

$$\Delta \text{ BEC(t) [stat]} = (k_3k_1)/(k_4+k_2)$$

and Figure 4 shows the predicted stationary weight for different values of k_2 and (k_3k_1), with k_4 = 0.

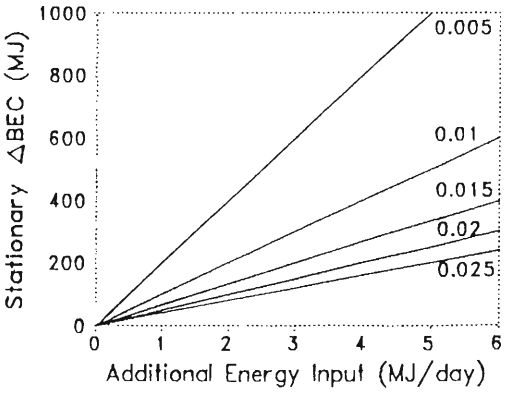

FIG. 4 Predicted stationary weight for different values of k_2 and (k_3-k1), with k_4 = 0.

Figure 5 shows the corresponding response times for achieving 95% of the stationary weight illustrated in Figure 4.

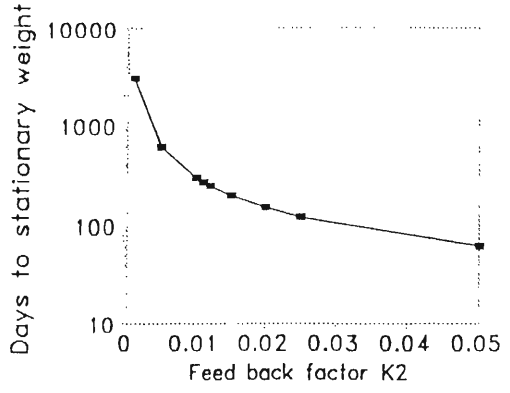

FIG. 5 Response times for achieving 95% of the stationery weight

Discussion

The validity of the results presented here depends primarily on the validity of the assumption that the feed back loops depend on the body energy content as such and that the dependency is linear. In this sense, our model is very similar to that used by Alpert (1). Available data do not permit the use of more realistic models,

example, that the body energy content is split up in different parts, each with their own feed back loop and that the relationship may be nonlinear.

The value of k_2 was calculated from (3) and (4) and we have estimated a reasonable range for k_2 as 0.0050.025. k_2 shows a very large variation between the subjects. Presumably, the largest part of this variation is due to measurement error, but this remains unknown.

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Energy metabolism and obesity: The thrifty gene hypothesis

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Abstract

Crosssectional studies of energy metabolism were conducted in a large group of subjects using an indirect open circuit wholebody calorimeter. These studies have led to the following conclusions: 1) Fatfree mass, fat mass and age account for about 80% of the intersubject variability in resting metabolic rate (MR); 2) Independent of body size and body composition, females have lower MR than males; 3) Resting and 24hour MR are familial traits; 4) Resting skeletal muscle metabolism and sympathetic nervous system activity are important determinants of MR, and 5) The "setpoint" of the human thermostat (body temperature) varies between individuals and this variability correlates with interindividual variations in MR.

Prospective studies in which nondiabetic Pima Indian subjects have been followed for more than 4 years, have shown: 1) A low MR for a given body size and body composition is a risk factor for body weight gain; 2) A low level of spontaneous physical activity, is also associated with greater weight gain; 3) A low rate of 24hour fat oxidation (independent of MR) measured in the whole body calorimeter under standardised dietary conditions is a predictor of body weight gain; and 4) In response to weight gain, MR, the energy cost of physical activity, and the rate of fat oxidation become "normal" for the new body weight and body composition.

"Thrifty gene hypothesis": over generations, cycles of food abundance and food deprivation promote an "efficient use" of food which is a selective survival advantage when food is scarce. In affluent societies, the "thrifty genotype" becomes a detriment and obesity and type II diabetes often ensue.

In conclusion, our results suggest that individual differences in energy and substrate metabolism, of possible genetic origin, contribute to individual differences in body weight. Thus, some people are obese due to intrinsic metabolic forces beyond their control. The commonly held belief that all obese people are gluttonous should be discarded.

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Functional consequences of iron supplementation to iron deficient female cotton mill workers in Beijing, China

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Introduction

Some previous studies have found that the productivity of the workers were reduced in both iron deficiency and iron deficiency anaemia (18). But it is not clear so far in which way this harmful effect occurs and what physiological mechanism it is. There were also few studies being directed at the functional consequences of iron deficiency and none of such studies have been done in China.

The present study conducted from 1989 to 1991 in Beijing, China, was designed to investigate the effect of iron supplementation on functional consequences in irondeficient Chinese women, with emphasis on energy expenditure at work (EEW), energy expenditure during leisure time (EEL), production efficiency (PE) and heart rate (HR).

Subjects and methods

Subjects selection

Eighty nonpregnant women between the ages of 19 and 44 years diagnosed as iron deficient were selected from an anaemia screening test among 558 female workers in 'spun yarn' workshop of a cotton mill in China. Only the patients involved in relatively heavy work and without abnormalities in the tests of GPT, Xray of chest, concentrations of folic acid in red blood cells and serum, stool occult bleeding and the eggs of hookworm in the stools were included.

Patients were classified according to the severity of iron deficiency using the following categories (9,10).

1. Iron deficiency alone (ID): Haemoglobin (Hb) >12 g/dl and serum ferritin (SF) <12 μg/l and free erythrocyte protoporphyrin (FEP) >35 μg/dl (N=36).
2. Irondeficiency anaemia (IDA): Hb <12g/dl plus SF <12 μg/l, or plus FEP >35 μg/dl (N=44).

Whereas mild anaemia having more than 80% of normal Hb value (N=34) and moderate anaemia having 60% to 80% of normal Hb value (N=10), were prevalent, none of the subjects belong to severe anaemia, ie having less than 60% of normal Hb value.

Experimental design

The selected ID and IDA subjects were randomly divided into two groups and then treated for 10 to 12 weeks

with either iron or placebo. Before treatment, all the subjects stayed overnight in the plant hospital. Next day in the early morning, the subjects were waken and their BMR were measured. Afterwards, the following steps were made in sequence: firstly, body weight (WT) and height (HT) and fatfree mass (FEM) were measured after 'voiding' and blood samples were collected before eating breakfast. Then the standard meal containing about 2100 KJ was offered. About 20 minutes after breakfast, the calibration procedure for obtaining the HREE correlation line was carried out. Just the day after or before calibration procedure was completed, physical activities were recorded and minutebyminute HR was monitored in freeliving situations on 3 consecutive days. After treatment with either iron or placebo, all the above assessments were equally repeated.

Anthropometry

Body weight and height were measured to the nearest 0.1 cm respectively, in the early morning after fasting and voiding using a beam weighing scale and measuring system (Seca. Model 220, Gmbh & Co, Germany). The weight of the patient's clothing was measured separately and subtracted from the total measurement.

Haematological measurements

Capillary blood was obtained by left ring finger stick using disposable blood lancet (Bloedlancet, lameris, Holland). Haemoglobin (Hb) was determined by HemoCue in duplicate.

Serum ferritin, (SF) was determined with a commerciallyavailable enzyme immunoassay (ELISA) kit (Ramco, Laboratories, INC., USA) and the instrument of Titertek Multiskan R plus (EFLAB), Labsystems and Flow laboratories, Finland). Free Erythrocyte protoporphyrin (FEP) was determined with the method of fluoprescence spectrophotometer (DaoJin, 12F510, Japan).

Basic Metabolic Rate (BMR)

BMR was measured under standard conditions in a comfortably warm room, with the subject lying at complete rest and having fasted for 13 hours. All the patients stayed overnight in the plant hospital. Immediately after the subject awaken in the early morning, BMR was determined in duplicate from two 10minute samples of expired air. The expired air was collected in a 1001 Douglas bag after 5 minutes warming up with a two way nonrebreathing and lowresistance valves. Analyses of oxygen and carbon dioxide contents and the measurement of the expired air volume were done soon after collection using 02 paramagnetic analyser (Servormex 570A, England), CO2 infrared analyser (Servomex 1410, England) and precision wet gas meter (MeterfabriekSchlumberger B.V., Holland) respectively. Gas volumes were corrected to standard temperature and pressure (STPD) with barometer (Prazisionsbarometer 485, Lambrecht, Bakker & Co, Holland).

FatFree Mass (FFM)

FFM was estimated by a bioelectrical impedance analyser with 4 terminal impedance plethysmography (Model BIA 101 RJL Systems, Detroit, MI).

Energy expenditure at work (EEW), energy expenditure during leisure time (EEL)

1. Calibration procedure

Energy expenditure was estimated by minutetominute heart rate recording. The principle behind this method is that a relationship exists between HR and EE (11,12,13). In order to determine HREE regression, an individual calibration procedure was done on each subject both before and after

treatment on the sam% day of measuring BMR. The procedure consisted of following 18 mixed different activities sequentially, i.e., twice basic metabolic status, sitting quietly, sitting with hands at work and with arms at work, standing quietly, standing with hands and arms at work, sweeping the floor, squatting and standing, cycling at 5 different workloads on a cycle ergometer (Monark 818E, Ergomed & Co., Sweden), stepping on a 23 cm high block, stepping forwards and backwards on a multiple stairs, as well as the activity of working in the cotton mill. Each activity lasted for 3 to 5 minutes, after 2 minutes preliminary equilibration. Usually the whole procedure lasted for the whole morning in the laboratory.

The calibration point for each activity was computed as the mean of the HR and EE values for the sampling period.

2. Heart rate monitoring

Minutebyminute HR was monitored in freeliving situations on three consecutive days just before or after calibration procedure was completed. Each subject was fitted with the HR monitor (sport tester TM, PE3000, Polar Electro, Kempele, Finland) early in the morning and it was worn until it was removed by the subject before going to the bed in the evening.

3. Calculation of energy expenditure at work (EEW) and energy expenditure during leisure time (EEL)

Eighteen points of HR (beats/min) and EE (KJ/min) were obtained from calibration procedure. A logistic regression line between HR and EE was simulated by SPPS computer programme. After the HREE regression was determined, EE of every minute in sampling period was derived from the minutetominute recorded HR by reference to the subject's regression line for the EE corresponding to the HR.

Production efficiency (PE)

In the spun yarn shop, there is a complete perfect system of guaranteeing product quality. A modern management model of overall planning, quality, economic accounting, manpower management and computer management has been established. Since each worker's monthly bonus depended upon the attendance rate, monthly and spot evaluations were made on the quantity and quality of the yarn produced individually. In this study we used basic income, expressed as basic salary plus or minus bonus mainly based upon the attendance rate to represent the individual production, i.e.,

$$\text{Production (yuan/day)} = \frac{\text{basic income of the month concerned}}{\text{working days of the particular month}}$$

Production Efficiency (PE) was calculated as:

$$\text{PE (yuan/MJ)} = \frac{\text{production (yuan/day)}}{\text{average total energy expenditure at work (EEW) over three days (MJ/day)}}$$

Medicine distribution

Ferrous sulfate pills containing 60 mg elemental iron and placebo with identical appearance were provided by Lomapharm Medicines, Emmerthal, W. Germany. The study was double blind. ID patients were given 1 pill per day of either iron or placebo, IDA patients were given 2 pills per day. Everyday expect holidays, the medicine distributor went to the workshop to distribute pills to each subject who had to consume the pills in his presence. All the subjects were followedup for 10 to

12 weeks. The frequency and severity of side effects were also recorded.

Statistic analysis

The changes between pre and post-treatment were determined by paired t test within placebo and iron groups. The difference of the changes between two groups was compared using t test. The correlation coefficients (r) were calculated by linear regression analysis using SPSS/PC (V3.0, Marija J Norusis/SPSS INC).

Results and discussion

General

The initial values of the age, educated years (education), years of working in the cotton mill (standing), weight, height and fatfree mass (FFM) of the subjects are given in Table 1. There are no significant differences between the initial values of iron and placebo groups using t test. None of the subjects had abnormal values in the tests of GPT, Xray of chest, the concentrations of folic acid in red blood cells and serum. Stool occult bleeding and the eggs of hookworm in the stools were not found, which suggest that all the subjects were apparently free of hepatitis, tuberculosis, folic acid deficiency, acute breaking out of hemorrhoids and hookworm infection.

Haematological measurements

General haematological data are shown in Table 2. The results show that the initial values of all the parameters were almost identical among the two groups. The increase in Hb values for irontreated subjects was statistically significant, while Hb values in the placebo group were almost constant after treatment. Although the changes in SF and FEP in the group receiving placebo were also significant, in comparison with the irontreated group, the subjects receiving iron supplementation exhibited much more significant increase in SF and decrease in FEP. The reason for the marked improvement in the values of SF and FEP in the placebo group is considered due to the attention paid by the subjects after a series of nutrition education combined with the project. As the subjects in our study benefited with iron supplementation, it is well accepted that iron deficiency do exist in this population.

TABLE 1

Profile of the initial values of the subjects (N=40)

Iron Parameter	Placebo (Mean ± SD)	(Mean ± SD)
Age (yr)	30.5 ± 5.9	29.7 ± 6.4
Education (yr)	9.6 ± 1.4	9.5 ± 1.2
Standing (yr)	11.0 ± 6.3	10.6 ± 7.0
Weight (kg)	55.9 ± 7.2	53.3 ± 6.4
FFM (kg)	40.3 ± 4.4	39.3 ± 3.7
Height (cm)	161.05± 5.65	160.60± 4.57

Energy expenditure at work (EEW), energy expenditur during leisure time (EEL), mean heart rate at work (HRW) and during leisure time (HRL)

The length of HR recording at work (LengthW) and during leisure time (LengthL), mean HR at work (HRW) and during leisure time (HRL), total and mean energy expenditure at work (EEW KJ/d and EEW KJ/min), total and mean energy expenditure during leisure time (EEL KJ/d and EEL KJ/min) are presented in Table 3. Figure 1 shows that the decrease of mean HR at work was well correlated with the increase of Hb, which indicates that there was less exertion or less cardiovascular stress to do the same work with improved nutritional status after iron supplementation.

TABLE 2

Evaluation of haematological status of patients before and after 12 weeks treatment with either iron or placebo

Parameters	iron (N=40)		placebo (N=40)	
	Mean	SD	Mean	SD
Hb (g/dl):				
Before treatment	11.4	1.5	11.5	1.4
After treatment	12.7	1.2	11.3	1.4
Difference(95%CI)	1.3	1.2 (0.9a1.7)**	0.2	0.8 (0.5a0.1)
SF (µg/L):				
Before treatment	9.7	5.6	10.6	10.9
After treatment	30.0	20.8	18.8	17.9
Difference(95%CI)	20.3	18.9 (18.5a22.1)**	8.2	19.4 (2.1a14.3)*
FEP(µg/dl):				
Before treatment	57.0	30.8	52.5	16.8
After treatment	27.7	11.3	37.2	15.0
Difference(95%CI)	29.6	26.4 (37.9a21.3)**	15.3	14.4 (19.9a10.7)**

*p< 0.05 and ** p< 0.001

TABLE 3

The length of HR recording, mean HR, total and mean energy expenditure both at work and at home for iron and placebo subjects (N=40)

Parameters	Iron Mean±SD	Placebo Mean±SD
LengthW[a](minutes)		
before	440±31	444±31
after	440±33	442±24
change	0±27	2±32
HRW[b](beats/min)		
before	95.5±7.6	97.6±7.3
after	91.1±8.0	98.0±6.5
change	4.4±4.4***	0.4±4.6 ###
EEW[c](KJ/d)		
before	4348±1204	4162±834
after	3881±1114	4233±836
change	467±631***	71±835 ##
EEW (KJ/min)		
before	9.9±2.6	9.5±2.2
after	9.0±2.5	9.4±1.7
change	0.9±1.5***	0.1±2.3
LengthL[a](minutes)		
before	377±59	391±59
after	412±64	376±70
change	35±65**	15±74
HRL[b](beats/min)		
before	86.5±8.2	89.6±5.1
after	85.7±7.5	88.3±6.3
change	0.8±5.7	1.3±5.5
EEL[c](KJ/d)		
before	2933±710	3047±888
after	3137±827	2762±791
change	204±775	285±869* #
EEL (KJ/min)		
before	7.9±2.0	7.8±1.6
after	7.6±1.6	7.4±1.6
change	0.3±1.6	0.4±1.8

[a] LengthW and LengthL: the length of HR recording at work and during leisure time respectively.

[b] HRW and HRL: mean HR at work and during leisure time.

[c] EEW and EEL: total (KJ/d) and mean (KJ/min) energy expenditure at work and during leisure time.

* $p<0.05$, ** $p<0.01$, *** $p<0.001$, using paired t test;

# $p<0.05$, ## $p<0.01$, ### $p<0.001$, using t test.

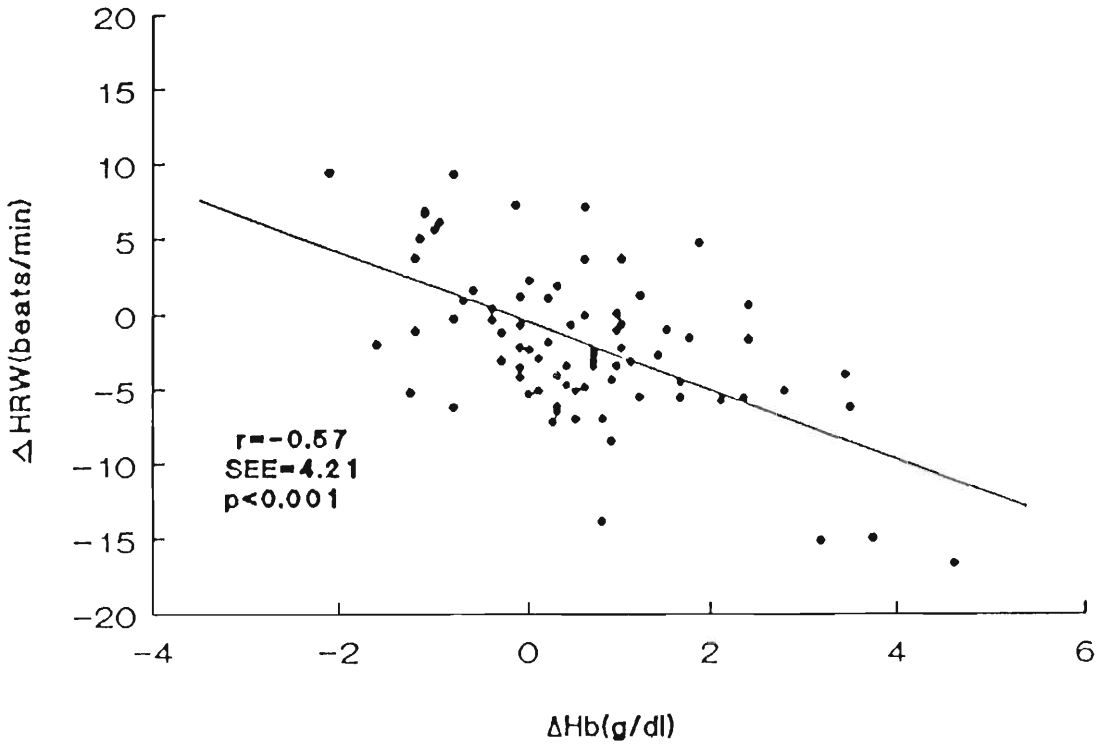

FIG. 1 Scatterplots for the change of mean HR at work (Δ HRW) against Hb in all the subjects (n=80).

The reduced total energy expenditure at work (EEW) after iron supplementation is of very important social and economic significance, which makes it possible for workers to accomplish their tasks without undue fatigue so that at the end of the working day, they are left with sufficient vigour to enjoy their leisure time and perform their duties to the family, such as taking care of the babies. This probably would also explain why the total energy expenditure during leisure time (EEL) after iron supplementation was increased for iron group as compared to a decrease in placebo group, and provide tangible evidence that tiredness and weakness are common symptoms of iron deficiency which could at least be partly attributed to inefficient energy yield and utilisation.

Production efficiency (PE)

The average production expressed in Chinese yuan earned per working day and production efficiency (PE) expressed as production divided by average energy expenditure at work over 3 days (yuan/MJ of per working day) in irontreated and placebo subjects were compared with the values in pretreatment (Table 4). The significant increase of PE for iron-treated subjects was obtained by paired ttest, even allowing for changes in placebo group and after correction for FFM. Our results also show that, for all the subjects, the change of PE after the trial was correlated with the change in Hb values ($r=0.56$, SEE= 0.39, $p< 0.01$) (Figure 2). But there was no significant correlation between the change of PE and the change of mean HR at work ($r= 0.00661$) and the change of PE could not be explained by the change in BMR.

TABLE 4

The average production and production efficiency (PE)[a] of 3 working days for iron and placebo subjects (N=40)

Parameters	Iron (Mean±SD)	Placebo (Mean±SD)
Production (yuan/day)		
before	7.34±1.09	7.44±0.51
after	7.72±0.64	7.47±0.98
change	0.38±0.97*	0.03±0.94
PE (yuan/MJ)		
before	1.83±0.57	1.86±0.40
after	2.15±0.65	1.85±0.52
change	0.32±0.44***	0.01±0.45 ###

a PE was expressed as production divided by average total energy expenditure at work for 3 days.

* $p< 0.05$ and *** $p<0.001$, using paired t test

$p< 0.001$, using group t test

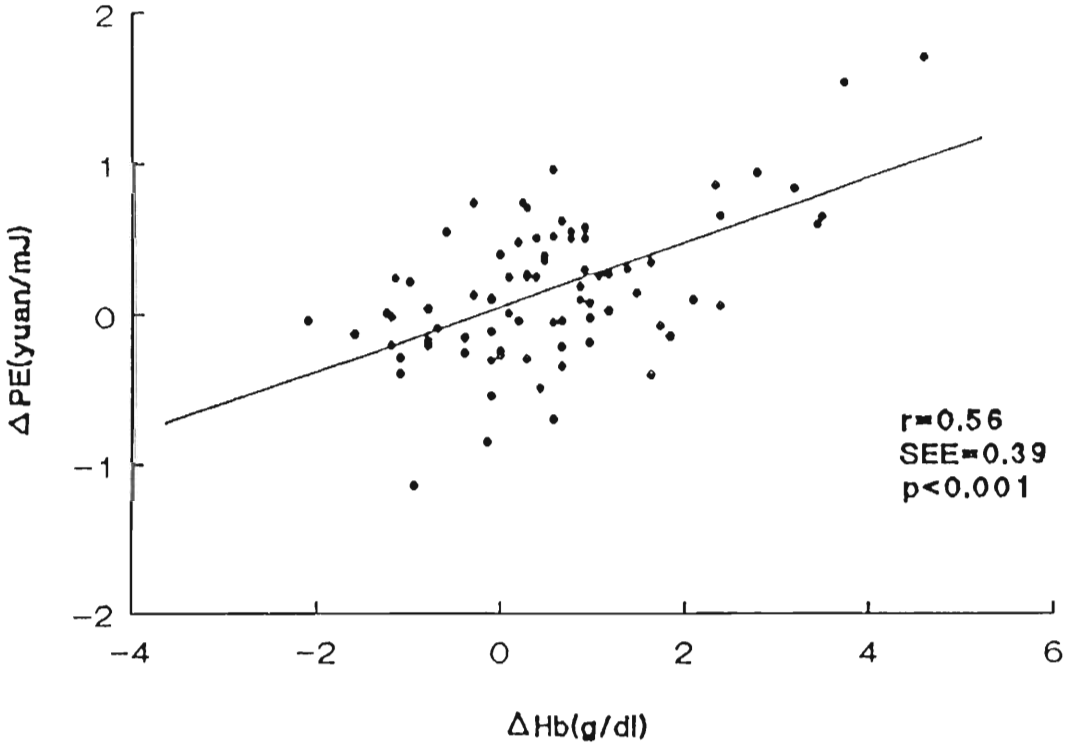

FIG. 2 Scatterplots for the change of PE against Hb in al the subjects (n=80).

Since the work pace in the cotton mill was determined by the machine and the weak people have to keep up with the strong, the response of production expressed as income to iron treatment in our study was not as significant as that obtained in the studies in Sri Lanka and Indonesia. However, after iron supplementation, energy expenditure at work was reduced and production efficiency was significantly increased for irontreated subjects, meaning the energy is conserved while doing the same work.

During prolonged, severe exercise or during ordinary daily activities, aerobic processes play a most important role. Under normal conditions, physical activity is the most important factor in determining total oxygen requirement, at least in quantitative terms. This is so because it induces significant increments in the metabolic rate of skeletal muscle and, to a lesser degree, of myocardium. Since the function of iron compounds is intimately linked to the essential roles of transporting and utilising oxygen involved in muscle work, the reduction in concentration of haemoglobin, myoglobin, and reduced activities or concentrations of several respiratory enzymes in the mitrochondria reflect, the diminution of the total capacity of transporting and utilising oxygen and impaired energy flux in the mitochondrial 'power plant'. As compensatory changes, heart rate could be increased and respiratory system adjusted to maintain adequate tissue oxygenation and meanwhile, the dependance on anaerobic energyyielding processes would increase lactic acid output. With the buildup of protons and a rapid depletion of carbohydrate substrates, muscular efficiency determined by the combined efficiencies of coupling of oxidation and phosphorylation and the coupling of phosphatebond energy and muscular contraction will be changed, leading to premature fatigue.

In summary, from a physiological and medical viewpoint, the blood tests for the evaluation of iron nutritional status are rather meaningless unless they are based on sound physical considerations. Our data illustrate that iron deficiency has a deleterious effect on the heart rate and energy metabolism, since after iron supplementation, the mean heart rate at work and energy expenditure at work of the patients were reduced and production efficiency was increased. The increased production efficiency has great potential social and economic consequences, especially so in developing countries.

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Dietary effects on iron status

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Introduction

The WHO collaborative study on iron supplementation in Thailand has shown that iron deficiency is the major cause of nutritional anaemia in Thai population (1). The three common causes of iron deficiencies in Thailand are low bioavailability of dietary iron, increased iron requirement, and increased iron loss.

Sequential changes of inadequate iron status

Inadequate iron status can be categorised into 3 stages: iron depletion, iron-deficient erythropoiesis, and iron deficiency anaemia. Subjects with iron depletion usually have serum ferritin (SF) of < 12.0 μg/L or total iron binding capacity of >400 μg/dL, whereas those with iron-deficient erythropoiesis are diagnosed by free erythrocyte protoporphyrin (FEP) of >70 μg/dL, transferrin saturation of <16%, and serum transferrin receptor of >9.0 mg/L, in addition to serum SF of < 12.0 μg/L. Subjects with iron deficiency anaemia have low hemoglobin levels: <13.0, <12.0, and 11.0 g/dL for adult males, adult females, and pregnant women, respectively, in addition to the aforementioned abnormal iron parameters (2, 3).

Factors affecting iron absorption

The three major factors influencing the absorption of iron from the diet are dietary iron content, iron bioavailability, and intestinal mucosal behavior.

Dietary iron content

The dietary iron content is determined by its constituent in foods. Typical Western diets usually contain 6 mg iron/1000 kcal (4). Our study has revealed that iron intakes in urban and rural adults are 6.3 and 5.4 mg/1000 kcal, respectively. The majority of the dietary iron is derived from non-heme iron (5).

Iron bioavailability

Compared with non-heme iron, heme iron is highly bioavailable. This is due to the fact that heme iron is not influenced by many ligands in the diet. It is directly taken up to the mucosal cell by an absorption mechanism different from that of non-heme iron, and it is unaffected by the high pH of the upper small bowel. Thus heme iron in

animal foods is much more readily absorbed than non-heme iron in vegetables and cereals. However, heme iron forms only 10 percent of the total intake of the dietary iron even in population with hight meat consumption (4).

The bioavailability of the non-heme food iron is variable and generally much lower than heme iron. When eaten alone, the iron in rice, wheat, maize, and black beans are poorly absorbed. However, when these staple foods form part of a mixed diet, the absorption of the dietary iron is markedly influenced by other dietary constituents which can be classified into inhibitors or enhancers of iron absorption (3,6).

Inhibitors of non-heme absorption from the common pool include polyphenols, phytates, the dietary fiber complex, calcium and phosphorus, and the dietary protein complex (4, 7). Indian tea and coffee inhibit the absorption of non-heme iron by the information of insoluble tannates. Similarly the poor absorption of the iron present in sorghum, horse beans, finger millet, cow peas, spinach and red wines appears to be attributable to the presence of polyphenols. Eggs cause a decrease in the percentage absorption of non-heme iron which is related to the presence of phosphoprotein in egg yolk and conalbumin in albumen. Though soy protein reduced iron absorption the amount of iron absorbed is not reduced by adding soy protein to a meal because of the usually high iron content of soy products. Carbonate, oxalate, phosphate and phytate have been shown to interfere with iron absorption due to the formation of insoluble complexes between these compounds and iron which are very poorly absorbed. Though fiber of wheat and maize binds iron the absorption study with specific dietary fiber including pectin and cellulose have yielded negative results (4,7).

Two major enhancers of non-heme iron absorption are meat and ascorbic acid. Heme iron in meat is well absorped and meat also potentiates the absorption of non-heme iron in other foodstuffs. Cysteine present in meat protein may play some role. Ascorbic acid has a profound effect in enhancing non-heme iron absorption which is due to its reducing property and binding iron in equimolar concentration to form a readily absorbed complex. Ascorbic acid present in foods or in pharmaceutical preparations has similar effect in promoting iron absorption which is dose-dependent. Numerous vegetables and beverages containing appreciable quantities of other organic acids including citric, malic, lactic, succinic, and tartaric acids have been shown to promote the absorption of non-heme iron absorption under certain condition (3,7).

The diets can be generally categorised into low, medium and high iron availability. Daily diets of low, medium and high availability contain <30, 30-90, and >90g of meat, respectively, or <25, 25-75, and >75 mg of ascorbic acid (3).

Intestinal mucosal behaviour

Though the percentage of iron absorption rises as the body content falls the actual amount of iron absorbed in the iron-deficient subjects depends on the bioavailability of dietary iron (4,7).

Dietary effects on iron status in Thai population

Since diets predominated with inhibitors have low iron bioavailability whereas diets rich in enhancers have high iron bioavailability, the prevalence of iron deficiency anaemia is higher in Thai villagers on rice-based diets than urban Thais on meat diets. Besides, iron deficiency anaemia usually coexists with protein-calorie malnutrition in

Thai villagers (8). Soybean and other legumes have been promoted to increase the protein content of the rice-based diets (9). However, this can affect iron bioavailability. Our study in free-living omnivorous and vegetarian adults have shown that vegetarians have significantly lower hematocrit and serum ferritin levels than omnivores though both groups have adequate intakes of iron and ascorbic acid (10). This indicates lower iron stores in vegetarians than in omnivores. Iron-deficient erythropoiesis is detected in 30 children who were forced by their parents to consume vegetarian diets for 16 weeks. Iron depletion is also found in adolescents receiving soybean supplementation for 8 weeks though their protein-calorie status is improved (9). Our results are consistent with the present knowledge of dietary factors influencing iron bioavailability and explain the high prevalence of iron deficiency anaemia in Thai villagers (1, 11).

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Strategies for anaemia control in India

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Introduction

Nutritional anameia continues to be a major public health problem in India, affecting large segments of the population. The incidence is particularly high among pregnant women and young children. Surveys conducted in different parts of the country show that 40-70% of pregnant women have haemoglobin levels below 11 gm/dl and about 10% have severe anaemia with less than 8 gm/dl (1). The deleterious effects of anaemia are well known. In pregnancy, severe anaemia is associated with increased risk of foetal wastage and maternal mortality (2). In addition, the high incidence of maternal morbidity, premature delivery and low birth weight among the population have been attributed to anaemia. Milder forms of anaemia are often neglected but now there is evidence to show that even moderate reduction in haemoglobin can lower resistance to infection (3) and reduce work efficiency (4). An effective programme to control anaemia in the population is therefore essential.

Iron deficiency is by far the commonest cause of anameia. Cereals form the major source of iron in the Indian diets. Poor availability of iron from these habitual diets is the most important cause of iron deficiency. Isotope studies show that iron absorption from a cereal based diet is only 2-5% (5). Dietary intake of iron is also low among poor income groups. Other factors include increased requirement due to repeated pregnancies and prolonged lactation, chronic infection and blood loss due to hookworm disease.

There are two major approaches to prevent iron deficiency anaemia. One is at-risk approach providing iron supplements to vulnerable groups like pregnant women and preschool children, and the other is fortification of foods with iron. Perhaps, the most rational approach would be to diversify the diets to enhance iron absorption. However, it is difficult to achieve this goal in the near future under the prevailing socioeconomic conditions. Emphasis is, therefore, laid on iron supplementation. A study carried out by NIN has shown that daily administration of 30 mg iron during the last trimester of pregnancy was sufficient to prevent anaemia (9). However, this was a hospital based study. In view of the wide prevalence of iron and folic acid deficiencies in the community, the Study Group on Nutritional Anaemias recommended that pregnant women should receive 60 mg of iron and 500 µg of folic acid daily for 100 days (7). Such a programme was initiated on a national scale by the Government of India, in 1970.

National programme for anaemia control

The National Nutritional Anaemia Prophylaxis Programme has been in operation for the last two decades (8). The target population comprises preg-

nant and lactating women, family planning acceptors and children between 1-12 years.

Implementation

Under this programme, sponsored by the Ministry of Health & Family Welfare, two types of "folifer" tablets are distributed; the `large' tablets containing 60 mg elemental iron and 500 µg of folic acid are given to the adult beneficiaries, while `small' tablets containing 20 mg elemental iron and 100 µg folic acid are given to the children. It is implemented through all the institutions providing MCH services like primary health centes, hospitals for women and children and maternity homes. The actual distribution of the tablets is carried out by the ANMs (Auxilliary Nurse Midwife) and Health Visitors. Each beneficiary is expected to receive 100 tablets and consume 1 tablet/day over a period of 100 days.

Evaluation

An evaluation study was conducted by the ICMR during 1985-86, to assess the current status of the programme and its impact on haemoglobin status (9). The study was carried out in 11 States covering 6 districts and about 60,000 population in each State.

The results of the study revealed poor performance in all the States. The coverage of pregnant women ranged from 3.6 to 26.6%. About 80% of them received less than 60 tablets. Only 2.6% of lactating women were receiving tablets at the time of the survey. The number of children covered was also negligible.

The reasons for poor coverage included inadequate supplies of "folifer" tablets, poor supervision and monitoring, lack of awareness among health functionaries, non-involvement of village level workers, poor compliance of women and sometimes refusal due to lack of knowledge and ignorance. Education component was found to be totally lacking.

Haemoglobin estimation showed a high prevalence of anaemia in pregnant women, with the mean value aroung 9 gm/dl. About 88% of the women had haemoglobin below 11 gm/dl. There was no difference between those who received the supplement and those who did not. Thus the programme has made no significant impact on the prevalence of anaemia.

Strategies to improve delivery of "folifer" tablets

There is an urgent need to strengthen the national anaemia prophylaxis programme, with better control over the actual delivery of the tablets. Monitoring and supervision are important to ensure regular distribution.

Supplies

The supplies of "folifer" tablets have to be increased to match the requirements of the target population. These should be based on demographic data. Logistic of supplies and distribution must be streamlined at the state, district and PHC level. The package of tablets should be made attractive to improve its acceptability.

Beneficiaries

All women and children can be considered as high risk groups. But with limited resources, prioritisation is essential. All pregnant women need supplements of iron and folic acid, regardless of their initial haemoglobin levels. Otherwise, they are likely to register a significant drop in haemoglobin with advance of pregnancy. Highest priority should, therefore, be given to pregnant women. Adolescent girls also need special attention as a high proportion of them

are anaemic. Pregnancy only serves to aggravate pre-existing anaemia. It is desirable to give iron-folate tablets to all girls soon after marriage so the anaemia is corrected before they become pregnant.

Distribution

The responsibility for distribution of "folifer" tablets rests with the health system. For pregnant women, "folifer" supplementation can be linked with tetanus immunisation and should from a part of the comprehensive package of antenatal care. Women attending the hospital or health centre receive "folifer" tablets during their visit. However, in order to reach all the target population, the health workers have to make house-to-house visits for identification of the beneficiaries and distribution of the tablets.

At present, the tablets are being distributed by the ANMs. But they are obviously unable to cover all the target population. Apart from lack of motivation, their heavy workload due to the multiplicity of functions appears to be an important factor. Since distribution of tablets is a simple measure, trained birth attendants (TBA/Dais) can be given this task. They can keep track of all pregnant women in their village. In addition, other village level workers like Health Guides and Anganwadi Workers should also be involved in the programme. Proper training and motivation of these workers are essential for efffective implementation of the programme.

Education

Education of the community is important for the success of any public health programme. However, this appears to be one of the weakest links. A recent study conducted by NIN revealed that many women do not know what `anaemia' is (10). They are neither aware of the programme of "folifer" supplementation, nor its purpose. Attempts were therefore, made to devise a multimedia educational strategy to create awareness about anaemia in the community. A kit of educational material comprising a pictorial booklet and a set of colour posters was prepared. A video film and slide-n-sound presentation covering all aspects of anaemia were produced. These educational materials were pretested, corrected and replicated. They are being used by the field level functionaries like ANMs, AWWs and Dais in the community.

Salt fortification for anaemia control

Although the prevalence of nutritional anaemia is high among pregnant women and children, other segments of the population also suffer from this condition. Fortification of salt with iron has been suggested as a public health approach to improve the iron status and prevent anaemia in the population. A successful method for salt fortification has been developed at NIN (11).

Iron fortified salt (IFS)

The formula suggested earlier for salt fortification was based on ferric orthophosphate and sodium acid sulphate (11). It was shown that ferric orthophosphate can be substituted with ferrous sulphate and phosphoric acid to reduce the cost (12). Salt fortified with this formula was found to be satisfactory with respect to iron availability, stability and acceptability. However, the fortified salt developed colour during storage. The formula was further modified, adding a stabiliser-sodium hexametaphosphate, to prevent colour formation (13).

The fortified salt provides 1 mg of elemental iron per gram of salt. The average salt consumption by an adult in India is about 10-15 gm/day. So the fortified salt will provide an additional 15 mg of iron.

Impact of IFS

Several community studies were undertaken to assess the impact of feeding fortified salt on the iron status of the population. The first study was conducted by NIN in residential school children aged between 5-15 years (14). The results showed that continued consumption of iron fortified salt was not associated with any untoward effects. At the end of one year, the haemoglobin levels had increased and the incidence of anaemia decreased significantly in those receiving iron fortified salt, while there was no change in the control children receiving iron fortified salt. These subjects were apparently healthy children living in urban areas with access to medical care. Most of the Indians live in rural areas, where they are exposed to recurrent infections and helminthic infestations, both of which contribute to anaemia. It was considered important to establish the beneficial effects of iron fortified salt in such populations.

Multicentric field trials were therefore carried out in four different regions in the country (15). Three areas were rural, located in Calcutta, Hyderabad and Delhi regions, while the fourth was an urban centre in Madras city. Each centre covered about 4000-6000 population. Iron fortified salt was found to be acceptable in all the four regions and no untoward effects were found due to its consumption. At the end of one year, consumption of fortified salt resulted in a significant improvement in the haemoglobin status and a reduction in the incidence of anaemia. In the Calcutta region, iron fortified salt showed a significant impact even in the presence of hookworm infestation.

Another community study was carried out in rural Hyderabad covering about 9000 population, wherein iron fortified salt was introduced following a therapeutic intervention (16). A haemoglobin survey was conducted initially to identify anaemic individuals. All such cases were treated with "folifer" tablets to improve the haemoglobin levels. During the next phase, the villages were divided into two groups; the experimental group received iron fortified salt while the control group received unfortified salt. One year later, there was a significant difference between the two groups in the mean levels of haemoglobin. The prevalence of anaemia increased from 48 to 53% in the control group and reduced from 44 to 30% in the experimental group. These observations indicate that additional amount of iron in the diet is necessary to control anaemia in poor communities. A combined approach of anaemia treatment with "folifer" tablets and supplementation of the diet with iron fortified salt appears to be the best strategy. In the above study, initial treatment of anaemia was not adequate. Once the existing anaemia is corrected, iron nutrition can be maintained through continued supply of fortified salt.

Production of IFS

Several enterpreneurs are willing to start bulk production of iron fortified salt. Recently, the Tamil Nadu Corporation (TNSC) has set up a plant at Valinokkam, Ramanathapuram district to produce iron fortified salt. Initially they were using 'spray mixing' process which needs expensive dryers and also poses several logistic problems. Therefore, a suitable technology for the production of iron fortified salt by `dry mixing' process was standardised with the technical assistance of NIN (17). Production capacity was found to be satisfactory and uniformity in iron distribution was also achieved by three stage mixing process. The plant is now producing 3 tonnes/hour with an annual capacity of 15000 tonnes. Similar plants are now being set up in other States like Orissa and Rajasthan.

Field Kit for testing IFS

Effective implementation of salt fortifi-

cation programme for the control of anaemia requires regular monitoring of edible salt for iron, particularly at the retail sales and household levels. A simple field kit for monitoring iron fortified salt has been developed by NIN (18). The test is based on the principle that ferrous iron in the fortified salt is converted into ferric iron by oxidation and the ferric iron when sprayed with ferrocyanide reagent gives rise to a blue colour. This kit can be used by any field level worker, merchant or housewife even without any formal training in chemistry.

Double fortified salt

Since iron deficiency anaemia and iodine deficiency disorders often coexist, the most effective approach to control these public health problems would be simultaneous fortification of salt with iron and iodine. A technology for double fortification of salt has been successfully developed at NIN (19). Laboratory studies have shown satisfactory results with respect to stability and bioavailability of iron and iodine. A large scale community trial is now underway for field testing the double fortified salt.

Conclusion

Iron deficiency anaemia is widespread in India, affecting almost all segments of the population. No single strategy will have an immediate impact on the problem. Salt fortification programme will improve the iron status of the entire population, but its effect will be felt only after a few years. Those who suffer from severe forms of anaemia, particularly pregnant women and children require therapeutic doses of iron to correct anaemia within a short period. A combined approach of "folifer" tablet distribution to the high risk groups and iron supplementation to the entire population through fortified salt, together with a mass education campaign is more likely to succeed in achieving the goal.

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Fortification of rice with iron: opportunities and constraints with particular reference to the Philippines

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Introduction

Several strategies for the control and prevention of nutritional anaemia have been suggested, and some are being carried out in various countries. The major ones are supplementation and nutrition education. Others include home gardening, and programs combining improved health care.

Food fortification offers another approach to alleviate anaemia, providing a daily increment of iron through a less expensive, more consistent and least obstrusive method. Food fortification is a practical approach in situations where anaemia is widespread and where the objective is to reach the widest population coverage. Rice offers a convenient vehicle for this purpose in rice-eating populations. However, a national rice fortification programme requires a strong commitment on the part of policy makers and planners. The purpose of this paper is to review the factors that have to be considered for a successful rice fortification programme, citing particular experiences in the Philippines.

Rice as a vehicle for fortification

When choosing a vehicle for fortification, two basic principles are kept in mind: (i) the commodity should be consumed in sufficient amounts by the general population, or at least by the at-risk group, and (ii) the production or processing of the commodity is centralised or centers for this are few so that quality control can be adequately maintained.

In the Philippines, corn, salt, sugar, fish sauce, fish paste and dried fish are prospective vehicles for fortification since these are being consumed more or less regularly by large groups of population. Rice, however, may be singled out as most suitable because Filipinos are basically a rice-eating population. Rice is consumed at relatively constant amounts within each age and sex groups, and is eaten by all income and occupational groups (1).

However, in the Philippines, rice cultivation and milling are certainly not centralised. Rice is cultivated predominantly in numerous small farms and milled in about 3500 mills throughout the country (2), thus posing administrative problems. Home pounding still accounts for even a small portion of rice consumption among some farming households who cannot afford milling fees, the accessibility of the fortification program therefore becoming limited although other segments of the nutritionally needy such as the rural landless laborer, urban poor, small

farmers producing cash crops will likely benefit (3).

Fortificants used in rice fortification

Several iron compounds can be considered as fortificants in rice enrichment activities. It is of course important that the bioavailability of the iron in the compound, the stability of the added iron over long periods of time and under extreme conditions of storage and cooking, and the organoleptic changes that may occur in the fortified rice with the addition of the fortificant, be considered.

Ferrous sulfate has a high relative bioavailability, and has therefore become the reference standard in bioavailability studies. It is the cheapest and widely used iron source in iron fortification activities. Other iron compounds can also be considered wuch as ferrous citrate, ferrous lactate, ferric chloride, ferric ammonium citrate and ferric glycerophosphate (4).

In fortifying cereals, the iron added, whatever the form, is usually poorly absorbed because of inhibiting factors present, although inclusion of meat and Vitamin C rich fruits and vegetables in the diet will improve absorption. Moreover, off-flavors or unacceptable color changes in cereals or bakery products are likely to occur with the use of ferrous sulfate. This however may be overcome with application of a coating treatment, such as with ethylcellulose; reducing undesirable organoleptic effects with little influence on bioavailability.

Fortification levels

The level of iron to be added is determined by the extent to which the target population is deficient in iron intake together with the level of rice consumption of the same population. In the Philippines, for example, iron in diet specifically among children 6 years old and below provides for 72.9% to 95.7% of the Recommended Dietary Allowances. Considering that daily rice consumption of a child 6 years old or below is 143g on the average, fortifying rice at 2 mg iron per 100 g rice grains will more than meet the iron gap. For the average adult male consuming about 308 g rice daily and with an adequacy level of already 91% (1), this will yield 6.16 mg iron or 51.3% RDA for iron from the enriched rice alone or 142% RDA altogether. The idea is to determine the optimum level of fortification which has no toxic effect to rice consuming groups, and studies along this area will have to be pursued.

In the Philippines, we investigated iron absorption levels using rice fortified at 0.5mg%, 2mg% and 5mg% (5). Results of our investigation indicated that fortification of the staple was successfully achieved at the 2% level, iron absorption increasing with increasing level of fortification. On the average, a 20% iron absorption was achieved at 2% level of fortification in this study where the subjects were normal males. There were reports on iron overload.

Technologies for rice fortification

It is to be emphasised that fortified rice to be acceptable should be indistinguishable from ordinary rice grains. It is very common among Filipino housewives to pick out small stones and other unacceptable objects including dark colored grains from the rice container prior to cooking, and if fortified rice or the premix appears as such, these are likely to be picked out and thrown away as well.

In addition, it is also a Filipino practice to wash rice grains two to three times prior to cooking. Unless the technology takes this custom into consideration, the fortificant will be washed off and rendered useless.

These problems are minimised with

the Surface Coating Method. This approach requires that a suspension of the fortificant be sprayed on to clean polished rice as it is tumbled in a large rotating cylinder. The solvent evaporates, leaving a relatively soluble in coating on the rice grain (6). The fortified rice grain is then encapsulated with a coating material to prevent discoloration and off-flavors that may result with the use of ferrous sulfate as well as minimise the washing off of the fortificant prior to cooking. The fortification technology tried at the Food and Nutrition Research Institute, Department of Science and Technology called for the use of a coating material prepared from ethyl cellulose-methyl cellulose - chloroform - isopropyl alcohol. With the coating, the fortified grains were creamy white in color, hardly distinguishale from the unfortified rice grains. Color change in the rice grains was very slight, turning into light beige after 20 weeks at room temperature storage. Rinsing test, done by stirring and gently rubbing the grains in water two times and throwing away the rice washing, showed approximately 9% loss of iron (7).

The fortified grains are then evenly mixed with ordinary unfortified rice grains at a 1:200 ordinary - premix rice ratio. The amount of ferrous sulfate should be calculated so as to yield the desired iron concentration in the fortified rice. The level of 12.5 g anhydrous ferrous sulfate per kilogram rice will yield approximately 400 mg Fe/100 g premix or, when added to ordinary milled rice at the ratio of 1:200 will result in enriched rice containing 2 mg Fe/100 g of rice (not yet taking into account the 1 mg Fe/100 g already present in ordinary milled rice). To compensate for possible losses from rinsing and storage, a level of 14 g anhydrous ferrous sulfate per kilogram rice is sufficient. Another technology is the Simulated Kernel Method. A dough consisting of wheat flour as binder, rice flour and the enrichment ingredient is either extruded through a macaroni press or passed through a noodle-making machine (6).

Strategies in rice fortification

Need for legislation

As in any intervention scheme, endorsement by government usually through legislation is necessary if it were to be adopted as a national program.

Rice fortification in the Philippines was required by law in the 1950's. This however, was enforced only for less than a decade primarily because enrichment which was done during milling made it easier for government to monitor taxable income of rice producers and millers based on the amount of premix they obtained from authorised premix distributors. Political will to enforce the law, understandably, also wavered. Thus, unless political commitment to enforce the law is strong, legislation is futile. Legislation is reasonable if the burden both operational and economic, that will have to be placed on the miller is minimal, otherwise strong dissension among millers is likely. Moreover, legislation requires additional cost to monitor compliance.

In the absence of an alternative scheme that a National Rice Fortification Program can adopt, another strategy is through selective enrichment - for example, only government rice is enriched in such a way that the lower income group will most likely be reached.

On the other hand, an enrichment scheme should be available to the other small farm households who home-pound their rice rather than pay for milling services. A home enrichment strategy can be carried out to make available premix for sale in retail stores, and in health centers. This approach however, will require strong promotion and social marketing.

Need for training educational and promotion component

Training, together with educational and promotion components targetted to both the millers and the households, is most important in the program. Among households, the importance of adding of the correct quantity of the premix to unfortified rice grains will have to be emphasised. On the part of the millers, operational difficulties arise because of a new step and a new ingredient is added in the milling process with fortification. The process in addition will require considerable care to assure the mixing of the correct quantity of the premix. Thus, unless the millers are properly trained and motivated, resistance to fortification may arise. Increased taxes, our experience has shown, was a disincentive to fortification.

Assuming a rough estimate of US $ 0.51 per pound of iron premix, the added cost of fortification will amount to at least PO.40 per kilogram enriched rice. The population, particularly the low income households and at the same time the at-risk group, will certainly object to the added cost especially in the light of present economic difficulties. Whether the government will subsidise the added cost of fortification and keep the price of NFA rice still the lowest in the market after it is fortified is an issue that will need to be addressed foremost by the trade and industry and agriculture sectors. Advocacy to policy makers for a subsidy scheme, and a rice enrichment program in general, will have to be strongly pursued by the nutrition group.

Need for monitoring and evaluation

If a rice fortification program were to be carried out, efficient monitoring and evaluation are important to ensure that the program's objectives are being met, thus providing basis for justifying program cost especially if a subsidy scheme were adopted. Monitoring will help identify loopholes in implementation and therefore allow for modification.

It is important to monitor the millers' compliance to the program, in particular to the premix : rice ratio requirement to ensure the quality of enriched rice. Compliance to packaging and storage requirements at the mill and in the retail outlets will also have to be checked as these affect the stability of fortificant (7).

Finally the monitoring and evaluation of the impact of the program on the iron status of at-risk groups, should be put in place if not already there. In addition, the incidence of iron overload should as well be monitored while health personnel should be trained to respond when such cases are reported.

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Effect of iron deficiency on physical growth, cognitive process, morbidity and work productivity

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Introduction

Iron deficiency is commonly devided into 3 stages. First, the loss of storage iron, as indicated by lowered serum ferritin concentration. Second, decrease in the availability of iron in the blood, as measured by a decrease in serum iron and iron binding capacity or transferrin saturation, but the circulating hemoglobin is not significantly decreased. The third and final stage is overt iron deficiency anaemia (1, 2).

There is reliable evidence from studies in experimental animals that iron deficiency, if sufficiently severe, can reduce physical capacity and performance (3, 4), learning and behaviours (5), immune function and resistance to disease (6), and temperature regulation (7). Isolated studies of one or another of these consequences provide confirmation that these findings also apply to humans (2). However, no previous study has attempted to look at these functions concurrently in a free living population at all stages of iron deficiency.

This paper will describe the quantitative functional consequences associated with the different levels of iron deficiency, and demonstrate the improvement of the consequences as the result of an improvement in iron status.

Methods

This is a double blind clinical nutritional trial to assess the functional consequences of iron supplementation among iron deficient and anaemic women and preschool children. The aims were to measure the effects of the supplementation on physical growth, morbidity and cognitive function of the children, and work productivity of the women.

Location

The study was conducted in three tea plantations - Kertamanah, Pasirmalang and Purbasari - owned by the Government of Indonesia in the district of Pengalengan, 50 km southeast of Bandung, the capital of West Java Province. The plantations are located about 1,300 to 1,800 m above sea level and cover on average, about 1,300 hectares. The average temperature in this part of Java is 17°C with a range of 12°C - 23°C. Generally, the rainy season lasts from November to April, while the dry season runs from May to

October. The average rainfall is 2,361 mm per year, with a range of 1,760 to 2,750 mm; the mean number of total days of rain is 167 with a range of 106-188 days.

Each plantation has housing facilities for most of the workers and their families. The houses have electricity and potable water; there are public bathrooms with toilets and separate areas for domestic animals including goats, ducks, and cattle. Some families own televisions, radios and other electrical appliances. Available on each plantation are a day care service, a kindergarten and a primary school. Medical (clinic) services are also available on each plantation. Four to six sites in the three plantations were chosen for sampling and included three sites in Kertamanah, three in Purbasari, and two in Pasirmalang.

The collaboration of the staff of the plantations, ethnic homogeneity, the small variability in the socioeconomic status of the population, accessibility to a large number of adult and children at risk of nutritional anaemia in a closed geographical area, and the low prevalence of infection, made these plantations an ideal location for the study.

Sample and iron supplementation

A total of 235 families were selected for the study on the basis of the following criteria: (i) the female of a household works as a tea picker; (ii) a husband is present in the household; (iii) there is at least one preschool child; (iv) the family lived inside a plantation.

Iron supplementation

The iron treatment consisted of ferrous sulphate, produced by an Indonesian pharmaceutical company (PT. Kimia Farma). The children received 50 mg/day of elemental iron in 10 ml of syrup for eight consecutive weeks. The women received two tablets of 100 mg/day of elemental iron for the first week and one tablet per day for the remaining seven weeks. A placebo in liquid and tablet form respectively, similar in appearance to those containing iron, were given daily to the other half of the sample following the same procedures. Distribution and consumption of the iron preparations were closely supervised.

Assessment of iron status

The assessment of body status of the subjects in the sample consisted of three hematologic surveys. The first survey was carried out three months prior to the iron supplementation; the second, immediately before (T1), and the last following the completion of the intervention (T2). These surveys determined Hemoglobin (Hb), hematocrit (Ht), serum ferritin, transferrin saturation, and free erythrocyte protoporphyrin (FEP). There were no significant changes from the first to the second surveys (both done before the intervention) in the mean values of each iron indicator. Accordingly, thereafter all references to the blood analyses at T1 are restricted to the results from the second survey which were closer to the beginning of the intervention.

Blood samples were collected via venipuncture. A small fraction from each sample was used to determine Hb, Ht and FEP. The blood remaining from each sample was allowed to clot in clean tubes. After separation the serum was frozen and stored at 20°C for later determinations. All samples were kept in an ice bath during transport to the Center for Research and Development of Nutrition (CRDN).

Hb was determined by the cyanmethemoglobin procedure using a Compur M 1000 Mini Photometer. Ht was determined by the microhematocrit method using a Comput M 1100 Mini Centrifuge. Serum iron was measured

using the method defined by the International Committee for the Standardisation in Hematology method (8); transferrin was measured by end-point radialimmunodiffussion (M. Partigen Transferrin Kit); serum ferritin was determined by a Clinical Assay radioimmunoassay method (Gamma dab 125 I (isotope Superscript). Ferritin Radioimmunoassay kit, Clinical Assay, Cambridge, MA); and FEP was measured on blood specimens dried on filter paper using the method described by Orfanis, *et al.* (9), and the FEP standard produced by the Sigma Chemical Co., St. Louis, MO.

Anthropometry

Measurements of body height, weight and skin fold thickness were obtained immediately before (T1) and after (T2) the intervention, using standard anthropometric procedures (10). Height was measured with a portable instrument designed by the Nutrition Research and Development Centre in Bogor, calibrated for an error of measurement of 0.1 cm. The weight of the children was measured with a Detecto scale with an accuracy of 0.1 kg. The triceps skinfold was measured with a Lange caliper to the nearest 0.1 mn. Anthropometric measurements were taken twice; when necessary, any discrepancies were resolved by a third measurement.

Cognitive function

The battery of tests included two discrimination learning tasks, three oddity learning tasks, and the Peabody Picture Vocabulary test.

(i) Two-choice Discrimination Learning:

1. Pictures - Two colored pictures, cut from children's books and pasted on black poster board, were presented to the child being tested. A happy face had been placed on the underside of the poster board on which one of the pictures had been pasted. The task was to discover which picture "hid" the happy face underneath it. After each trial the left-right position of the pictures was rearranged out of the child's sight. The procedure continued until a learning criterion of seven correct in a row is met; at this point a reversal shift was introduced into the problem, so that the correct stimuli were those that were previously incorrect. Again the task is administered to the same learning criterion.
2. Color-Form Figures - The procedures is identical to that for the pictures described above, except that the two stimuli were colored, geometric figures. Two colors were used - red and blue - and two forms - X and O. While the colors were randomly paired on consecutive trials with the happy face. Again seven consecutive correct responses defined the learning criterion; at that point reversal shift was introduced.

(ii) Oddity Learning:

Three pictures, two of which were identical, were presented simultaneously on a 7 x 18 black poster board. The only instructions given to the child were to "find the winner". The correct response was to point to the picture that was different from the other two. Feedback was given about response correctness. In the first series of problems, new stimuli are used on every trial. In the remaining series, the same stimuli were repeated twice or thrice. In each case the nature of the stimulus does not determine its correctness, but rather its relationship to other stimuli in the array.

(iii) Peabody Picture Vocabulary Test (PPVT):

Forms A and B from the 1965 version (11) of the PPVT were used. The administration procedures followed the instructions of the original test manual.

Morbidity

Nurses and nurse assistants of the health clinics in the respective plantations visited the houses of the women enrolled in the studies three times in a seven-day period, six weeks before and after the intervention. A morbidity questionnaire was used to interview the women regarding the presence or absence of signs or symptoms on a list of specific disease categories. The questions did not address issues of disease severity or duration. The disease categories included were the following: gastrointestinal disorders including diarrhea, respiratory tract disorders, measles, smallpox, conjunctivitis, otitis media purulenta, dermatitis and scabies.

Work productivity

The daily weight (kg/day) of tea leaves picked was recorded for each woman in the sample. For the purposes of this study the average amount of tea picked in a picking rotation (i.e. 7 days), expressed as a percentage of the plantation's quota, represents the unit of analysis of work productivity. This measure controls fr the possible differences between plantations due to differences in skills between plantation workers, the age of the plants, or on the quality of the respective lands.

Statistical analyses

The statistical analyses in each of the studies on the functional consequences of iron deficiency focus of within group changes (T_2-T_1) and between group differences before and after treatment. Student t-tests, chi-square test, analyses of variance and covariance have been used for this purpose. In the analyses of behavioral data, age was included as a covariate. The use of the test scores at T_1, as a covariate for the analyses of the results at T_2 assumes that the potential effects of those extraneous variables (not related to iron), which may account for the differences at T_1; and differences observed at T_2 should reflect the sole effect of the experimental intervention.

TABLE 1
Criteria for the classification of subjects according to iron status

Children

Iron deficiency anaemia:	Hb< 11 g/dl; plus two of the following three criteria: ferritin < 12 µg/L; TS* < 16%; FEP** > 1.77 µmol/L RBC
Iron deplete:	Hb < 11 g/dl; plus two of the following three criteria: ferritin < 12 µg/L; TS < 16%; and FEP > 1.77 µmol/L RBC
Iron replete:	Hb > 11 g/dl; plus two of the following three criteria: ferritin > 12 µg/L; TS > 16%; and FEP < 1.77µmol/L RBC

Women

Iron deficiency anaemia: Hb < 12 g/dl; plus criteria for children
Iron deplete: Hb < 12 g/dl; plus criteria for children
Iron replete: Hb > 12 g/dl; plus criteria for children

*Transferrin saturation; ** Free erythrocyte protoporphyrin

Results

The preschool children and the women were classified into one of the three categories: iron-replete, iron deplete, and iron deficiency anaemia. The term anaemic is used to refer to the last group. Table 1 presents the criteria for the definition of these three groups.

Iron status

Table 2 presents the means and standard deviations of each of the five indicators of the women and their children assigned to the iron and placebo treatment groups, independent of their iron status before treatment. For the women and the children treated with iron, the changes (T_2-T_1) in all indicators were statistically significant ($p < 0.05$); conversely, none of the changes in the placebo group were significant.

Table 3 presents the data on response to treatment based on iron status for the three iron groups. The numbers of iron-replete subjects increased significantly ($p < 0.05$), and the numbers of iron-depleted and anaemic subjects decreased significantly ($p < 0.05$) in the iron groups but none in the placebo groups for both women and children.

TABLE 2

Hematologic values, before and after treatment*

Parameters	Treatment	Children (N=207)		Women (N =177)	
		Before	After	Before	After
Hemoglobin (g/dl)	Fe	$12.8^{a}\pm1.45$	$13.7^{a}\pm1.38$	$12.5^{f}\pm1.38$	$13.4^{f}\pm1.45$
	Placebo	12.9 ± 1.56	13.3 ± 1.51	12.7 ± 1.48	12.9 ± 1.46
Hematocrit (%)	Fe	$40.4^{b}\pm3.96$	$41.9^{b}\pm3.70$	$39.2^{g}\pm4.19$	$40.9^{g}\pm4.09$
	Placebo	40.7 ± 4.01	41.3 ± 4.18	40.0 ± 4.02	40.4 ± 4.09
Ferritin (µg/L)	Fe	$18.5^{c}\pm22.70$	$32.5^{c}\pm34.30$	$21.2^{h}\pm23.20$	$36.5^{h}\pm38.50$
	Placebo	22.6 ± 25.95	18.7 ± 16.65	23.3 ± 25.76	19.7 ± 15.80
Transferrin saturation (%)	Fe	$19.1^{d}\pm6.15$	$24.3^{d}\pm7.78$	$18.4^{i}\pm5.88$	$23.6^{i}\pm7.53$
	Placebo	20.2 ± 7.17	18.7 ± 5.28	19.5 ± 6.21	18.5 ± 4.57
Erythrocyte protoporphyrin (µmol/L rbc)	Fe	$1.79^{e}\pm0.50$	$1.52^{e}\pm0.34$	$1.88^{j}\pm0.51$	$1.60^{j}\pm0.34$
	Placebo	1.77 ± 0.51	1.75 ± 0.37	1.74 ± 0.40	1.81 ± 0.34

* Within rows, figures with the same superscript letters are significantly different at $p < 0.05$.

TABLE 3

Number of iron-replete, iron-depleted, and iron deficient anaemic, before and after intervention*

Iron status	Intervention	Children		Women	
		Before (n)	After (n)	Before (n)	After (n)
Iron replete	Iron	37[a]	73[a]	33[a]	72[d]
	Placebo	47	44	34	40
Iron depleted	Iron	35[b]	15[b]	21[e]	3[e]
	Placebo	37	53	26	22
Iron deficient anaemic	Iron	25[c]	7[c]	35[f]	14[f]
	Placebo	26	15	28	26

* Within rows, figures with the same superscript letters are significantly different at $p < 0.05$.

Growth

Table 4 presents the pretreatment for weight, height and skinfold thickness of the groups, classified by their iron status and assignment to treatments. The three (iron replete/iron depleted/anaemic) x two (iron/placebo) analyses of covariance failed to yield statistical significant differences. Body iron status and physical growth were independent of each other before treatment. Accordingly, there is no evidence that the iron treatment resulted in an acceleration of physical growth.

Psychological testing

None of the psychological tests administered descriminated between iron-replete and iron-depleted children, either before or after treatment. The following report is therefore restricted for comparing between the iron-replete and anaemic children. The results of these psychological tests have been published in the American Journal of Clinical Nutrition by Soesmalijah Soewondo *et al.* (12)

TABLE 4

Mean body weight, height and skinfold thickness of the children at before and after treatment

Measurement	Intervention	Before treatment			After treatment		
		Replete	Depleted	Anaemic	Replete	Depleted	Anaemic
Weight (kg)	Fe	13.34	13.68	13.78	14.21	14.15	14.30
	Placebo	14.02	13.83	13.79	14.19	14.16	14.11
Height (cm)	Fe	92.69	63.90	94.77	95.03	95.47	96.35
	Placebo	94.67	94.07	93.06	95.35	95.31	94.39
Skinfold (mm)	Fe	7.44	7.26	6.68	7.51	7.26	6.74
	Placebo	7.08	6.88	7.01	7.08	6.88	7.02

Peabody Picture Vocabulary Test

Table 5 presents the mean scores for the groups compated at T_1 and T_2. The T_1 scores for the iron-replete and anaemic children are similar to each other. Unexpectedly, because of randomisation, the main effect at T_1 of assignment to treatment ($F_{(1,114)}$= 3.81; $p < 0.05$) and the interactive term for treatment by iron status ($F_{(1,114)}$=4.11; $p< 0.05$) were statistically significant. The mean score of the children who received a placebo (42.71) was higher than that of the children treated with iron (39.42). This difference was explained by the mean values in each of the four cells in the analyses. Among the anaemic children, those who received iron had a higher mean score (41.34) than that of the children who received placebos (40.56). Conversely, among the iron-replete children the mean score of the placebo children (44.85) was higher than that of the children who received iron (37.90). Because of randomisation these pretreatment differences must be distributed to chance.

The T_2 ANCOVA controlled for the potential effects of age and T_1 measures on the outcome variables. Thus, the differences that might be observed between iron or treatment groups could not be attributed to regression to the mean effects. The iron status variable was not statistically significant in the ANCOVA of the T_2 PPVT scores. Across iron status groups, the mean PPVT raw score of the children treated with iron (46.00) was somewhat higher than that of the children who received a placebo (42.97). The treatment variable had $F_{(1,113)}$= 3.21 with p=0.07. Finally, the interactive factor was not statistically significant.

Discrimination learning

Table 6 presents the mean trials to criterion of the original and reversal presentations of the discrimination learning tasks before and after treatment. The analysis of covariance of T_1 scores in the DL original presentation failed to yield statistically significant findings.

TABLE 5

Mean raw scores in the Peabody Picture Vocabulary Test of iron-replete and anaemic children before and after treatment*.

Nature treatment	Before treatment			After treatment		
	Iron - replete	Anaemic	Total	Iron - replete	Anaemic	Total
Iron	37.90[a]	41.34	39.62[b]	44.60	47.39	46.00
Placebo	44.85[a]	40.56	42.71[b]	43.62	42.31	42.97
Total	41.38	40.95	–	44.11	44.85	–

* Within rows or columns, figures with the same superscript letter are significantly different at $p < 0.05$ or better.

TABLE 6

Mean trials to criterion in the orginal and reversal presentations of the discrimination-learning task among the iron-replete and anaemic children before and after treatment

Treatment	Before treatment			After treatment		
	Iron - replete	Anaemic	Total	Iron -	Anaemic replete	Total
Colour: original presentation						
Iron	22.46	22.41	23.44	22.48	22.58	22.53
Placebo	22.49	23.29	22.89	23.87	21.82	22.57
Total	22.47	23.57	–	23.18	22.13	–
Colour: reversal presentation						
Iron	17.87	25.02	21.44	30.61[a]	16.29[a]	23.22
Placebo	18.09	22.81	20.45	26.11	27.16	26.59
Total	17.98	20.45	–	28.14[b]	21.68[b]	–
Form: original presentation						
Iron	22.56	24.41	23.44	13.50	11.93	12.71
Placebo	22.49	23.29	22.89	10.60	11.54	11.07
Total	22.47	23.57	–	12.05	11.74	–
Form: reversal presentation						
Iron	14.43	16.13	15.26	15.43	14.80	15.12
Placebo	16.31	17.84	17.08	14.58	15.18	14.99
Total	13.37	16.99	–	15.01	14.99	–

* Within rows, figures with the same superscript letter are significantly different at $p < 0.05$

The analysis of covariance of the T_2 reversal presentation of the color DL task shows that the main effect of iron status was statistically significant ($p < 0.05$). The mean trials to criterion of the iron replete children (28.14) was greater than that of the anaemic children (21.68). However, the interactive factor was also statistically significant ($p < 0.05$)). This suggested that the effects of iron status was not the same among the iron treated and the placebo children. The iron replete children treated with iron took more trials (30.61) to criterion than the anaemic children treated with iron (16.29). Planned comparisons showed that this difference was statisticlly significant ($p<0.05$). On the other hand, the anaemic placebo children had a slightly higher score (27.16) than the iron replete placebo-children (26.11). This difference, however, was not statistically significant. Also the main effect of treatment, across the groups classified by iron status, was not statistically significant.

The analysis of covariance of the reversal DL-form scores failed to yield statistically significant findings.

Oddity learning

As observed in Table 7, the iron replete children learned faster at T_1 than did the anaemic children in the non repeated and the repeated - once, - twice, and - thrice, however only in two (ie, twice and thrice) of the four comparison were statistically significant.

There were no statistically significant findings in the analysis of the two first OL tasks at T_2. Likewise, the main effects of treatment and iron status were not statistically significant in the third and fourth OL tasks. However, the interactive factor was statistically significant ($p < 0.05$) in both of these tasks. This finding suggested that the differences between the iron replete and iron deficient anaemic children differed in the iron treatment condition as compared with the placebo condition. As observed in Table 7 the results of the third OL tasks shows that among those treated with iron the anaemic children had more correct responses (9.02) than the iron replete children (7.32). Conversely, the performance of the iron replete placebo-children (8.52) was better than the anaemic-placebo children (7.78). Planned comparisons showed that the respective differences were statistically significant ($p < 0.05$). The anaemic children treated with iron obtained the highest scores among the four subgroups.

The comparison between cells in the fourth OL task showed that the anaemic children treated with iron had a larger number of correct responses (8.90) than the iron replete children (7.27) treated with iron. This difference was statistically significant ($p< 0.05$). Among those that received a placebo the iron replete children had a slightly higher number of correct responses (7.76) than the anaemic children (7.36). This small difference was not statistically significant. In this task, as in the third OL task, the anaemic children treated with iron had the best performance among the four subgroups.

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TABLE 7

Mean number of correct responses in the four oddity-learning tasks among the iron-replete and anaemic children before and after treatment.

Treatment	Before treatment			After treatment		
	Iron-replete	Anaemic	Total	Iron-replete	Anaemic	Total
Nonrepeated task						
Iron	11.53	10.46	10.99	11.43	12.37	11.90
Placebo	11.23	9.98	10.60	12.88	11.82	12.10
Total	11.38	10.22	–	12.16	12.10	–
Repeated once						
Iron	8.21	7.84	8.04	7.96	8.00	7.48
Placebo	8.04	7.86	7.95	8.49	8.33	8.41
Total	8.12	7.67	–	8.27	8.41	–
Repeated twice						
Iron	7.58	6.78	7.18	7.32b	9.02[b]	8.17
Placebo	8.15	6.73	7.44	8.52c	7.78c	8.40
Total	7.87a	6.76[a]	–	7.92	8.40	–
Repeated thrice						
Iron	7.50	5.90	6.70	7.27d	8.90[d]	8.08
Placebo	7.52	6.62	7.07	7.76	7.36	–
Total	7.51c	6.26c	–	7.51	8.13	–

* Within rows, figures with the same superscript letters are significantly different $p < 0.05$.

Morbidity

Morbidity information was collected on the preschool children and their mothers six weeks before and after the treatments. Data on the following disease categories were obtained: gastrointestinal disorders including diarrhea, respiratory tract disorders, measles, smallpox, conjunctivitis, otitis media purulenta, dermatitis and scabies. Table 8 presents the information for both children and adult women at before and after treatment. For each of the two types of treatment (iron/placebo) the data are pooled for subjects with different iron status. Otherwise statistical comparisons between groups would be precluded because of a small number of subjects per cell. The difference between the pre- and post-treatment measures of gastrointestinal and respiratory tract disorders for both iron and placebo children are the only statistically significant findings.

Work productivity

The average of tea leaves plucked by each individual over a tea plucking period is the measure of work productivity. An individual's score was expressed as a percent of the standard of tea picked per period in her respective plantation. There were 68 and 64 women exposed to the iron and placebo treatments respectively. As observed in Table 9 the pretreatment mean work productivity score of the women on both groups were very similar to each other. However, the change in the mean work productivity of the women treated with iron was statistically significant ($p < 0.05$). On the other hand, the change score was not statistically significant among the women who received a placebo. The work productivity scores of the iron-replete women were higher than those of the anaemic women at the beginning of treatment. However, these differences were small and not statistically significant. As observed in Table 10, the t-

TABLE 8

Morbidity, children and adult women at before and after treatment

Age group	Intervention	N	G.I. tract		Resp. tract		Measles		Chicken pox		Conjunc. toxitis		OMP		Skin infection	
			A (n)	B (n)	A (n)	B (n)	A (n)	B (n)	A (n)	B (n)	A (n)	B (n)	A (n)	B (n)	A (n)	B (n)
Preschool children	Fe	148	32[a]	7[a]	58[b]	12[b]	9	6	7	0	9	4	4	0	19	4
	Placebo	169	25[a]	15[a]	59[b]	27[b]	8	9	8	2	13	5	4	0	17	7
Adult females	Fe	108	19	6	31	14	2	1	3	0	6	3	5	0	11	3
	Placebo	127	18	8	40	19	1	2	3	0	5	2	3	2	11	4

B = Before treatment
A = After treatment
G.I. tract = Gastro intestinal tract infection includes diarrhea and dysentri
Resp. tract = Respiratory tract (upper, lower) infection
OMP = Otitis Media Purulenta
* Within rows and columns, figures with the same superscript letter are significantly different at $p < 0.05$.

test values of the change scores for the anaemic and iron-replete women treated with iron were statistically significant. On the other hand, the delta of the normal women treated with iron was not statistically significant. Therefore, the salutary effect of the iron treatment varied as function of the iron status of the subjects at before intervention. Likewise, the placebo was not associated with a statistically significant change in the women's work productivity from the pre to the post-treatment evaluation in any of the three groups.

TABLE 9

Means work productivity* of iron and placebo groups before and after treatment

Time of evaluation	Intervention	
	Iron (N=68)	Placebo (N=64)
Pretreatment	93.7	93.4
Postreatment	103.0	96.4
Difference	9.3	3.0
T-test	3.71**	1.06

* Percentage of tea picked of plantation's standard
** $p < 0.01$

TABLE 10

Means work productivity* based on iron status, before and after treatment

Time of evaluation	Anaemic		Iron-depleted		Iron-replete	
	Iron (N=26)	Placebo (N=25)	Iron (N=17)	Placebo (N=16)	Iron (N=25)	Placebo (N=23)
Pretreatment	92.1	94.1	92.8	90.0	96.2	94.8
Posttreatment	104.8	99.9	102.1	90.6	101.8	96.6
Difference	12.8	5.8	9.4	0.7	5.6	1.8
T-test	3.33***	1.14	2.16**	0.14	1.19	0.40

* Percentage of tea picked of plantation's standard
** $p < 0.05$
*** $p < 0.01$

Discussion

Iron deficiency anaemia with its reduction in hemoglobin levels is a major health problem especially in developing countries. There is already evidence that iron deficiency impairs resistance to infection, cognitive performance, physical capacity, and work output (2). However, there are still very few studies to demonstrate that iron deficiency per se, as diagnosed by levels of serum iron, ferritin, and transferrin saturation, was sufficient to affect those functional consequences. This current study has attempted to look at these functions in a free living population.

This present study has shown that none of the psychological test administered discriminated between the iron replete and iron deplete children either before and after treatment, therefore the analysis in this study restricted for didactic purposes to comparisons of the iron replete and anaemic children.

The pretreatment data on the three cognitive test (PPVT, DL and OL) administered showed that although there were no difference in IQ between the anaemic and the iron replete children, there were differences in the expected direction in the reversal presentation (ie, DL color sore) of the DL and OL tasks (ie, repeated twice and thrice). A total of nine statistical comparisons was made involving the T^1 IQ and cognitive test data. Three, or 33%, of these nine comparisons yielded statistically significant findings in favor of the iron-replete children as compared with anaemic children.

Three of nine ANCOVAs of the test results after treatment yieled significant interaction terms (ie, treatment x iron status). Anaemic children treated with iron performed significantly better in two (ie. repeated twice and thrice) of the four OL tasks and in one of the DL reversal rasks (ie, color) than did anaemic children who received placebos. This evidence in conjunction with strength of the study design attributes internal validity (13, 14) to the relationship between iron status and cognitive test performance. The comparatively low performance of the anaemic children at T_1 was due to their low iron status, and their improvement in performance from T_1 to T_2 was due to the iron treatment. This study strongly suggests that iron deficiency produces alterations in specific cognitive process related to visual alteration and concept acquisition. These alteration were fully reversed after 8 weeks of iron treatment.

This present study shows the differences between the pre and post-treatment measures of gastrointestinal and respiratory tract disorders for both iron and placebo in children are the only statistically significant. While studies on iron deficiency and infection in adults are very few, several studies on infant and children have shown similar results. One of the earliest clinical study was conducted by Andelmen and Sered in 1966 (15), included 603 infant fed a proprietary iron formula containing vitamins and 12 mg of iron per quart. Their indicence of respiratory infection was approximately half that of a group of 445 infants fed a formula with the same added vitamins but no iron. Another study in Alaska showed that diarrheal and respiratory infections were more common in Eskimo and native children with iron deficiency anaemia, and meningitis was often fatal in anaemic children but not in those with hemoglobin levels above 10.1 g/dl (15). There are a wide range of possible mechanism that iron deficiency reduces resistance to infections. Among of many possibilities, the importance of cell-mediated immunity and related mechanism have been showed a positive results (2, 6).

The results of the present study revealed that iron deficiency, as diagnosed by levels of serum transferrin

saturation (TS), ferritin, and free erythrocyte protoporphyrin (FEP), was sufficient to affect work productivity. It is also clearly demonstrated that iron status, not only of iron deficiency anaemia, but also of iron deficiency not severe enough to cause anaemia significantly impaired the functions. Therefore, the significance of iron deficiency on reducing work performance and productivity is greater than has been recognised.

It is important, however, to obtain some confirmation, that the effects of lowering work productivity were due to iron deficiency and not to other factors. In general, the amounts of tea leaves picked per day are influenced by the skills of the workers, the age of the plant, the soil and the quality of the land, and the seasonal factors. In obtaining the true effects of iron deficiency, the influences of the above factors were minimised by expressing the amount of the leaves picked in a percentage of the plantation's quota (standard), represents the unit of analysis of work productivity.

The supplementation with ferrous-sulphate for the eight weeks duration resulted in significantly greater improvement when compared to the placebo group. These findings provide strong evidence that the economic implications of increased work productivity with iron treatment are very significant, particularly in developing countries such as in Indonesia.

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Iron deficiency in Thai children: problems and perspectives

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Introduction

Anaemia affects approximately 30% of the world's population. The majority is due to iron deficiency (1). Iron deficient pregnant women seem to transfer less iron to the fetus causing increased risk of premature birth, low body weight, fetal death and low serum ferritin in the neonates (2). In Thailand (3), the prevalence of anaemia in pregnant women ranges between 30-70%.

Infants with iron deficiency anaemia (IDA) had poor Bayley Scales of Infant Developmental tests scores (BSID) (4,8). Treatment with iron increased scale scores in some IDA infants. This suggests that IDA affects adaptive behaviors. The effect was no restricted to infancy since study from Indonesia showed that IDA affects learning. This study replicated the effect of IDA in a different ecological setting, population and culture.

Method

Study design

This is a double-blind clinical trial conducted in 16 elementary schools in a non malarial area of Chonburi province approximately 110-150 kilometers from Bangkok with good road access. Each school has at least 150 children. Some 2268 students (about 23% of the total number of grade 3-5 students in the province) were screened. Case selection was based on (a) absence of thalassemia diseases, (b) age, 108-144 months (c) never had menstruation. The inclusion criteria included (i) pre and post treatment hemoglobin (Hb), transferrin saturation (TS), serum ferritin (SG) and free erythrocyte protoporphyrin (FEP), (ii) pre and post treatment IQ and educational achievement tests scores derived from different forms of the same respective tests; (iii) pre to post treatment change in IQ < 40 points. Ingestion of > 3 mg elemental iron /kg/d to those treated with iron. 1775 children represent the sample selected for analysis.

The children were classified into one of 3 groups according to their body iron status:iron replete (IR), iron deplete (ID), and iron deficient anaemia (IDA) (7) (Table 1).

Physical examination

Every child was examined before (T1) and after (T2) the intervention, minimal infections were treated and recorded but included in the study.

Hematology

The venous blood was drawn for

TABLE 1
Criteria to identify iron status. Hemoglobin plus 2 out of the 3 following parameters

	Hgb g/L	FEP µg/L	TS* (%)	SF (µg/L)
Iron deficiency anaemia (IDA)	< 120	> 70	< 16	< 10
Iron deplete (ID)	> 120	> 70	< 18	< 10
Iron replete (IR)	> 120	< 70	> 16	> 10

complete blood count, iron status (TS, SF, FEP) and determination of thalassemia/ hemoglobinopathies as described elsewhere (8).

IQ and achievement tests

The Colored Raven Progressive Matrices was used to measure IQ. The school achievement tests for Thai language and mathematics (Math) developed by the Ministry of Education of the Government of Thailand for the public school were used.

Socioeconomic status

The parents answered questions on family income and size, parental education, land owned, quality of housing, and availability of home electrical appliances.

Treatment

An antihelminth, albendazole 2 tablets were given to every student on the day of the blood test before, and 3 months after the iron/placebo intervention. The iron treatment consisted of 50 mg tablets of ferrous sulphate daily, for the first 2 weeks, and 100 mg tablets per day for the remaining 14 weeks. The placebo was a tablet containing sweet cassava powder with a color and appearance similar to the iron tablets. The pills were distributed daily by the school teacher.

Analytical design

The analyses of the treatment effects were based on an unbalanced multiway analysis of variance (MANOVA) with repeated measures. The between group factors included treatment and iron status. The repeated measure methodology was introduced as a "blocking" factor at an individual level.

Results

Hematology

There is a gradient from the IDA to the iron deplete and iron replete subjects in the mean Hb at T1 (Table 2). Iron treatment significantly increased the Hb, SF & TS in iron deficient subjects, but not in the iron replete one. As expected the FEP follow the opposite direction. Accordingly, the ANOVA showed significant effects ($p<0.01$) of iron status and of the interactive term ($p<0.01$) between time, time and treatment, iron status and treatment.

IQ and achievement test

The between group analysis shows significant effects of IQ, language and math for school & grade. The main effect of iron status was significant for IQ and Thai language (Table 3). Except for the comparatively high IQ at T1 and T2 of the ID children treated with a placebo, the scores of the IR children were consistently higher than ID & IDA children.

The within group analyses yielded a powerful effect of time (T2-T1) for the

TABLE 2
Means and confidence intervals of the haemoglobin (g/L)

	IDA (101)		ID (47)		IR (1210)	
	Iron (47)	Placebo (54)	Iron (27)	Placebo (20)	Iron (598)	Placebo (612)
Pre Rx	99 (94-104)	99 (94-101)	125 (123-127)	126 (123-130)	129 (128-130)	129 (128-129)
Post Rx	129 (126-132)	113 (109-117)	130 (127-133)	125 (121-129)	130 (120-131)	127 (126-128)
Change	29 (24-34)	5 (11-17)	5 (2-8)	0.2 (-3-3)	1.5 (1-2)	-1.5 (-2-1)

TABLE 3
Mean of IQ and education tests among the iron status groups

	IDA (101)		ID (47)		IR (1210)	
	Iron (27)	Placebo (54)	Iron (27)	Placebo (20)	Iron (598)	Placebo (612)
IQ	87.8	98.2	88.74	93.1	93.3	93.47
Thai (%)	49.39	52.2	52.2	48.2	58.2	57.7
Math (%)	47.15	44.2	47.2	47.15	53.6	52.64

three outcome variables: the children in the three groups improved their scores from T1 to T2 probably from learning but was not associated with treatment.

Analysis of covariates

Since iron intervention has no effect on any of the three outcome measures places in question that statistical association between iron status on the other are indeed causal. Conceivably, iron replete children are taller, heavier, and come from higher income and educated families than the iron deplete and IDA children. Analyses of covariance (ANCOVA) were done to control for anthropometric and socioeconomic variables, the main effect of iron status on IQ and Thai language was still statistically significant ($p<0.01$). Treatment, treatment by time, and treatment by iron status by time were still non significant.

Discussion and conclusion

Contrary to the study in Indonesia at which iron treatment improved scores in education tests. According to this study, IR children had significantly higher IQ and Thai language than the ID ones, but no evidence that iron treatment had an effect on IQ, mathematics and language even though significant improvement in the iron status were observed after 16 weeks of treatment. These changes were significantly greater than the control group that received only the antihelminthic agent. However, there were some hematologic changes in iron status in the placebo group. Could this be due

to the erradication of the hookworm or the unexplained effect of albendazole on hemoglobin?

The prevalence of anaemia in the study was 28.8%, 5.6% was IDA, 22.7% was IRA (iron replete anaemia or anaemia other than iron deficient). The number of student of the IRA at T2 was decreased, especially in the iron supplemented group that decreased from 190 cases at T1 to 73 cases at T2 (Table 4). It means that more than half of IRA in Thai School children are probably iron deficient; their iron profiles are low but not enough to be classified as iron depleted. The rest of IRA may be due to other nutrients or thalassemia traits. The incidence of thalassemia trait in Thailand is approximately 1% of the population.

Even though the causal relationship between IDA and development defect of children has not been proved. The failure of improvement in psychoeducational achievement in this study could be due to short duration of iron supplementation or the permanent damage that had occurred. For the time being, IDA should be prevented and treated in all children. Countries where thalassemia prevails, typical thalassemia features, and history of transfusion help to avoid a therapeutic trial of iron in the severe thalassemic patients.

Apart from public education and based on this study, the school is an appropriate vehicle for the delivery of iron tablets to children.

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TABLE 4

Number of students in various iron status at T1 & T2: Iron group

		No at T2				
	No at T1	IDA	ID	IR	IRA	Others
IDA	47	1	1	39	6	1
ID	27	0	0	26	1	0
IR	598	0	0	563	35	0
IRA	190	1	0	116	73	0
Others	7	0	0	5	2	0

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The changes in nutritional and health status in Japan after the 2nd World War

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Immediately after the 2nd World War, the people in Japan experienced serious food shortage and critical socioeconomic conditions. The Japanese Government conducted three important activities to improve nutritional status: (i) a national nutrition survey, (ii) determination of recommended dietary allowances and (iii) compilation of a food composition table for locally-available foods in Japan. These activities were necessary to calculate accurate daily intakes of nutrients and to determine "which and how much" nutrients had to be caught up. These activities were conducted by the Ministry of Health and Welfare and by the Agency of Science and Technology. The Ministry of Agriculture, Forestry and Fishery, and the Ministry of Education and Culture also conducted some valuable activities to improve the nutritional status of people living in rural areas and school children.

The pilot project of the national nutrition survey was conducted in December of 1946 in the Tokyo area. After 1948, the survey area was expanded to the whole country. The survey was conducted among households selected randomly in statistically selected areas for three successive days in February, May, August and November of each year. After 1955, the survey was conducted in November only.

In 1946, the average intake of total protein and animal protein was 59.5g and 15.2 g respectively in urban areas and 58.8 g and 5.9 g respectively in rural areas. By 1987, the national average daily intake of total and animal protein had risen to 78.5 g and 40.1 g respectively. Likewise, in 1946 the fat intake was only 16.6 g in urban areas and 12.7 g in rural areas, but in 1987, the national average figure was 56.6 g.

The physical status of Japanese males and females improved remarkably. Immediately after the War, we suffered from serious symptoms and diseases caused by undernutritional conditions. For instance, the symptoms caused by protein deficiency such as the loss of body weight, oedema, bradycardy, amenorrhoea and insufficient lactation were most prevalently observed, and the symptoms caused by deficiency of vitamin A and vitamin B group such as xeropthalmia, abnormal tendon reflex were also frequently observed.

The life expectancy of Japanese males and females in 1947 was 50.06 and 53.96 years respectively, but subsequent improvement was remarkable in reaching 75.61 years for the male and 81.39 years for the female in 1987. It took only 24 years to improve from a level of less than 50 years of life

expectancy for both the male and female to a level of over 75 years.

A remarkable change in the causes of death has occurred in Japan. The leading cause of death/100,000 population was communicable diseases such as tuberculosis, pneumonia, bronchitis up to 1950. Since 1965, cardiovascular diseases have decreased substantially. It is noteworthy that the death from heart diseases such as coronary heart disease have not increased, although intake of animal fat has increased markedly during the past 40 years.

In Japan, the daily fat supply of both animal and vegetable origin has increased remarkably (animal fat: 40.8 g and vegetable fat: 40.9 g in 1980). However, the levels are much lower than those of western countries such as Sweden (daily supply of animal fat: 107.8 g and vegetable oil: 66.0 g in 1980). It seems likely that the decrease of death from cerebrovascular diseases may be due to the increase of intake of animal fat containing cholesterol, since the recent epidemiological data suggest an inverse correlation between cholesterol intake and the incidence of cerebrovascular diseases.

The lower prevalence of coronary heart diseases in Japan compared to the western countries may also be due to the much higher consumption of marine fishes.

Recent reports strongly suggest that the n-3 polyunsaturated fatty acids, especially eicosapentaenoic acid which are abundant in marine fishes, are able to prevent coronary heart diseases through the inhibition of undesirable functions such as platelet aggregation which leads to ischemic heart disease by eicosanoids from arachidonic acid, n-6 metabolite from linoleic acid.

Therefore, n-3/n-6 polyunsaturated fatty acid ratio in the diet is an important factor for the incidence of coronary heart diseases or allergic diseases. The n-3/n-6 fatty acid ratio (0.26) in the diet of Japanese in 1946 was much lower than that (0.36) in 1985. The ratio for Americans in 1985 was 0.12. Eskimos who have a much lower incidence of coronal heart diseases showed a high ratio of 2.80. The n-3/n-6 ratio for Japanese school children was 0.15 which is almost similar to that of Americans. This suggests that the eating habits among the younger generations in Japan are similar to that of western countries.

We have overcome the undernutritional status caused by serious food shortage and poor economy after the 2nd World War. Deaths due to communicable diseases and cerebrovascular diseases have also decreased. As a result, the quality of life including the health status and life expectancy of Japanese has improved remarkably.

However, new nutritional problems are now being confronted especially among the younger generation.

Conclusions

1. The health and physical status of Japanese have improved remarkably with the improvement of nutritional status after the 2nd World War.
2. Appropriate animal protein intake should be the most important factor to consider for decreasing the incidence of communicable diseases.
3. The appropriate amount and quality of animal fat intake can effectively prevent cerebrovascular disease.
4. The most effective preventive factor of coronary heart disease in the diet is n-3 polyunsaturated fatty acids especially eicosapentaenoic acid in fish. The ratio of n-3/n-6 fatty acids in the diet may be avail-

able as an important nutritional parameter for the incidence of coronary heart disease.

5. The eating habits of the younger generation are now changing and the new nutritional problems such as obesity, arteriosclerosis, and ischaemic heart disease may be on the increase.

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The land of milk and honey: a good survival strategy gone wrong ?

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The western diet and lifestyle represents a brief moment in the course of human history. As argued by Eaton and Konner (1) humans have spent by far the greatest part of their history as hunter-gatherers. Agriculture is a relatively recent phenomenon, being less than 10,000 years old in even its earliest forms. Whether we begin in paleolithic times with Homo habilis, the tool-making ancestor with identifiably human characteristics (2 million years before present), or later with modern man, Homo sapiens (40-60,000 years BP), humans have lived as hunter-gatherers for most of their past. Eaton and Konner argue that this is the diet and lifestyle for which we, as modern humans living a westernised lifestyle, are genetically programmed: that the hunter-gatherer diet and lifestyle is a benchmark by which subsequent changes should be judged.

Australian Aborigines are one of the relatively few hunter-gatherer societies which survived into the 20th century. By the latter half of this century most of these people had been subjected to a rapid and radical lifestyle change and began to develop a disease pattern characteristic of other groups around the world which had been exposed to similarly rapid westernisation; a high prevalence of obesity, non-insulin dependent diabetes mellitus (NIDDM), hypertension and coronary heart disease (2). There is no evidence that they experienced these conditions when they lived as hunter-gatherers.

The diets traditionally consumed by Aborigines from all over Australia (tropical, coastal, desert, temperate) were very varied, often containing a high proportion of animal foods: mammals, reptiles, birds, fish, crustaceans, molluscs. However, the diet was not high in fat since wild animals have a much lower carcase fat and intramuscular lipid content (1-2% wet weight) than domesticated animals such as sheep and cattle (5-20% wet weight) (3).

A wide range of vegetable foods was eaten by Aborigines traditionally: starchy tubers and other roots, large legume-like seeds such as Acacia, wild grass seeds, fruits, nuts (4). They were generally rich in micronutrients, high in fibre, and with a low energy density - typical of uncultivated vegetables around the world. The carbohydrate in these wild vegetables was slowly digested and absorbed, which would have minimised postprandial glucose and insulin responses - possibly having implications for protection against both obesity and NIDDM.

Probably the most significant characteristic of both the animal and vegetable components of the diet in relation to body weight was their low

energy density. Energy expenditure is also important in body weight regulation. In this context, it is important to note that food procurement and preparation were energy-intensive processes: walking long distances, digging (for tubers, reptiles, eggs, honey ants etc.), chopping with a stone axe (wild honey, witchetty grubs etc.), winnowing and grinding seeds, digging pits for cooking large animals, gathering wood for fires.

Food intake of traditionally-living Aborigines varied widely both on a day-to-day and a seasonal basis ("feast-and-famine") - subsistence interspersed with feasts. The women were primarily responsible for the subsistence component: vegetable foods, small mammals, reptiles, fish, shellfish, crustaceans, insects. Although the men did assist with these activities, they were primarily hunters and provided the less regular, but highly valued, "feasts" from large mammals and reptiles.

There are numerous reports of Aborigines eating 2-3 kg of meat at one long sitting, taking maximum advantage of an abundant food supply on those irregular occasions when it was available. Almost without exception, food was consumed at the time it was available, little was processed into a form in which it could be stored and wastage was rare. This was indeed a thrifty way of life. It can be argued that the feasts were critical to the survival of Aborigines as hunter-gatherers as they provided excess energy which could be converted into fat and deposited as adipose tissue, thereby providing an energy reserve to tide an individual over periodic food shortages. The hyperinsulinemia reported in Australian Aborigines may have facilitated this process (2).

The most highly-prized components of the Aboriginal hunter-gatherer diet were the relatively few energy-dense foods: depot fat, organ meats, fatty insects, and honey. In general, muscle provided the bulk of the energy from a carcase. Although some animals were actively hunted at those times of the year when their fat depots were largest, the fat depots on most animals were usually small through most of the year (and needed to be shared among many people). Thus, high fat foods were either only available seasonallyy, or were present in small quantities on the animal. Likewise, wild honey was available only at certain times of the year and its procurement was often associated with high energy expenditure.

Nevertheless, it is significant that in a diet which was generally characterised by its low energy density, the foods which were most actively sought and most highly valued were those which had a high energy density. Clearly this was an important survival strategy. From the foregoing discussion it appears that two important components of the survival strategy of Aborigines as hunter-gatherers were to maximise energy intake and minimise energy output. The reality of the lifestyle, however, resulted in a generally low energy intake (subsistence) in combination with a relatively high energy expenditure. The scenario changed dramatically with westernisation.

After westernisation these hunter-gatherer food preferences have been retained by Aborigines in an environment where the availability of energy-dense foods (primarily fat and sucrose) is no longer limited and the energy output involved in their procurement is minimal. In the western context Aborigines have a very high intake of sucrose (primarily as sugar in tea and as carbonated beverages) and fat (from cheap fatty meats from domesticated animals, and more recently from a wide variety of processed foods). If the same eating behaviour is applied to beef and lamb as had been applied to kangaroo meat (2-3 kg at one long sitting), 2-4 times as much energy would be

consumed: 4,000-12,000 kcal instead of 2,000-3,000 kcal! This is due to the much greater fat content of meats from domesticated animals relative to wild animals.

From the hunter-gatherer perspective, the most logical developments in the food supply would be to increase the availability of the "survival foods", i.e. those foods with a high energy density (high in fat and sucrose). Our ancestors applied this principle in the early years of agriculture - seeking "The Promised Land - The Land of Milk and Honey". Since the industrial revolution, a very short time in human history, this principle has been applied assiduously by the food industry. Our "Promised Land" is one in which fat and sucrose are very readily available in an ever-increasing array of delectable, appetising and hidden forms. No longer do we have the natural constraints imposed by a traditional lifestyle on what may well be an in-built appetite for fatty and sweet foods.

There are probably two main strategies which could be developed to cope with this paradox - behaviour change and changes in the food supply. In terms of behaviour change, we need to learn to curb our natural instincts to seek out energy dense foods. There is evidence that changes along these lines are already taking place. Obesity is less common among the higher socio-economic, better educated classes in western societies where health promotion messages (e.g. Dietary Guidelines, regular exercise, anti-smoking) generally have more impact than in the socially disadvantaged groups. This type of behaviour change can be seen as a rational adaptive response to changed circumstances but may well have only limited success. The second approach, changing the composition of the food supply, is one which would complement and facilitate behaviour change. In order for this to occur, there will need to be radical changes in philosophy and direction in both the primary and secondary food industries towards producing foods with a lower energy density. Examples of such changes are the production of much leaner animals used for meat production, the production of reduced-fat milks, and in food manufacturing, the modification of existing products and the development of new products with less fat and refined carbohydrates, and more fibre. However, as it is clear from the foregoing description of the hunter-gatherer lifestyle, it was not only the composition of the diet (in particular its low energy density) which was important in preventing obesity, but also the lifestyle itself which was characterised by relatively high energy expenditure. Thus, future programmes aimed at obesity prevention would need to incorporate not only dietary chage, but also the adoption of a more physically-active lifestyle.

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Third World chronic diseases and their emergence

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Other contributors to this Symposium will highlight their experience of the emergence of chronic diseases in the Third World. A Western perspective, based on experience directing the Rowett Institute with its history of health issues linked to farming and food production, seems appropriate. Secondly, involvement in changing nutrition and health policy at the national level (1,2). European (3) and global levels (4) have revealed many of the barriers to change.

Barriers to change in public health

Four themes permeate an analysis of the emergence of chronic diseases. First, we need to recognise that the same processes are now involved in the Third World as were evident in Western Europe and North America post-war, i.e. in the 1950s; these processes are now well advanced in the Second World, i.e. Eastern Europe. Secondly, in all three worlds there are major forces of conservatism within the medical community, amongst nutritionists and in government circles. These groups are often obsessed with the concept of nutritional deficiencies and view the incidence of chronic diseases in moral terms of self-indulgence and excess. Next, we should emphasise the conceptual gap between those who view illness in public health terms linked to the need for prevention through national strategies and those who are in the majority in society who personalise the issues of disease. This then tends to focus on the importance of individual susceptibility to disease and therefore on its genetic basis. Finally, nutrition is unlike most branches of science because we have to contend with huge industrial interests in the agriculture and food business; companies involved in food and in the agribusiness perceive it as their legitimate interest to promote that scientific evidence which suits their business and to neglect or criticise nutritional ideas and discoveries which run counter to their financial interest. The distorting effect on scientific process and public health could become serious as illustrated by the experience of the anti-smoking campaign where tobacco interests use a variety of tactics to undermine public health initiatives. Since several of the large US tobacco conglomerates have now diversified into the food business, it will be interesting to see whether the same unscrupulous processes described by Taylor for the tobacco industry emerge in the food sector (5).

Three nutrition revolutions

Elsewhere I have highlighted (6) the three revolutions in nutrition this century. The first was the discovery of vitamins and the concept of specific diseases arising from selective micronutrient deficiencies. The second is the post-war revolution in animal

nutrition and in agriculture generally. The third is the recognition that nutrition plays a pivotal role in the development of the chronic non-communicable diseases of public health importance.

The early recognition of vitamin deficiencies was coupled before the War with widespread concerns about the general poor health and stature of the British and other European people. Boyd Orr and others linked poverty to a bad diet which in turn led to ill-health (7). Food supplementation with meat and milk to provide "first class protein" was recognised as needed, particularly by vulnerable groups such as children, pregnant and nursing mothers and the elderly. Government intervention with a strong bias towards a welfare state led to health, economic, educational and social policies which permeated society in order to prevent "undernutrition".

This concept of malnutrition led to the second revolution in farming and now dominates thinking in UN circles. With it is linked, in the public mind, the desirability of eating an American or British diet since these countries led the way in promoting health by mass education and rapid changes in the agricultural system. In all three worlds it is the automatic assumption at every level of society that meat and milk are "good" foods and that national policies should be geared to their provision as plentiful foods available to all sectors of society as cheaply as possible. Thus American and British agriculture is distorted by the pervasive subsidy over decades of the farming industry to provide meat and milk. The USDA and Canadian Ministry of Agriculture and indeed all EC country agriculture departments behave towards the agriculture and food industry in a manner which would astonish other Ministries with industrial interests. The Agricultural Ministries see it as their prime responsibility to support and nurture the farming industry. This has moral overtones because society has to eat to survive so it is little wonder that strategic thinking in government circles has always attached a high priority to agriculture. This in practice means that the dairy and beef industries have also received intense support, with research and development costs provided free. Marketing systems have also been subsidised to ensure the proper distribution of food, and government health and nutrition education constantly highlights the health benefits of dairy and meat products. These pervasive pressures all go back to the first revolution in nutrition thinking and the concept of undernutrition.

Eastern Europe

These same assumptions, agricultural support and public priorities pervade second world agriculture. The Polish people in the early 1980s were rioting because there were inadequate supplies of meat. Yet Polish meat consumption is greater than in some Western European countries and far in excess of Third World countries. The Polish people had been told for decades that meat was a luxury, prized food with health-promoting properties and the Communist regime in the early 1980s was convinced that a responsible Marxist state must provide more meat and milk. The Soviet Union today spends billions of dollars on grain imports; these import decisions affect the world grain prices but the grain is needed for animal feed because meat and milk are seen as primary national priorities. Yet Poland and Russia in the Soviet Union have escalating problems of heart disease and cancers of dietary origin. Thus political crises and international economic policies are linked to distorted perceptions of food based on concepts promoted to improve child health by my predecessor, Boyd Orr. He went on to found FAO as a strategy for coping with the desperate food supply problems in Europe and

the Third World after the War.

The Third World

The Third World is triply handicapped because it still has widespread deficiency diseases relating to stunting, iron, vitamin A and iodine deficiency, with society dominated by deficiency concepts. The second agricultural revolution is also underway but has not achieved the production gains seen to such spectacular effect in the West. Genetic engineering of plants, intensive livestock husbandry, monoculture systems with control of plant growth by growth modifiers and the widespread use of fertilizers, fungicides and pesticides are all being transferred to the Third World with substantial changes already evident, e.g. in the great revolution of rice growing in Asia. In Europe food gluts are the norm with productivity gains from scientific research providing 2-3% gains per annum in productivity. Social changes stemming from a transfer of people from the land are substantial in Europe and likely to become extraordinary in Asian countries, such as China. Yet still the priorities are to produce more meat and dairy products for supposed health reasons. Given this all-pervasive view of what is required, it is little surprise that the emergence of chronic disease in Asia is seen as either unexpected or of little significance. In practice it reflects the expected outcome of inappropriate national policies which continue to be based on concepts of nutrition and health developed in the 1930s. The Third World is therefore contending simultaneously with the strategies for combating deficiency diseases, a huge drive to enhance agriculture output and at the same time the development of chronic diseases in urban societies throughout much of Asia.

The WHO approach

On a global basis, we advocated an early recognition of the problems of co-existing deficiency and adult chronic diseases. Health, nutrition and food policies need to change dramatically if primordial prevention is to be institutionalised. Adult as well as child surveillance is needed and a coherent re-evaluation is unlikely at a national level without the formation of some form of national council driven by the Ministry of Health. Following our WHO Report many Western governments are rethinking their policies with a dramatic change revealed in the UK (8). We at WHO advised, however, a major change in strategy if effective political help was to be provided to Health Departments who have traditionally lost their battles with other government Ministries with huge vested interests in the status quo, e.g. agriculture. The potential solution is the active involvement of lay organisations and public opinion by the Health Ministry operating an open policy of consensus building to effect change in government policy and prevent the apparently inexorable aping of inappropriate Western lifestyle in Asia.

Solutions developed locally will involve economic and development policies; international agencies and trading organisations will often operate to sabotage appropriate initiatives. Western food firms, with huge economic leverage together with current economic priorities based on the desirability of unfettered free markets, will all propose that healthy nutrition demands that the public be well educated to allow them to make "free choices" and thereby determine consumption patterns. No society exists where the choice is free and undistorted by pricing, marketing, subsidy and educational policies which limit the public's ability to make balanced judgements even if in theory they were provided with suitable information. The present approach neglects the manipulative power of advertising,

subtle but progressive changes in marketing, structural adjustments which favour Western style societies where food processing is concentrated in a few hands, and where agricultural science imports Western solutions of intensive agriculture in Asia where labour is abundant and rurally based. On this basis it is unlikely that Asia can avoid Western mistakes despite the benefit of modern nutritional science and the recognised policy failures in the West. We have taken on average 30 years for health needs to be recognised, accepted and translated into action. If the same inertia applies in Asia then the agricultural and societal distortions of current policies will take several decades to overcome.

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Food and nutrition transition in Thailand

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Introduction

There seems to be little dispute that remarkable increases in food production have been achieved in providing for the nutrition needs of all human being over the past decades by many developing countries and developed countries alike. Yet the number of hungry people has increased because rapid and uneven population growth and more importantly, the lack of effective food distribution and political will to solve the problem. Moreover, food chains and food webs for any creatures, which are the processes of transferring energy from sunlight to life on earth, are more and more vulnerable to disruption when human beings try to manipulate the ecosystem of the biosphere as never before. For human beings, utilisation of food to sustain life is the end point of the complex and interlocking processes of transferring energy from the sun, through production of foods, distribution, and consumption, to cells in our body. There are threats along the pathway i.e. ecological degradation (greenhouse effect, acid rain, drought etc); inefficient distribution or unequal access to foods due to adverse economic and political situations; ignorance, lack of education or nutritionally inconsistent food taboos or habits; and diseases and utilisation of foods. In response to these threats, human beings have attempted to improve (i) the production process by means of science and technology, (ii) the distribution process by social and economic systems, (iii) consumption by modifying culture and food habits, and (iv) medical and health care to cope with diseases. However, interventions are usually confined within disciplinary boundaries and are not always concerted to the betterment of the community being targeted. Thus, the human nutrition and food system are in a rapid transition and the challenging and economic access to food, arising from unequal purchasing power and rapid environmental deterioration.

Thailand's economy and food production

Thailand has been cited as one of the successful countries of the developing world over the past two decades. The economy has undergone rapid and sustainable growth resulting from an industrial and export-oriented agricultural development policy. During the four National Economic and Social Development Plans (NESDP, 1961-1981), Thailand's economic growth rate averaged over 7%, which generated a fourteen-fold increase in the national income, and an average eight-fold increase in the per capital income (1).

Thailand's food production consistently exceeds the annual domestic requirement and is not only self-reliant in rice, the country's main staple, but

is also the world largest exporter of rice and cassava in 1986 (34.6% and 89.2% of the world market respectively), along with several other agriculture and livestock commodities. Year in year out, Thailand's exports on agricultural commodities and food products far exceed food imports in term of cash value. In 1981, Thailand earned 74.16 billion baht from food and exports which constituted 48.6% of total export. Food import amounted to 5.96 billion baht or 2.7% of total import (2).

Food and nutrition in transition

Amid such an overall economically thriving condition with a bounty of food, there is still considerable poverty and undernutrition. Thailand's income distribution and poverty profile are of major concerns. The Gini Coefficient was widening from 0.426 in 1976 to 0.500 in 1986 and the percentage of population under the poverty level showed no sign of improvement over the period (3). The expeditious introduction of predominantly capital-intensive, large-scale technology has failed to create sufficient jobs and incomes to eliminate absolute poverty in rural areas. The future economic outlook will also more likely benefit the already better-off households with non-agricultural occupations due to foreign capital inflows which largely finance development in non-agriculture activities. On the other hand, since world agricultural production is expected to be high, lower international prices and demand will limit Thailand's export of agricultural products (4) and thus, negatively affect the already worse-off agricultural households.

The prevalence of protein energy malnutrition (PEM) by weight-for-age in children under five that reflects macronutrients deficiency was 53% between 1979-1982 and 18.9% in 1990. Although it is considered to be a marked improvement thanks to the nationwide growth monitoring and community-based nutritional program by the Ministry of Public Health (5), the present PEM magnitude still undermines the quality of Thailand's future human capital and the prospect of better quality of life. Micro-nutrients deficiencies are also quite common and prevail in certain vulnerable groups. Iron-deficiency anaemia among pregnant women in 1986 was wide-spread being highest in the eastern region (35.9%) and lowest in the North (20.4%) (6), and also among children aged 0-5 yr (29.2%) in the 1988 national nutrition survey (7). The northern region and some provinces in the northeast are also categorised as goiter endemic.

The goiter prevalence among school children could be 10% and higher in 31 districts in the endemic areas (7). At present, although tremendous commitments and efforts are given to tackle the goiter problem, intervention strategies, activities and resources to alleviate nutritional anaemia are far from adequate.

In addition, due to uneven prosperity in the society, inadequate consumer protection and unmitigated environmental dangers, Thailand is now enduring a new chapter of nutrition related health threats. Obesity (120% weight-for-height NCHS reference) can be found in 4.3% and 16.2% of the primary school students in public and affluent private schools respectively. Heart diseases have been the number one killer (>30 deaths per 100,000 persons per year) in recent mortality statistics since 1980 (8). Prevalence of diabetes mellitus increased from 2.5% in all age groups in the 1971 national survey (9) to 3.4-4% in urban settings in the 20-80 years age group in 1987. Prevalence of hypertension is also alarming and can be as high as 17% in Bangkok slum area (10) and 16.9% in urban area in the northeast (11). Certain kinds of cancer which relate to overconsumption of fat (e.g. breast and

colon cancer) and contamination of toxic substances in the food chain (e.g. aflatoxin-induced liver cancer) are on the rise as a price of uncontrolled environmental hazards and changing food habits.

Other elements, both economic and social, can also indirectly influence nutritional status. Agricultural production, food prices, purchasing power, marketing systems and food habits are examples of important socio-economic factors (12). The rapid changes in dietary, food acquisition and food expenditure patterns have created concern among scholars and policy makers alike. In the rural areas, because of the pressure on the land and its resources due to population growth and rapid rural development, household food acquisition and food security rely more and more on monetary terms and market systems, rather than on domestic cultivation and partial hunting and gathering way of life. These rather primitive manners of food entitlement in the past were shown to provide food varities and adequate nutritional balance though they might suffer intermittently in some periods of "hunger season". However, the recent development in terms of electrification, communication and transportation is also conducive to poor nutrition especially among the poor and under-educated. Commercial bombardments and invasion of processed food in rural areas may result in an adverse situation when people sell more nutritious food in favour of buying less nutritious but more prestigious food. Nutritive value obtained with regard to the money spent is quite critical among the poor who have little disposable income.

In the urban areas, there is an accelerated shift from home-based food preparation to processed or pre-cooked food. Hectic lifestyle in the city also force people to eat out more. As a result, people have less control of what they eat. National and international agribusinesses are also clearly visible in their presence and will certainly claim an increasing share in people's daily life. Consumer behaviour, as never before, is being modified by intensive advertising and quite often by unfounded claims for the health benefits of special foods and food faddism. In these circumstances, although nutrition education may contribute to improve food choice and better utilisation of available food supplies, it needs good communication strategies to change people's value and perception.

Future challenges

The effect and impact of this transition on consumption, food expenditure and nutrition situation are inevitable. It is also quite indefinite whether the change is a blessing and propitious change. No single body of knowledge and field of discipline is sufficient to provide the direction and means to cope with this transition effectively. A growing body of knowledge of nutrient requirements and a healthy diet may exist, but interventions to ensure adequate food entitlement and consumption both at the community and household level are far from clear. Meeting the food security and dietary needs of people depends on improvement in every link along the energy transferring path or food chain. Research, training and technology development in food production, food storage and distribution, nutrition and public health, nutrition education and communication, food habit modification and food and nutrition policy are required. It is also quite clear that cataloging of each element is not sufficient; analysis of each of them and their interactions need to be done in order to understand the whole spectrum of the food and nutrition security issue. To identify the elements and the specific links in the chain that are missing or particularly weak in the

context of Thailand's rapid societal transition so as to generate information to fill those gaps is challenging agenda in food and nutrition research.

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Changing dietary patterns - policy intervention

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Abstract

Increasing urbanisation, changing lifestyles and diminishing gender specific roles in the family and the society are the major forces that are contributing to changes in the dietary patterns. The proliferation of fast food joints and the blooming of processed/semi processed food industry prove beyond doubt that convenience is going to overtake over considerations, including nutrition, in the choice of food. With women playing a greater role in economic activities, time constraint on processing, cooking methods and meal pattern are the major determinants of changing dietary patterns which will have profound bearing on nutrition. Changes in agriculture, trade and economic policies can turn nutrition priorities upside down. When indigenous dietary patterns, evolved on their proven ability to support healthy lifestyle, are drastically eroded by the tides of changing lifestyles, nutrition is at greater risk especially in populations where nutrition awareness is low and illiteracy is high. The need for integration of nutrition concerns in development programmes and nutrition advocacy to policy makers and planners is imperative at this point of time when the developing countries are in the race for faster economic growth. Protecting consumers from nutrition deprivation, because of the lopsided market oriented food policies, deserves better attention of policy makers and nutritionists.

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Contrasting nutrition experience in the east and west: a case study of China

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The objective of this paper is to demonstrate the dietary changes and disease transition in China. All the data used for the following interpretation are originated from an international collaborative study entitled "Diet, Lifestyle and Disease Mortality in China: A study of Characteristics of 65 Chinese Counties" which was directed by Drs. Colin Campbell, Richard Peto (Oxford University), Li Junyao (Chinese Academy of Medical Sciences), and Chen Junshi (1).

In 1983, an ecologic study on diet, nutrition and other lifestyle characteristics in 65 Chinese rural counties was conducted. A total of approximately 6500 adults were included in the survey, with 50 individuals per village (100 per county), half of each sex. Five kinds of information were collected and recorded, i.e. 3-day food intake measurements; questionnaire on lifestyle characteristics; blood analyses of nutritional, viral and metabolic characteristics; urine analyses for selected minerals, vitamins and food contaminants, such as aflatoxin; and food analyses for various fibre fractions, trace minerals, heavy metals and pesticide residues. The national mortality data of 1973-75 served as an important basis for this ecologic study. The combined data for these 65 counties and 130 villages were comprised of 367 items of information on life and death characteristics. These included age-standardised county mortality rates for many cancer and non-cancer diseases and a comprehensive group of nutritional, metabolic, hormonal, environmental, reproductive, demographic and socioeconomic status variables.

Geographic patterns of mortality rates were investigated as follows. Mortality rates that were significantly correlated ($p<0.05$) with each other were grouped together and two distinct groups of disease emerged. Every disease in the first group was found to be significantly inversely correlated with every disease in the second group (Table 1).

Most diseases in group A (diseases of poverty) are communicable and are generally more common in poor societies, while most of those diseases in group B (diseases of affluence) tend to be chronic degenerative diseases characteristic of more affluent societies. An empirical division of disease in this way suggests that diseases within each group share overlapping geographic distributions and common causes. To investigate what these common causes might be, aggregate mortality rates for each group of diseases were determined

TABLE 1

Self-clustered disease groups*

Group A	Group B
Pneumonia (16)	Stomach cancer (5)
Intestinal obstructions (12)	Liver cancer (10)
Peptic ulcer (13)	Colon cancer (9)
Other digestive disorders (17)	Lung cancer (16)
Nephritis (12)	Breast cancer (1)
Pulmonary tuberculosis (10)	Leukemia (15)
Infections diseases (other than schistosomiasis) (10)	Diabetes 92)
Parasitic diseases (other than schistosomiasis) (10)	Coronary heart diseases (1)
Eclampsia (13)	Brain cancer (ages 0-14) (13)
Rheumatic heart diseases (13)	
Metabolic and endocrine disease (other than diabetes) (10)	
Diseases of pregnancy and birth (other than eclampsia) (15)	

* Each disease category, when significantly correlated ($p<0.05$) with any other disease category is positive for disease categories in its own group and negative for disease categories in the second group. Numbers in parentheses indicate the number of correlations (of 20 comparisons) which are statistically significant at $p<0.05$

for each county. Associations between these group rates and various dietary and lifestyle characteristics were then determined using univariate correlation coefficients and those that were statistically significant at $p<0.01$ are listed in Table 2.

As expected, diseases of poverty are associated more with agricultural than with industrial activity. These diseases are more common in the higher elevation inland areas where overall economic activity, literacy and population density are lower. Diets in these areas involve fewer eggs, less beer and less soy sauce. In contrast, diseases of affluence are found in the more densely populated areas nearer the seacoast where industrial activity and literacy rates are higher and more fish, beer and processed starch and sugar products are consumed. It must be emphasised, however, that these particular food associations do not provide strong evidence of causal relationship with disease, because only small amounts of these foods are consumed. For example, mean egg consumption in China nationwide is very low by Western practices, with mean daily intake being about 5-10% of that for the United States. Therefore, consumption of these particular foods is probably more indicative of general economic conditions and other local circumstances than of plausible biological relationships to disease.

Differences in nutritional status between populations who suffer from these diseases may be examined by several indicators (Table 2). The physical stature of adults (both height and weight) is greater in areas where diseases of affluence are more common. Also, diseases of affluence are associated with higher levels of

TABLE 2

Correlations of aggregate mortality rates by disease group with selected characteristics.

Characteristic	Diseases of Poverty	Diseases of Affluence
PLASMA		
Total cholesterol		0.48+
Urea nitrogen	- 0.47+	0.40
Albumin		0.44
Antibody to core HB	0.44	- 0.32
Continine	0.37	- 0.50+
Prolactin (35 – 44 yr)	0.44	
URINE		
Riboflavin excess	- 0.41	0.45
Chloride	0.48	
RED BLOOD CELLS		
Hemoglobin	- 0.39	
Total n3 fatty acids (RBC)		0.44
QUESTIONNAIRE		
Height	- 0.59	0.51+
Weight	- 0.45	0.41
Beer (per day)	- 0.32	0.59+
Egg (per year)	- 0.54+	0.31
Total pregnancies	0.53+	- 0.38
Stillborn	0.51+	- 0.34
Infant mortality§	0.69+	- 0.47+
DIETARY SURVEY		
Fish (g/day)		0.56+
Processed starch and sugar		0.51+
Soysauce	- 0.41	
Arsenic	0.41	
GEOGRAPHIC CHARACTERISTICS		
Mean elevation	0.43	- 0.39
Mean longitude	- 0.48+	0.40
Gross value of industrial and agricultural output§	- 0.44	
Population density§	- 0.45	0.41
Literacy rate§	- 0.51+	0.39
Agricultural employment§	0.64+	- 0.58+
Industrial employment§	- 0.63+	0.58+

+ $p<0.001$; all others $p<0.01$.

§ Based on 1982 data reported in the Population Atlas of China (1987).

plasma cholesterol, plasma urea nitrogen and plasma albumin, each of which indicates a diet richer in fat and protein, and lower in fibre and other plant food constituents. Nutritional enrichment of this kind is most effectively and commonly obtained by increasing the intake of animal foods in the diet. The proportion of a 5mg experimental supplement of riboflavin that was excreted in the urine within the following 4 hours is significantly greater in affluent disease areas, indicating greater tissue repletion with this vitamin. Riboflavin intake is significantly correlated with consumption frequency of meat ($r=0.36$, $p<0.01$) and milk ($r=0.81$, $p<0.001$).

One of our statisticians, Dr Qu Y.S. used the data of five variables (height, weight, plasma urea-nitrogen and albumin and blood hemoglobin) to form a non-observable variable named GNS (general nutrition status), by using the LISREL statistical model. From the nutrition point of view, GNS is a variable for assessing the general nutrition status of a given population, mainly based on their protein status. When GNS is used to compare with various disease mortalities, it shows a strong positive correlation with all cancers as well as a strong inverse correlation with all non-cancer causes, mainly comprised of communicable diseases (Table 3). This inverse relationship between GNS and total death indicates that in the 1970s, communicable disease was still the major cause of death in China. Further analysis shows that GNS is positively correlated with most cancers and also heart disease. On the other hand, GNS is negatively correlated with most communicable diseases, including pneumonia, chronic bronchitis-emphysema, tuberculosis etc. These findings are consistent with the data shown previously.

Although general in nature, these various correlations hint at findings that could be useful for public health policy purposes. The ideal future policy, of course, would be to reduce mortality from the diseases of poverty without causing a large compensatory increase in the diseases of affluence. Among the characteristics listed in Table 2, however, some of the nutritional characteristics which are correlated positively with one disease group and inversely with the other suggests that there could be a trade-off in disease mortality trends with a so-called improvement in nutritional status. There are, however, some characteristics that are significantly correlated only with one disease group. For example, relatively high levels of plasma cholesterol, plasma albumin and omega-3 erythrocyte phosphatidylcholine fatty acids (directly correlated

TABLE 3

Correlation coefficients between GNS and mortalities of cancers and non-cancer causes in 65 counties

Causes of death	Male	Female	M+F
All causes	- 0.448	- 0.454	- 0.490
All cancers	0.463	0.601	0.547
All non-cancer causes	- 0.660	- 0.561	- 0.638

$p < 0.01$ in all cases

with fish consumption: $r=0.61$, $p<0.001$) reflect increased mortality only from diseases of affluence without simultaneously being associated with decreased mortality from diseases of poverty. Diseases of poverty are correlated with increased urinary chloride and decreased hemoglobin levels whereas diseases of affluence show no relationship to either. If these correlations do at least partially reflect causal relationships, then a diet low in protein, fat and salt, but sufficient to allow for adequate synthesis of hemoglobin should be associated with reasonable low mortality rates for both disease groups. This diet should minimise the intake of animal food, yet supplies an adequate intake of a variety of high quality plant foods. It should also minimises fat intake, decreases caloric density and enhances the intakes of various fibre fractions and a large group of antioxidant nutrients and nutrient analogs. This, then, is the dietary and nutritional lifestyle which is optimum for all societies, not only because it provides for optimum health, but also because it would provide for more equitable welfare for a larger number of people.

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Soluble fibres in diabetic diet - how useful?

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Introduction

Guar gum, a form of soluble dietary fibre obtained from the Indian cluster bean, has been first suggested to have a positive role in the management of diabetes mellitus by Jenkins *et al.* (1-3) in 1976. Most studies (1-7) but not all (8) have proven the beneficial effects of guar as shown by the improvements in fasting blood glucose levels and/or glucose/insulin responses to test meals. As these previous studies were performed with Western foods as test meals which are obviously different from Asian diets, the objectives of this present study were to investigate the glycaemic and insulin responses of Malaysian diabetic patients taking three common ethnic breakfast meals and the effects of guar in altering these responses.

Materials and methods

Patients

A pool of 12 non-insulin dependent diabetes mellitus, NIDDM (M:9, F:3) volunteer patients of mean age and BMI, 56.8 $\pm$ 13.3 yrs and 23.3 $\pm$ 2.9 kg/m2 was recruited from the Endocrine Clinic, UKM. Informed consent was obtained from each subject prior to the study. Six subjects completed all the three test meals. Only three of the patients were treated with dietary measures alone, while the remainder were on supplementary oral hypoglycaemic agents. The subjects had fairly good diabetic control with fasting plasma glucose values ranging from 5-12 mM.

Protocol and laboratory techniques

Blood samples were obtained after an overnight fast, and 15-30 mins up to 3 hr after ingestion of 75g glucose or a test meal with/out a pre-drink of 5g guar gum (Guarem, Finland). The description and composition (9) of the three test meals are listed in Table 1. Plasma blood glucose was measured by a Beckman analyser (Beckman Instruments, USA), intra-assay CV 5%; while serum insulin was measured by a commercial RIA kit (Novo, Denmark), CV 15%.

Statistical analysis

Results were analysed by ANOVA and Student's paired t-test where appropriate.

Results

Peak glucose levels among the three test meals were not significantly different but were lower ($p<0.05$) than oral glucose (Table 2). Addition of guar significantly lowered the peak times for oral glucose ($p<0.03$), increased for *nasi lemak* ($p<0.002$) but had no effect with *roti* and *mee sup*. In contrast to no glycaemic changes obtained for *roti telur*, significant lowering of plasma

TABLE 1

Composition of test meals

Test meal	Energy (kcal)	(kJ)	Protein (g)	Fat (g)	Carbohydrate (g)
Nasi lemak	570	(2386)	31	29	45
Roti telur	525	(2198)	19	20	67
Mee sup	640	(2679)	20	24	85

Nasi lemak: Rice in coconut milk (160g), anchovies in chili
(Malay) paste (30g), fried anchovies (15g), cucumber
(15g), groundnuts (15g), half-boiled egg (25g)

Roti telur: Fried pancake with an egg (165g),
(Indian) dhal curry (120g)

Mee sup : Wheat noodles (180g), egg (50g), chicken (20g)
(Chinese) cabbage (30g), mustard leaves (10g)
tomato (30g)

TABLE 2

Peak plasma glucose level and peak time achieved after ingestion of glucose or meals with/without guar

Test meal	n	Peak glucose level mean ± SD (mM)	Peak time mean ± SD (min)
Glucose load	11		
without guar		16.6 ± 3.6	95.4 ± 27.3
with guar		15.1 ± 2.3	77.7 ± 14.0 (b)
Nasi lemak	10		
without guar		13.4 ± 2.6 (a)	67.5 ± 15.4
with guar		13.2 ± 2.0	111.0 ± 39.8 (c)
Roti telur	7		
without guar		13.0 ± 2.2 (a)	98.6 ± 29.8
with guar		13.2 ± 2.1	122.1 ± 28.3
Mee sup	8		
without guar		12.2 ± 2.6 (a)	106.9 ± 47.7
with guar		11.8 ± 2.6	118.1 ± 38.6

(a) $p<0.05$ versus glucose
(b) $p<0.03$, (c) $p<0.002$ versus respective meals without guar

glucose levels between 15 to 45 mins postprandial, was obtained by addition of guar to *nasi lemak* and *mee sup*. No significant changes in insulin responses with the meals was obtained with guar, but an increase ($p<0.02$) was seen at 30 mins after glucose loading.

Discussion

Despite the differences in carbohydrate content, ranging from 45 to 85g, the plasma glucose levels were not significantly different among the three test meals. In contrast to the report (10) that similar glycaemic responses can be obtained with same contents of carbohydrate, protein, fat and energy in mixed meals, our study shows that these effects can be reproduced using normal servings of test meals with different composition. This study also shows that although there were beneficial effects for free glucose, *nasi lemak* and *mee sup*, guar may not be useful for all local breakfast meals such as roti telur. The reasons for this are still unknown and thus, results obtained with western meals cannot be extrapolated to local settings. Although guar was effective in decreasing the rate and delaying the peak time for glucose absorption, it did not lower peak glucose levels for the three meals. Moreover, since insulin responses were unchanged by guar, lowering of plasma glucose was probably due mainly to a delay in absorption of digested carbohydrates. There is a need for further and longer term studies on the effectiveness of guar with other common traditional Asian meals given to local diabetic patients.

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Fatty acid composition of adipose tissue in Korean diabetics

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Indroduction

Diabetes mellitus is a chronic condition characterised primarily by an elevation of plasma glucose due to insufficient action of insulin owing either to its absence or to resistence to its action. Resistance to the effect of insulin on glucose metabolism is a characteristic feature of both obesity and non-insulin dependent diabetes mellitus. In most developed countries above five percent of the population has diabetes mellitus, and an equal number are liable to develop this disease.

The prevalence of diabetes in Korea is estimated at two to three percent (3). Non-insulin dependant diabetes mellitus (NIDDM) accounts for a great majority of diabetics. NIDDM is associated with hyperlipoproteinemia, enhanced platelet aggregability, and a marked predisposition to development of atherosolerotic complications, especially coronary artery disease (4).

Changing the nature of fat consumed profoundly influences fatty acids available to the body. Thus, modifying the source of dietary fat may alter the composition of adipose tissue (5,6). Animal research has provided convincing evidence for enhanced deposition of linoleic acid in carcass fat with an increase in the proportion of this fatty acid in the diet (7).

The fatty acid composition of human adipose tissue does not appear to be constant. Despite quantitative differences within an individual there appears to be little difference in fat composition sampled from subcutaneous or deep body sites (8). Reasons for these differences might be attributed to de novo synthesis rates (9), although diet could also be an important factor. The role of genetics in determining adipose tissue composition has not been established. Differences reported between racial groups are complicated by dissimilar fat intakes. In this regard, individuals consuming diets that differ from their habitual intake develop adipose tissue fatty acid composition which is radically different from their kinsmen (10,11). However, there is little information available as to what extent fatty acid composition of adipose tissue is altered by diet or diabetes.

Experimental

Therefore, we analysed fatty acid composition of adipose tissue in Korean patients with non-insulin, dependent diabetes mellitus and non-diabetic subjects. Samples of subcutaneous and visceral adipose tissues for the analysis of fatty acid composition were obtained from 10 patients and 13 controls by surgical methods. Samples of subcuta-

neous adipose tissue were obtained from 6 patients and 5 controls by aspiration biopsy. The results in Group I showed no significant differences in the proportions of fatty acids except for the palmitic acid between subcutaneous and visceral adipose tissue. In non-diabetic adult population, the amount of linoleic acid, which reflects dietary intake of linoleic acid, is greater than that of Western population. In patients with NIDDM, content of palmitic acid, linoleic acid, and alpha-linolenic acid in subcutaneous adipose tissue were increased, and that of oleic acid were decreased compared with those of non-diabetic subjects.

Furthermore, increased contents of linoleic acid, and alpha-linolenic acid, and the decreased proportion of oleic acid in subcutaneous and visceral adipose tissue of NIDDM, which are related to hyperglycemia and to increased plasma glycosylated HbAlc levels, were observed in surgical biopsy. Aspiration biopsy showed NIDDM patients had decreased proportion of arachidonic acid, docosahexaenoic acid and oleic acid in subcutaneous adipose tissue. The ratios of docosahexaenoic acid to alpha-linolenic acid and arachidonic acid to linoleic acid were decreased in patients with non-obese NIDDM. These results suggest that the desaturation and elongation of fatty acids are impaired in patients with NIDDM.

Therefore, to obtain better understanding of the physiologic significance of altered fatty acid desaturation in diabetes mellitus, we have investigated fatty acid compositional changes and delta-6 desaturase activity of streptozotocin induced diabetic rats and confirmed these results.

A great deal of evidence has accumulated indicating that there is a defect in fatty acid desaturation in both experimental and human diabetes (12). Studies of diabetic animals *in vivo* showed that alterations of tissue fatty acid composition, consistent with depressed desaturase activity (13). Tissues from diabetic animals have reduced ability to desaturate stearic to oleic acid (delta-9 desaturation) and linloeic acid to arachidonic acid (delta-6 desaturation).

Microsomal delta-6 desaturase is a key enzyme in the metabolism of polyunsaturated fatty acids, the activity which is regulated by insulin. There have been many reports that omega-3 fatty acids, such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which are abundant in fish oils, produce beneficial effects on blood viscosity through changes in fatty acid composition of the RBC membrane lipids (14). To determine if changes in delta-6 desaturase activity in experimental diabetes correspond to the changes of fatty acid composition of microsome and RBC membrane and if dietary omega-3 fatty acid supplementation can produce any alterations in fatty acid metabolism, 30 Sprague-Dawley rats were studied for 6 weeks. The animals were divided into 5 groups with 6 rats in each group. The first group was the controls, the 2nd and 3rd groups were streptozotocin diabetic rats but insulin was injected in the 3rd groups. The 4th and 5th groups were supplemented with omega-3 fatty acid, among them diabetes was induced in the 5th group. The delta-6 desaturase activity was suppressed with diabetes induction ($p<0.05$) and was recovered with insulin treatment ($p<0.05$). The linoleic acid which is a substrate of the enzyme was increased ($p<0.05$ in microsome, $p<0.01$ in RBC) and the arachidonic acid, one of the products, was decreased ($p<0.01$, both) in both the microsomal fraction of liver and RBC membrane. The fatty acid composition changes were reversed ($p<0.01$, both) with insulin treatment in the microsomal lipids but not in the RBC membrane. The delta-6 desaturase activity was also suppressed ($p<0.05$)

in the rats supplemented with omega-3 fatty acids. The EPA was increased in both the micorsomal lipids ($p<0.01$) and RBC membrane ($p<0.01$), but there were no changes in the plasma glucose levels with dietary omega-3 fatty acids.

To summarise, the delta-6 desaturase activity was changed with insulin deficiency, replacement and the dietary omega-3 fatty acids and these changes can explain the fatty acid composition changes in microsomes. The dietary omega-3 fatty acids might improve the blood viscosity through the increase of EPA microsome lipids but did not prevent the induction of the diabetes by single toxic dose of STZ. These findings suggest that adequate insulin therapy is required for the correction of the polyunsaturated fatty acids metabolism as well as blood glucose control. Omega-3 fatty acids might be recommended for the prevention of chronic complications of diabetes in the insulin dependent diabetics.

These results suggest that fatty acid composition of visceral adipose tissue is comparable to abdominal subcutaneous alipose tissue in man, and secondly, desaturation and elongation of essential fatty acids are decreased in Korean patients with non-obese NIDDM. However, adipose tissue composition may not be helpful in speculating dietary fatty acid composition in patients with NIDDM.

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Lipid metabolism in non-insulin-dependent diabetes mellitus and treatment

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Introduction

Subjects with non-insulin-dependent diabetes mellitus (NIDDM) have an increased incidence of atherosclerotic vascular disease, which is partly explained by the concomitant occurrence of other cardiovascular risk factors including dyslipidemias. The present study was designed to see the prevalence of hyperlipidaemias in patients with NIDDM whose glycaemic control was improved by treatment for diabetes mellitus. In addition, long-term effects of pravastatin (1), an inhibitor of HMG CoA reductase, and bezafibrate (2), a fibric acid derivative, on serum concentrations of lipoproteins and apolipoproteins were examined in hyperlipidaemic, diabetic patients.

Patients and methods

Serum levels of triglyceride, cholesterol and HDL-holesterol were measured in 212 patients with NIDDM: 130 on sulfonylurea, 46 on insulin, and another 36 on diet therapy alone. They all had regular visits at the Division of Endocrinology and Metabolism, Department of Medicine, Hyogo Medical Centre for Adults at the time of the study. Their age and duration of diabetes averaged 60.4 ± 0.6 (SE) years and 9.7 ± 0.5 years, respectively. Mean fasting plasma glucose and haemoglobin Alc were 143 ± 3 mg/dl and 8.4 ± 0.1%, respectively.

Pravastatin (5-15 mg twice daily) was given to hypercholesterolaemic patients for 12 months, and bezafibrate (200 mg twice daily) was administered in hypertriglyceridemic patients for 6 months. Lipoproteins were isolated ultracentrifugally by the method of Havel *et al.* (3) in samples taken before and after treatment with the two drugs. These experiments were done in a separate group of hyperlipaemic patients.

Blood was drawn after overnight fasting and lipid levels were measured by the respective enzymatic methods. Data are expressed as the mean ± SE. Statistical analysis was done by paired Student's t test.

Results and discussion

Eighty-nine (42%) out of 212 patients were receiving hypolipidaemic drugs (Table 1). Type II and type IV hyperlipidaemias had been found in 67 and 22 patients, respectively, at the start of the drug administration. Diag-

nosis of hyperlipidaemias was done at the time when glycaemic control was improved under treatment of diabetes mellitus. Although their serum levels of lipid and apolipoproteins were remarkably improved during treatment with probucol, inhibitors of HMG CoA reductase, or fibrates alone, or in combination, their ratio of total to HDL-cholesterol and the ratio of apo B to AI were greater than normolipidemic NIDDM. These two ratios are well-known to be strongly associated with coronary artery disease (4,5). Therefore, they are still at a high risk for atherosclerotic vascular disease even when their glycaemic (haemoglobin Alc = 8.5 ± 0.2%) and lipid controls were improved.

Pravastatin (10-30 mg daily) produced a 20%-decrease not only in total cholesterol and apo B but also in serum triglyceride levels in NIDDM (Table 2). These changes were associated with a decrease in the ratio of LDL to HDL-cholesterol and the ratio of apo B to AI, and continued throughout a 12-month treatment period. Bezafibrate (400 mg daily) produced not only a decrease in serum cholesterol, triglyceride, and apo B but an increase in HDL-cholesterol and apo AI. Although LDL/HDL-cholesterol did not change, the ratio of apo B to AI were reduced by 30%. Both pravastatin and bezafibrate produced no serious side effects during the observation period. Thus, these two drugs appear to be useful in reducing

TABLE 1

Serum concentrations (mg/dl) of lipids and apolipoproteins in 212 patients with NIDDM: 123 normolipidemic patients and 89 hyperlipidemic patients before and after treatment with various hypolipidemic drugs

	Patients with hyperlipidemia (n=89)		Patients without hyperlipidemia (n=123)
	Before treatment	After treatment	
Total cholesterol	256±6	202±4**	179±3
Triglycerides	238±19	173±13**	113±6
HDL-cholesterol	46.2±2.0	37.5±1.3*	42.6±1.0
Apolipoprotein AI	129±5	120±4	124±2
Apolipoprotein B	136±5	107±3**	86±2
Total/HDL-cholesterol	6.05±0.21	5.92±0.23	4.45±0.11
Apolipoprotein B/AI	1.10±0.04	0.94±0.04	0.71±0.02

Mean±SE

Asterisk indicates significant difference vs. normolipidemic patients; *p<0.01, **p<0.001

cardiovascular risk through the corrections of dyslipidemias found in the present study.

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TABLE 2

Effects of pravastatin (10-30 mg daily for 12 months) and bezafibrate (400 mg daily for 6 months) on serum levels (mg/dl) of lipids and apolipoproteins in hyperlipidemic patients with NIDDM

	Pravastatin		Bezafibrate	
	before	12 months	before	6 months
Total cholestrol	273 ± 14	220 ± 7^{c}	246 ± 8	199 ± 12^{b}
Triglyceride	280 ± 57	211 ± 47^{b}	277 ± 42	166 ± 26^{a}
HDL - cholestrol	48.8 ± 3.6	48.9 ± 2.3	34.7 ± 1.8	38.1 ± 1.6^{a}
Apolipoprotein AI	162 ± 10	179 ± 10	130 ± 7	144 ± 7^{b}
Apolipoprotein B	169 ± 11	136 ± 6^{b}	153 ± 12	122 ± 9^{a}
LDL/HDL-cholestrol	3.67 ± 0.40	2.72 ± 0.19^{c}	4.03 ± 0.54	3.09 ± 0.27
Apolipoprotein B/AI	1.10 ± 0.12	0.78 ± 0.04^{b}	1.19 ± 0.10	0.84 ± 0.05^{b}

Mean ± SE in 12 and 8 patients in pravastatin- and bezafibrate-treated groups, respectively

Significant differences between before and after respective treatment: a = $p<0.05$, b = $p<0.01$, c = $p<0.001$

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Effect of nature of starch on *in vitro* starch digestibility and *in vivo* blood glucose and insulin responses

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Introduction

Different glycaemic responses to rice has been attributed to many factors (1-2) including amylose content. Amylose because of its linear structure do not swell or gelatinise as readily upon cooking and therefore are digested slower and also result in lower blood glucose and insulin responses. However, it has been shown that rice with similar chemical composition but varying amylose content has shown conflicting results. Discrepancies in glycemic responses to rice maybe due to differences in the varieties and cooking procedures. However, they also indicate that amylose content alone may not be a good predictor of starch digestion rate and blood and insulin responses to rice; the physico-chemical properties of the starch may also exert an influence. Since rice is a staple food in many parts of the world, it is important to study those factors which may help predict its glycemic responses. Thus the objective of this study was to determine the rate of *in vitro* starch digestion and the *in vivo* blood glucose and insulin response to three varieties of long grain, non-waxy rice (IR62, IR36 and IR42), all with a comparable high amylose content and to determine whether the differences are related to their physico-chemical properties.

Materials and methods

In vitro digestibility and *in vivo* test were done using freshly cooked rice samples. In the *in vivo* test, finger prick samples were collected with autolet lancets and analysed for glucose by the glucose oxidase method and insulin by radioimmunoassay. Breath samples were collected and analysed for hydrogen.

Chemical analyses for proximate composition and dietary fiber were made. Physico-chemical properties such as alkali spreading, gel consistency, photometric final gelatinisation temperature, minimum cooking time, amylograph viscosity and volume expansion were determined. Light microscopy was also carried out on the samples.

Statistical analysis

The results are presented as means ± standard error of the mean and the significance of the difference was calculated by one way analysis of variance followed by Student's t-test for paired (*in vivo* study) and unpaired (*in vitro* study) data. *In vitro* and *in vivo* results were correlated with the physico-chemical properties of the rice samples using linear regression.

Results

In vitro digestibility test

The *in vitro* rate of sugar release during the three- hour digestion period was faster in IR42 than the other two

rice varieties (Figure 1, Table 1). However, significance ($p<0.05$) was observed only at the third hour when the sugar released in IR36 and IR62 were 15-17% lower than in IR42.

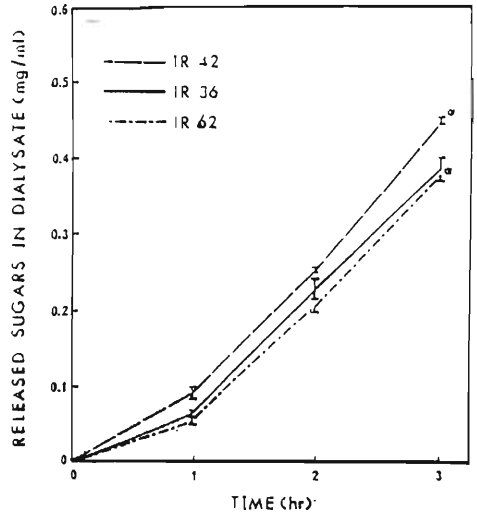

FIG. 1 The in-vitro rate of sugar release during the 3-hour digestion period.

In vivo tests

Blood glucose responses to the different rice samples showed significantly higher values ($p<0.05$) for IR42 than the other two rice varieties at 30 and 60 min but not at the other periods (Figure 2). The incremental blood glucose area and the glycaemic index (GI) of IR42 were also higher in IR42, in general agreement with the *in vitro* data. However, no significant differences were seen in plasma insulin, insulin area and hydrogen produced among the rice samples.

Chemical composition, physico-chemical and microscopic properties

The three varieties had very similar chemical composition (Table 2) but differed significantly in physico-chemical properties (Table 3). Compared to IR62 and IR36, IR42 showed the highest values for alkali spreading amylo-

TABLE 1

In vitro starch digestion and *in vivo* responses to rice varieties cooked under the same conditions*

	Rice Varieties		
	IR 62	IR 36	IR 42
In vitro study			
Total sugars released in 3 h (mg/ml)	0.38±0.01a	0.39±0.02a	0.46±0.01b
In vivo study			
Glycemic area, mmol/L. min	55.22±6.46a	64.70±3.88ab	81.02 ± 7.62b
Glycemic Index	61±9a	72±10ab	91±12b
Insulin area, pmol/L. min	9,240±1340	7,131±1633	9,415±1390
Total H_2 production, ppm	22.2±7.2	19.0±12.5	17.9±6.0
Carbohydrate unabsorbed g	2.58±1.29	1.17±0.85	1.08±0.86
Carbohydrate unabsorbed %	5.16±2.58	2.34±1.70	2.18±1.72

* Means in the same row followed by different letters are significantly different ($p<0.05$)

graph peak, setback, consistency and percent volume expansion and the lowest values for minimum cooking time, gel consistency and final starch gelatinisation temperature.

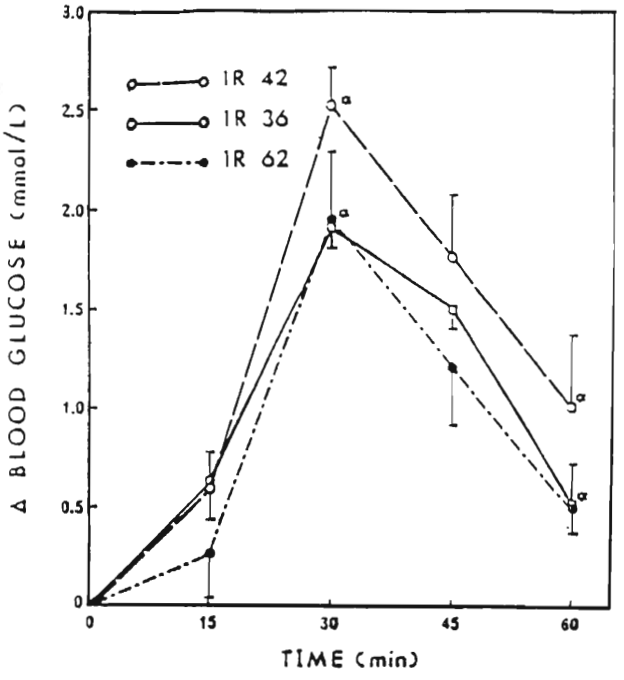

FIG. 2

Blood glucose responses to the different rice samples.

TABLE 2

Chemical composition of different high amylose rice varieties (% wet basis)

	Rice Varieties		
	IR 62	IR 36	IR 42
Moisture	12.41	11.24	11.24
Ash	0.44	0.65	0.86
Protein	9.28	8.11	8.30
Total Lipids	1.33	1.15	1.51
Starch	0.92	0.75	0.87
Non-starch	0.41	0.40	0.64
Total Carbohydrates	76.54	78.85	78.09
Dietary Fibre	1.05	2.00	1.73
Available Carbohydrate	75.49	76.85	76.36
Amylose*	27.00	26.70	26.70

* Dry basis

The *in vitro* digestibility data, glycaemic area and GI had negative relationships. i.e. values, with the gel consistency, final starch gelatinisation temperature and minimum cooking time, but positive relationships with alkali spreading value, amylograph viscosity (peak, setback, and consistency), volume expansion and weight increase after cooking (Table 4). The cooked rice sample differed in the degree of hydration as indicated by the size and number of water spaces between the starch granules (Figure 3).

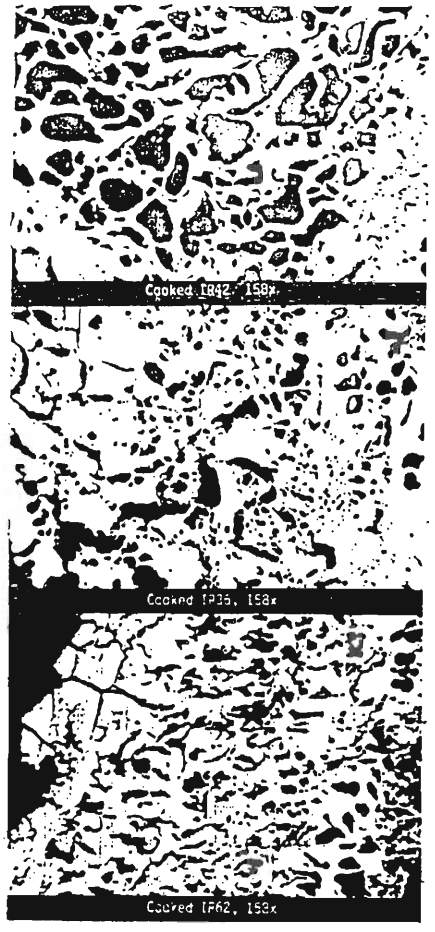

FIG. 3 Size and number of water spaces between the starch granules in the cooked rice samples.

Discussion

The investigation showed that differences can exist in the *in vitro* rate of starch digestion and blood glucose response to rice varieties with similar amylose content and cooked under the same condition. These differences may be due to variability in the physicochemical properties of the rice samples.

The higher alkali spreading value of IR42 rice indicates its easier gelatinisation at a lower temperature. The higher amylograph peak, setback and consistency values of IR42 compared with the other two samples also indicate its greater degree of hydration, when heated under the same conditions. This view was supported by the microscopic data and the higher volume expansion and increase in weight after cooking of IR42 compared to IR36 and IR62 rice varieties.

There was a high negative correlation between minimum cooking time and the *in vitro*, as well as *in vivo* results (Table 3) although only the relationship with *in vitro* digestibility reach statistical significance. This suggests that IR42, with the shortest minimum cooking time requirement (14 min) was digested the fastest because it was the most gelatinised at the cooking time (22 min) used for all samples.

Amylograph consistency was positively correlated with digestibility values indicating that samples which are easy to hydrate such as IR42 (hard gel), digest faster than those harder to hydrate, such as IR36 (medium gel) and IR62 (soft gel). This study has shown that, even in rice varieties with the same amylose content, amylograph viscosities can be predictors of the rate of starch digestion.

Starchy foods which are digested slowly and result in low blood glucose have been suggested to be more beneficial to health and in the management of diabetes and hyperlipidemia (38-41). Hence, the identification for food such

TABLE 3

Physico-chemical properties of different high amylose rice varieties

	Rice Varieties[#]			$r^{@}$		
	IR 62	IR 36	IR 42	GI	GR	*In vitro*
Alkali spreading value	5.0±0a	4.1±0.1a	7.0±0b	0.89	0.89	0.91
Gel consistency, mm	65.0±1.44a	34.0±0.4b	28.0±0c	-0.87	-0.87	-0.83
Final starch gelatinisation temp. C	72.0±0a	73.5±0.4a	65.0±1.4b	-0.86	-0.86	-0.96
Minimum cooking time, min	20±0a	19±0a	14±0b	-0.98	-0.98	-0.999**
Amylograph viscosity						
Brabender units						
Peak	655±7a	863±12b	870±35b	0.81	0.81	0.63
Setback	88±22a	13±12b	425±25c	0.85	0.85	0.96
Consistency	268±12a	305±4a	630±42b	0.96	0.96	0.999**
Volume expansion, %	200±0a	205±0b	220±0c	0.99*	0.99*	0.992*
Wt increase after cooking, %	184±2.0a	179±2.1a	190±1.6a	0.66	0.66	0.83

[#] Means for rice varieties followed by different letters are significantly different ($p<0.05$).

[@] Correlation coefficient between the physicochemical properties and glycaemic index.

(GI) glycaemic area (GR) or *in vitro* starch digestibility (*in vitro*)

* Significant at $p<0.05$

** Significant at $p<0.01$

TABLE 4

In vitro starch digestion and *in vivo* response to rice varieties cooked at their minimum cooking time

	Rice Varieties		
	IR 62	IR 36	IR 42
In vitro study			
Total sugars released in 3 h. mg/ml	0.61±0.24	0.56±0.18	0.52±0.00
In vivo study			
Glycaemic area, mmol/L. min	110.80±11.99	118.02±11.19	110.39±10.44
Glycaemic Index	75±4	78±5	81±5
Total H production, ppm	51.45±11.56	48.27±8.37	59±23.14
Carbohydrate unabsorbed, g	4.36±1.39	3.59±0.85	5.26±2.71
Carbohydrate unabsorbed, %	5.40±1.70	4.69±1.25	6.55±3.23

No significant difference between rice varieties ($p>0.05$)

as rice with low glycaemic indices such as IR36 and IR62 should be of continuing research interest.

In conclusion, rice varieties with similar amylose contents can differ in physico-chemical (gelatinisation) properties and this, in turn, can influence the starch digestion rate and blood glucose. For physiologically lower responses, good predictors include high gelatinisation temperature and minimum cooking time, and lower amylograph consistency and volume expansion upon cooking.

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Glucose intolerance, hyperlipidaemia, obesity and dietary patterns of Malaysian rural communities: are we heading for disaster ?

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Abstract

It has been implicated that excessive dietary consumption of refined carbohydrates and saturated fatty acids are partly responsible for obesity and the development of diseases related to diabetes mellitus and arteriosclerosis. Most Asians are known to be having a much lower dietary animal fat content compared to their Western counterparts, yet we are beginning to see a shift for the worse. The change is seen both in their dietary patterns as well as in the national mortality statistics.

In two recent surveys of diseases related to glucose intolerance involving a Malaysian rural agricultural redevelopment scheme and an oil palm plantation, predominantly inhabited by Malays and Indians, a surprised overall prevalence of about 12.8% glucose intolerance, about 30% of hypercholesterolaemia and a diet high in refined sugars were found in the former and an alarming 20% glucose intolerance in the later. There were striking differences between the various ethnic groups, with the Indians significantly more prone than the Malays. Relationships between the glucose intolerance, lipid profiles, indices for obesity and dietary patterns may be important factors influencing the rapid rise in the prevalence of diabetes and arteriosclerosis related conditions. The relatively high Epidemicity Index in the rural areas may indicate strong tendency towards full-blown diabetes in the near future.

The proportion of saturated fatty acids in the diet is considered a very important factor in the development of hypercholesterolaemia. Yet, in a community which do not traditionally indulge in excess animal fat intake, the high total calorie consumption (mainly carbohydrate derived), may be part of the reasons for the high prevalence of hypercholesterolaemia, more so than dietary fat. Immediate interventional programmes must be instituted to change food habits of the community in order to stop the deterioration of the mortality statistics.

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Food and Nutrition Policies in National Development

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Abstract

Food policy can be examined from its two important aspects: Food policy that significantly contributes in the socio-economic development of a country by exporting various food commodities; and food policy that is primarily aimed at food security and improving nutrition of the people by making the right kind of food available in sufficient quantities and thus improving nutritional status and significantly enhancing the productivity of people which is much needed for national development. In the national development plan documents of the developing countries of the Asia-Pacific region food and nutrition components as policy recommendations are stated under a number of sectors such as agriculture, health, education, trade and industry. The FAO Nutrition has discussed these components as they exist in some countries of the region. It was felt that the present food and nutrition policy components were inadequate in general and lacked specific details; the financial allocations for the ensuing programmes were meager and coordination in implementation was precious little. It was proposed that for the best use of limited resources in the developing countries, food and nutrition policy should be recognised as a sector in its own right in national development plans. For this purpose it was considered necessary to establish statutory food and nutrition policies and programmes and for negotiating their coordinated implementation in various sectors. Implications of such bodies will be presented.

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Food and nutrition policy development in the Western Pacific Region of WHO

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Introduction

All countries, even if by default, have policies and legislation in place that impinge upon the nutritional status of their populations. These may simply be import policies that result in imported foods being cheaper in urban areas than more traditional foods; agricultural policies that favour cash crops or are designed to assist a particular group; or, most commonly, policies that discriminate in favour of urban voters (1).

In this paper we briefly review the development of national food and nutrition policy, the constraints and difficulties, facilitating factors, the current situation in the Region and future developments.

The development of food and nutrition policy

A food and nutrition policy has been defined as: a coherent set of principles, objectives, priorities, and decisions adopted by the State and applied by its institutions as an integral part of the national development plan in order to provide all the population, within a specified time, with the food and other social, cultural, and economic conditions essential to satisfactory nutrition and dietary well-being (2).

Consequently, there are different paths towards the ideal defined above, e.g. one model that has been proposed is seen in Figure 1. The outcomes to the above could include dietary guidelines, changes in agricultural policy, nutrition education strategies, or a more comprehensive food and nutrition policy.

Different national requirements may mean that different stages of the scheme shown are more appropriate at a particular time or phase of development. For example it may be more appropriate politically to endorse dieteray guidelines on a voluntary basis rather than starting from the outset with legislative change. Although the latter is generally more effective and will almost certainly be required in some form eventually, legislation will also meet with considerable opposition from entrenched commercial and sometimes agricultural interests, as e.g. in the United States of America and Norway (3).

Consequently the initial food and nutrition policy may not be comprehensive, it may be intended to attack outstanding problems that are perceived to be priorities (2).

It is therefore impossible to describe a single intersectoral planning system suitable for all countries.

BASELINE DATA OR NUTRITIONAL ASSESSMENT

- collection and collation of data
- identification of basic problems

FORMULATION OF POLICY

- nutritional implications of existing policies
- objectives and goals
- alignment of projections of food supply and demand
- proposals
- formulation of policy

SURVEILLANCE &/OR EVALUATION & RE-FORMULATION

- continuing surveillance, evaluation, amplification & adjustment

INTEGRATION WITH NATIONAL PLAN & PRIORITIES

IMPLEMENTATION & MONITORING

Figure 1. Steps in the development of a national food and nutrition policy [adapted from Bengoa & Rueda-Williamson (2)].

In the definition given earlier, the end target is defined as all the population. However within this group, and with genereally limited resources, there will be groups at greater risk or considered of higher priority.

Conventionally, many countries and all the international agencies and nongovernmental agencies have considered infants and young children, and more recently, women as the prime target. Subsequently, the more affluent countries have identified adults as at risk of nutrition-related noncommunicable diseases and even more recently, the elderly. These latter two categories may be achieving increased recognition, not only because the policy makers in all countries can be found in one or both of these categories but also because the emergence of these categories as at-risk groups has increased with increasing longevity and relative affluence.

Constraints

One of the major constraints has already been identified i.e. that often the groups most at risk are those with the least capacity to influence policy.

Another related constraint is the perceived lack of priority in most government concerning nutrition. This is despite the fact that malnutrition has such a major role in the development, and outcome, of the childhood infectious diseases, and in the noncommunicable disease. The recent attempts to quantify the enhanced risk to mortality of vitamin A deficiency has helped to focus the interest of policy makers in this area.

Health Ministries are also often of relatively low priority. This presumably reflects the emphasis on curative medicine for much of century and the fact that, with limited national resources, investments in health are seen as not immediately productive, never satisfied and increasing.

A further consideration is that the major factors involved in nutrition are not only from health. Agriculture is the

most obvious but the urban/rural dirft, economic policies, education policies and industrial, commercial and agricultural lobbies can all be influences. The education of women, shown to have a measurable positive impact on health and nutrition (4) is not infrequently perceived as a relatively low priority in some cultural contexts. This multisectorality of nutrition policy has proven to be a major constraint that has caused some earlier policy development attempts to fail (5). It is no longer generally considered that 'because malnutrition has multiple causes, integrated interventions are obligatory' (4).

A related problem is the relative hierarchical position of those sent to sit on such intersectoral nutrition committees. The level of representation will often be low, the perceived rewards little and the attendance lessens, falters and finally fails.

Not infrequently, the different interests involved will have conflicting priorities. Nutritionists and agriculturalists have often had different priorities and desired outcomes e.g. the production of saturated fat products, cash cropping etc (1). As their products are generally producing revenue, the economists have usually supported the agricultural lobby. The relationship between nutrition and productivity is currently not well enough understood to be a strong positive factors.

Where consumers have dictated change e.g. low fat products, farmers, despite being seen as traditionally conservative, have shown themselves to be remarkably flexible. The food industry and nutritionists have also not infrequently been in conflict when it comes to national policy. The food industry, while claiming great difficulty and expense in responding to nutritionally-derived goals, show considerable agility in responding to consumer demands.

Facilitating factors

Much information needed for the development of national food and nutrition policy will already be available although probably under-utilized.

As has been alluded to, the target groups of nutrition policy are often emotionally positive target groups e.g. women and children. Earlier nutrition policy was often stimulated by nationally important issues, e.g. food policy in the United Kingdom during the first World War.

There has been a dramatic change in many countries over the last thirty or so years in the public interest in health and nutrition. While this is still positive there is a possibility of frustration as more and more foods come under suspicion of one sort or another or where advice conflicts or changes too often.

The increase in mortality caused by the noncommunicable diseases is now widely recognized. Of the 29 countries in the Region that have such data available, almost 90 percent have, their five major causes of mortality, 3 caused by the noncommunicable diseases (6).

Another faciltating factor is the body of experience and expertise that has been built-up over the last fifty years. Increasingly we have examples of what has worked and what has not.

Current situation in the Western Pacific Region

Using the broad categories of the figure above, we asked of countries what steps that had chosen to take, starting from the availability of national dietary and food intake data. A surprisingly large number had this. Those that did not usually had apparent consumption data.

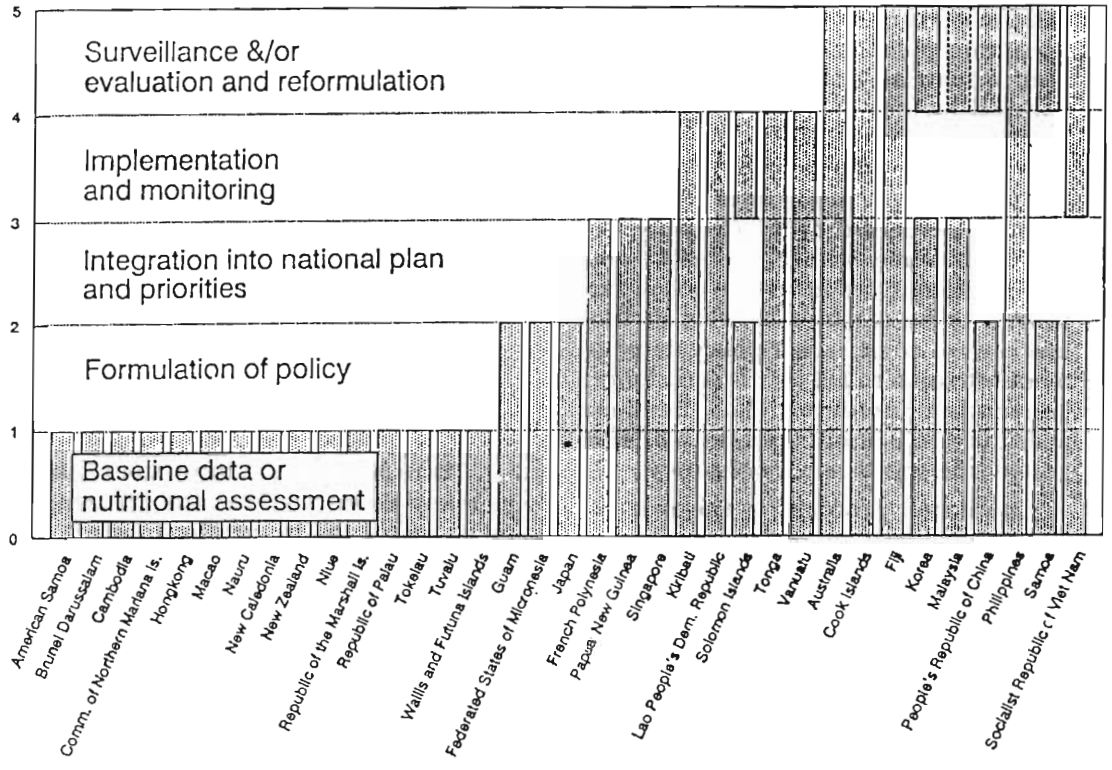

FIG. 2 Current status of food and nutrition policy in the Western Pacific Region of WHO July 1991.

As can be seen from Figure 2, just over a third (34.3%) of member countries or areas have national food and nutrition policies of varying types in place. National nutrition data are available from 31 of the 35 countries and dietary goals/guidelines and monitoring mechanisms are available in 40% and 28% of countries respectively (7).

Future developments

In collaboration with member countries, WHO has the aim that all countries in the Region should have a national food and nutrition policy in place. To this end, countries will be encouraged to have an identifiable unit in government dealing with food and nutrition, to collect national data, develop a policy and institute some appropriate monitoring and/or surveillance system.

As in other public health policy it is probably best to win strong public support before tackling entrenched interests. This will require extensive education of the public, health professionals and policy makers. It is also generally clear that educational campaigns are only effective when backed by policy measures favouring similar outcomes. Segments of the public are sometimes well ahead of the policy makers, having decided their own priorities, e.g. in the demand for high fibre products and for foods without the addition of unnecessary additives.

Conclusion

The answers will depend on all the above. However in the successful examples around, some common factors appear likely to be important.

Whereas governments will probably need to set some priorities and put such policies on the national agenda, success is almost guaranteed if it is following a public consumption trend or perception. In many cases governments will need legislation to facilitate changes to ensure economic policy, taxes etc., are not inhibiting positive changes. As always, the more that all participants can see the changes are to their advantage, the better. More specific strategies such as price subsidies, government intervention in the market, nutrition education and so on need to be tailored to each country's situation and needs, and hence is beyond the scope of this overview. However, as has been seen there are some very encouraging activities occurring in National Food and Nutrition policy in the Region. These should be continued and strengthened, remembering always to consider equity and the effects of policies on vulnerable groups.

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Food and nutrition policies for national development: case study of Pakistan

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Development of human resources leads to higher levels of human capabilites which in turn enhance the well being of the community and contribute to the national-development. This is achieved through improved nutrition, better health care, population planning, mass education and higher skills.

Malnutrition is both one of the consequences of social injustice and one of the factors contributing to its maintenance. It bears hardest on small children. Contributing to the masssive death toll among the young ones, and together with other adverse environmental factors, it interferes with growth and development of the survivors. It reduces their capacity to learn during childhood and earn during adult-hood. The inevitable result is a downward spiral in which poor malnourished parents produce malnourished children who in line become poor and malnourished parents.

The costs of malnutrition to an economy of a country have never been calculated, partly because of the numerous ways in which the problem interacts with other variables. It is no exaggeration to say that their future economic advencement is, to a large extent dependant upon solving this problem. Therefore improving nutrition of the people should be seen as an objective of development planning in its own right and the whole range of sectoral policies and programmes need to be drawn and harmonized. Without this multi-sectoral approach, the objectives carried out directly with the population to promote better nutrition and cure malnutrition will not achieve desirable results.

In the past, economic development has been considered synonymous with increases in output and GNP. Pre-occupation with physical capital has been paramount while human capital has been ignored. Yet the historical experience of many countries has been that capital formation has not meant a better life for all. Countries which started out with similar natural resource endowments and similar inverstment shares have achieved different degrees of economic development depending on the emphasis they placed on human development.

Human beings are both the means and the end of economic development. It is now recognized that the extent of poverty in a country is closely associated with its per capita income. Malnourished and unskilled people living in hunger and poverty make little contribution to economic progress and national output. On the other hand, a healthy, educated and active population contributes more to the prosperity of a nation not only because it is more efficient and productive but because human beings are the source of new ideas, innovations and opportunities.

Human development is more than just income equality or poverty alleviation. While both help in increasing the income share of the poor, it is clear that adequate resources must also be devoted to increasing the level of nutrition and opportunities for education, and providing adequate health coverage, clean weter and sewerage facilities and opportunities for employment.

Human resource development aims at building the human capital stock of the nation. It seeks to achieve this through better opportunities for education, health, nutrition and income.

Economists tend to view nutrition as one of the unproductive personal and social expenditure that competes with investment. Improvement in nutrition is thus seen as hinderance to economic development. The case can be made as nutrition, being an investment in is own right that malnutrition during pregnancy, infancy and early childhood may produce consequences for physical and mental development. Large expenditure in health and education may be necessary later to partly reverse these effects, where as proper nutrition during growth contributes to productivity.

Any lasting changes in the nutritional status of population must be affected by a combination of non-nutritional and nutritional measures. For this, a systematic approach is needed on the nutritional and income distributional implications of food production and supply policies, food distribution policy and public health policy.Limitations inherent in the economic system of the country also constitute serious financial obstacle to the solution of food and nutrition problems.

Before any plan of action is formulated, consideration must be given to the feasibility of its implementation. The executing agencies often lack the resources, or the scale of action proposed exceeds the financial capacity of the country.

Universally, it is held that the prime goal of a national development plan should create conditions which enables every individual to have an access to food for meeting nutritional requirement and to permit him to achieve his inherited physical and mental potential.

Thus many measures have an important role to play, in overall nutritional improvement, including measures to influence to the composition and adequacy of the national food supply, directed nutrition intervention, health measure and nutrition education. They cannot substitute for strategies and measures which increase the real income of the poor.

In order to achieve that, nutritional considerations have to accomodate in different sectors like health, agriculture, education and rural development, basic economic framework of a country i.e. fiscal policies, wage structure.

It is the Ministry of Planning which not only determins the administrative budget and is responsible for articulation of overall national development strategy on behalf of political authority but it is also in a position to require various ministries to join in dialogue and provide information on nutritional impact and cost of their activities.

Food and nutrition policy planning for national development in Pakistan

Food and Nutrition Policy Planning for National Development in Pakistan, is a relatively new concept that has been introduced in the form of consumption planning and Nutrition Planning.

Consumption planning

The consumption planning was incepted in the national development

planning process since 1972. The aim of consumption planning in Pakistan has been to ensure the availability of essential consumption items at reasonable price. It is imperative to ensure adequate supplies of such goods which are in demand. Demand, however, is not static and the level of demand is subject to growth in income and population. The objectives of consumption planning, therefore, is to formulate policies so that consumption goods at higher levels of demand are available at reasonable prices. Consumption planning has concentrated on the provision of essential items of mass consumption and the policy has been to maintain adequate availability of essential consumer goods, particularly increase availability of goods which are consumed by the low income groups like food grains, edible oils and cloth.

Ideally all consumption goods should have been included in the planning exercise but on account of non-availability and inadequacy of data, the initial exercise in the field of consumption planning covered only essential food items and cloth.

The consumption plan is primarily based upon the commodities which would meet the basic minimum needs of the common man to maintain the quality of life within acceptable standards. The present Seventh Plan (1988-93) has been formulated keeping in view the demand generated at different income levels and the daily nutritional requirement, which would ensure healthy living. The consumption plan also aims to supplying the basic commodities adequately both qualitatively and quantitatively at a cost which is within the reach of consumers.

Nutrition planning

Nutrition planning was institutionalized late in 1974 with the establishment in the Planning Division of a Nutrition Cell, demonstrating the Government's conviction that malnutrition is a significant development problem and signalling its determination to find solutions systematically in the economic planning process. A Nutrition Syndicate composed of representatives of the various nutrition-related disciplines was established to integrate nutrition planning into the mainstream of planning. Nutrition Section of the Planning division is the Secretariat of the body. The Nutrition Syndicate meets periodically to review nutrition issues and activities and formulates action plans in the field of nutrition. The work of gathering data on the nation's nutrition problems and potential improvement programmes, analysing the findings, and developing policy and project plans is being carried out under the Syndicate's guidance. At the provincial level identical bodies namely Provincial Nutrition Boards have been constituted, which have inter-departmental representatives, and Provincial Nutrition Units work as their Secretariat.

Nutrition planning efforts, so far, have been directed towards the inclusion of specific programmes of acute nature in the Annual, Five Yaer and Perspective Plans since 1975-76 as a supplement to consumption planning. As far as consumption planning is concerned, the demand for various items is projected for the target year on the basis of the expected rate of growth of income and population. Besides, assumed income elasticities of demand and the estimated population and growth are applied to obtain the demand for the various commodities. These projections are linked with nutritional requirements so that in the first instance malnutrition and undernutriton are gradually eliminated and essential requirements in terms of calories, proteins, vitamins etc., are met.

Although severe malnutriton is uncommon and the availability of food items generally satisfactory, still nutritional deficiencies exist. The gap between the total food availability and food requirements is not very large but it is aggravated by inequitable distribution in various segments of the society both inter and intrafamily due to poor distribution infrastructure and lack of nutrition education. However, the problem of malnutrition is not dramatically visible as in many Asian, African and South American countries.

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Nutritional surveillance for disaster preparedness and prevention of nutritional blindness: the effectiveness of the vitamin A capsule distribution in disaster-prone areas in Bangladesh

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Introduction

Vitamin A deficiency is a systemic disease with the most prominent manifestations occuring in the eyes. However, recent studies in Indonesia, Tanzania, Thailand, Australia, and India show that even mild vitamin A deficiency leads to higher rates (4-12 times) of child morbidity and mortality (1-4). Furthermore, intervention with a single high dose of vitamin A (200,000 IU) can reduce the mortality rate in preschool children by 30-50% (5, 6).

In 1987, Bangladesh experienced one of the worst and longest floods in its history. The flood covered 36 percent of the country and caused widespread damage which had been only partially repaired by mid 1988. However, in 1988, there was an even more severe flood that affected 61 districts out of 64 covering 84 percent of the national territory and directly affected 45 million people. The general health situation in Bangladesh is very poor, morbidity and mortality, especially among young children and mothers are extremely high (7, 8). The frequent floods, droughts, cyclones, etc. which affect Bangladesh invariably cause a deterioration in the already poor health status of its people, particularly women and young children, through decreased access to food due to crop and employment losses (9-11). The nutritional status of young children is a very sensitive indicator of sudden changes in food supply and health conditions. It is also a forerunner of changes in child mortality (12). The monitoring of children's nutritional status in disaster-prone communities is thus a vital tool to assess, plan and coordinate the response to ongoing and unforeseen crises related to floods and other natural disaster (13). Cyclic floods in the past, and particularly the one which occurred in August 1988, and other natural disasters, underline the need for strengthening the capacity to collect timely and reliable nutrition data and early warning information on which to base appropriate responses to acute food shortages. After the floods of 1988, there was no such information on health and nutritional status for effective allocation of relief programs.

Objectives

The overall goal of the project is to create an interactive mechanism for planning, monitoring and evaluation of multisectoral development and relief activities to increase their effectiveness.

Methodology

The Nutrition Surveillance Program is a collaborative effort by NGOs, the Institute of Public Health and Nutrition (IPHN) and UNICEF to establish a sentinel surveillance system. The project is financially supported by USAID and coordinated by Helen Keller International (HKI). Bimonthly each of the participating NGOs collects data from a random sample of 800-1000 children aged 6-59 months from different disaster-prone communities in rural and urban areas. Data are collected on nutritional and health status of children aged 6-59 months, socioeconomic status of the household, and distress factor (14). In this section we want to discuss our epidermiologic findings with major reference to the June 1990 data, because vitamin A capsules had been distributed in April and the effect of the capsule on nightblindness is highest within the first two months after the distribution. At the same time, the mother's memory is less biased.

The following aspects are considered important in attemping to distinguish causal from non-causal associations: strength consistency, temporality, biologic gradient, plausibility and coherence (15). We have investigated the association between vitamin A capsule (VAC) coverage and nightblindness in two ways:

a. For each round (April, June, August, October) we carried out a regression analysis between the VAC coverage and the prevalence of nightblindness per area;

b. For each round we conducted a case-control study on nightblindness. In order to adjust for confounding factors, we used logistic regression analyses.

Results and Discussion

In October the differences in VAC coverage explained 51% of the variance in nightblindness. The case-control studies showed that significantly more children with nightblindness did not receive the vitamin A capsule than children without nightblindness. In addition, children with nightblindness were older and has a higher prevalence of diarrhea than the controls. Education level of the mother shows a negative association with nightblindness. However, this association is not significant. No differences in other socioeconomic conditions have been observed. The logistic regression analyses demonstrated that VAC coverage, age, and diarrhea remained significant. By a comparative analysis of the June data we found that the VAC coverage was lower among the children whose mothers were not educated (52%) than among the children whose mothers were educated (59%; $p<0.001$). In August we found 57% and 63% respectively ($p<0.005$). One possible explanation may be that educated mothers are more assertive than non-educated mothers and demand vitamin A capsules. At the same time, however, it may also be that health workers have better access to educated mothers than to non-educated mothers (16).

For each round we conducted the same analyses. The strength and the significance of the association between VAC coverage and the point prevalence of nightblindness were the same for each round. We found 59%, 25%, 48%, 51% and 40% of explained variance in April, June, August, October, and all four months together respectively.

Temporality refers to the necessity that the cause precedes the effect in time. VAC coverage is defined as the percentage of children who have received a vitamin A capsule during the previous six months. Nightblindness is defined as the point prevalence of nightblindness (17%). Only children with nightblindness on the examination day are defined as cases.

Biologic gradient refers to the presence of a dose-response curve. The study areas of the NSP project varied considerably by VAC coverage. In areas with a high coverage (80-100%) almost no nightblindness was found. The prevalence of nightblindness was high in areas where the coverage rate was between 10-40%. When the coverage rate was between 40-80% the prevalence of nightblindness was dependent on differences in the efficacy to targeting. Further analyses of the June data showed that in the central Ganges-Padma basin near Madaripur and Gopalganj the coverage rate in the NGO project area was 62% while in the non-NGO area it was only 45%. At the same time we observed a higher prevalence of nightblindness in the NGO project area (1.7%) than in the non-NGO area (1.0%). Further analysis of who received the capsule by area shows no differences in the socioeconomic and nutritional status between the VAC recipients and controls in the non-NGO areas, whereas in the NGO area the richer groups in particular received the capsule. In the rural area the GOB is responsible for delivering the vitamin A capsules. We do not have information on VAC distribution by NGOs.

Plausibility refers to the biologic plausibility of the hypothesis and coherence implies that a cause and effect interpretation for an association do not conflict with what is known of the natural history and biology of the disease. Previous studies on the impact of either universal, or targeted VAC delivery systems showed lower prevalences of xerophthalmia, improved iron status and growth, and reduced mortality rates (6, 18-20). A study in the Philippines showed that a 70% reduction in mild xerophthalmia could directly be attributable to universal vitamin A capsule delivery (21), and a recent article from India shows a 54% mortality reduction among preschool children through a low-dose vitamin A supplementation (5).

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Summary of the Pre-Congress Asian Workshop on Nutrition in the Metropolitan Area

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A four-day pre-congress workshop was organised by the IUNS Committee 1/3 "Urbanisation and Nutrition", the Nutrition Society of Malaysia, the SEAMEO-TROPMED, and the GTZ - German Agency for Technical Cooperation. The workshop was located at the Continuing Education buildings of the University Pertanian Malaysia.

The workshop was attended by senior staff from government, academic and non-governmental institutions, concerned with nutrition related programmes and research. The participants brought a great variety of expertise to the discussions, which included nutritionists, urban planners, economists, sociologists, physicians and public health specialists. Eighty-two participants came from 16 countries, most of which were located in the South-East Asian region.

The purpose of the workshop was to stimulate nutrition projects and programmes through research and interventions in the metropolitan areas of Asia. The workshop was intended to leave participants with a greater awareness of the current state of knowledge of nutritional problems in urban areas, as well as produce specific proposals for action.

Urban nutrition is a relatively new concept which describes nutritional aspects of an environment that requires people to develop different skills. At the same time the urban environment provides different and often changing sources of support.

In order to exchange information on current problems, the workshop provided overviews of the nutritional situation of Asian metropolises in some countries. In each case the demography, ecology and socioeconomic situation was presented, together with risk groups and special aspects.

Almost all presenters showed high rates of increase in the urban population within the period of a single generation. Increases in recent years appeared to be due less to increases in the fertility of the urban population and was attributed to a larger extent to migration from rural areas.

Such demographic changes were identified as contributing to the vulnerability of different population groups, such as elderly and street children. The participants discussed the situation of these new risk groups at some length.

Besides malnutrition, participants presented evidence of over-nutrition in

many cities, with the associated chronic disease prevalence observed in industrialised countries. The health risks of overnutrition were documented not only for high-income groups, but also for middle class groups. Such observations suggest the particular influence of the urban environment on nutritional health.

Anaemia appears to be common problem, mentioned by all presenters. Even vitamin A deficiency was identified in several cases as an urban public health problem, although prevalence might be higher in rural areas.

Pollution of the environment in all urban conglomerations was recognised as a serious health problem, which may contribute to poor nutritional status of certain groups of inhabitants at higher risk. Particularly those at risk of infectious disease and appetite suppression. The exposure to parasitic organisms is higher due to the population density in urban areas.

In some cases intervention programmes aimed at specific urban problems were shown to be successful where the special circumstances of the physical and social environment of the city were taken into account in planning and implementation.

An entire day was devoted to presentations by professionals from a variety of disciplines related to nutrition describing urban problems and opportunities from different points of view.

* First, an analysis of the food supply and marketing systems peculiar to urban areas was presented, advocating the integration of national policies with urban ones.
* A second view presented the relative importance of income and other factors affecting nutritional status of the population, concluding that in several instances factors other than income, such as sanitation and access to essential services, were more important.
* Next the concept of individual action to change nutritional status was introduced, asking participants to consider the relationships between choices open to people and their ability to control personal health.
* A fourth view of social stresses observed among low-income groups in urban Malaysia concluded that several interventions were required to minimise the evident effect on health and nutritional status.
* A further analysis of the environmental problems led to the understanding of the differences in environmental management between Malaysia and other countries.
* A separate analysis of the health systems in urban Asia showed the limitations of health resources in minimising the health problems experienced in urban areas and concluded that Health-for-All can only be achieved through coordinated planning at city and national levels.
* The modern metropolises of developing countries also present problems with regard to the increasing number of elderly persons. Understanding the fundamentals of aging biology well as the unique influences of migration are critical to research on urban gerontology.
* The importance of the information sector was recognised in an analysis of economic interactions of the metropolis, advocating that the contributions from this sector be integrated with overall urban planning.

A unique feature of the workshop was the opportunity for participants to discuss and formulate research proposals and interventions for nutrition problems in urban settings. The outcome of the working groups

contributed concrete products for use by the wider nutrition community concerned with urban aspects.

The participants identified four research topics and two project topics for analysis and discussion. The research topics dealt with new approaches, such as

* the influence of pollution on nutritional status which focussed particularly on the problems of traffic pollution and the associated appetite depressant effects and anti-nutritional effects of pollutants;
* household level decision making on food distribution and whether the relationship between adults in urban households affects the distribution of food in the household sufficiently to change the food available to members.
* and new urban risk groups,
  - specifically the elderly, dealing with great variety of measurements and indicators to determine how aging influences nutritional status, within a causal model that identifies six main groups of determinants relevant to the urban situation;
  - and street children, proposing action to confirm or change assumptions and pre-conditions about the nutritional situation of street children, as many assumptions are based on knowledge of relationships and influences from rural models.

The two project topics dealt with

* the improvement in the quality of street foods, describing a programme aimed at making more street food available, with improved quality and safety, while recognising the importance of formalising the sector in providing this service;
* and the role of nutrition in urban primary health care, proposing a programme for nutrition, dealing with problems that can be addressed by either the health care providers or the community.

Participants used a common procedure for the formulation of causal models, variable and indicator lists. The reports of the working groups are not complete blueprints for action, as the time was too short for such an achievement. But the six proposals contain elements that professionals in the region can adapt for their own work.

At the end of workshop, it was felt by the majority of participants that a second meeting in Urban Nutrition should be held, possibly at the next Asian Congress of Nutrition. It is to be hoped that more research findings specific to the urban environment will be available to such a meeting and new experience of interventions can be presented. The proceedings of the workshop will be published in the Southeast Asian Journal of Tropical Medicine and Public Health.

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Epidemiological correlations between poor plasma levels of essential antioxidants and the risk of coronary heart disease and cancer

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Introduction

Aggressive oxygen species (superoxide anion radical, hydroxyl radical, singlet oxygen, etc.) can damage DNA, proteins, carbohydrates and unsaturated lipids and could thus be involved in many diseases. Unfortunately, free radicals are not easily detectable *in vivo* because of an extremely short half-life. But indirect information on the impact of free radicals may be obtained by comparisons of the antioxidant status since any pathogenic onset of radicals depends also widely on the body's multilevel defence system against radicals. The latter consists of enzymes (e.g. superoxide dismutase, glutathione peroxidase), non-essential endogenous radical scavengers (e.g. glutathione) and essential radical scavengers, i.e. the antioxidant vitamins C and E (α-tocopherol) as well as the singlet oxygen-quenching carotenoids (e.g. β-carotene, a potential vitamin A precursor with additional effects) and finally the thyil radical scavenger vitamin A. The status of essential antioxidants is in contrast to that of other antioxidative defence lines mainly determined by dietary supply. In consequence, if free radicals were indeed involved in pathological mechanisms, an optimum status of essential antioxidants should reduce the risk of disease and thus be a prerequisite of "optimum health" as defined by WHO. This working hypothesis is based on a series of observations (1). At first, many epidemiological studies have led to the general assumption that vegetable-rich diets are associated with a higher life expectency. Secondly, the calculation of the dietary intake of essential antioxidants has revealed inverse correlations to the risk of the major causes of death in westernized societies, i.e. of cancer and of coronary heart disease (CHD) (1). Thirdly, the actual plasma status of essential antioxidants (below) demonstrates more conclusively inverse associations, too.

Cancer

Prospective/Longitudinal surveys

A series of studies comparing the plasma antioxidants in subjects who subsequently developed cancer (of the lung, gastrointestinum or other organs) with that of surviving controls have revealed a significant correlation of low levels of β-carotene, in part also of vitamins E, C and A, with subsequent cancer in follow-up periods up to 12

years (2). Whereas prospective studies have mostly a "blood-bank" design (storing frozen serum for years which unfortunately causes some antioxidant loss) the Basel Prospective Study measured the antioxidants not only at once but was also unique by simultaneous comparison of all principal plasma antioxidants (2). The Basel Study has consistently revealed a satistically significant predictive power of a poor carotene status for most cancers in accordance with a series of other study sites. In addition, the Basel Study has established a statistically significant increase of the risk of gastrointestinal cancers at low plasma concentrations of vitamin C and at low levels of lipid-standardised vitamin A. Finally the Basel Study has indirectly supported results from other study cohorts showing a higher cancer risk at a truly poor vitamin E status. Thus vitamin E levels in Basel lacked a consistent correlation to subsequent cancer but the vitamin E levels of the Basel population were unusually and uniformly high and very probably above any level of risk. Clearly, an increased risk of a poor antioxidant level can only be detected if the latter occurs in a statistically appropriate percentage of study subjects. Taking together the previous prospective studies the potential cancer-preventive properties of essential antioxidants may have the following rank order for:

- lung cancer: carotene (β-, possibly also α-carotene) > lipid-standardised vitamins A and E;
- gastrointestinal cancer: vitamin C > carotene (as above) = vitamins E and A;
- all cancers: carotene > vitamins A and C.

The combination of low levels of several antioxidants, e.g. of carotene and vitamin A, increased the risk additively (2) or in part over-additively (3).

Current intervention trials

At present, more than 20 intervention studies in randomised subjects with high cancer risk (e.g. in smokers) and mostly sponsored by the US National Cancer Institute, NIH, Bethesda, Md, try conclusively to test the cancer-preventive potentials of specific supplements of β-carotene and/or of vitamins A, C and E (4). Results can be expected within a few years.

Conceivable mechanisms of action

The mechanisms by which essential antioxidants counteract mutagenic actions and cancer in mammals *in vivo* is poorly understood. Since radicals are known to damage DNA and independently to act as tumour promoters, the radical scavengers conceivably reduce tumour initiation and/or promotion, the latter presumably by modulating the expression of proto- and antioncogenes. Indeed, in the human vitamin A as well as β-carotene reverses the precancerous leukoplakia and reduces the occurrence of pathological micronuclei even on continuous exposure to mutagens from betel nuts and/or tobacco chewing (5). But all essential antioxidants might also act more through special mechanisms, e.g. via immunoresponses. Protection of the gastrointestinum by vitamins C and E involves conceivably also inhibition of nitrosamine formation and diminution of faecal mutagens.

Coronary heart disease

Evidence for association of a poor plasma status of essential antioxidants and an increased risk of CHD has emerged first from cross-cultural comparisons in Europe (where CHD mortality varies up to six-fold similar to world-wide differences and where the antioxidant levels differ up to about two-fold), secondly from comparisons of individuals without and with previously

undiagnosed angina pectoris, i.e. early CHD, in Edinburgh/Scotland (where plasma antioxidants vary from sufficient/fair levels to biologically poor levels), and finally from complementary observational data.

Cross-cultural epidemiology

The Vitamin Substudy of the WHO/MONICA Project (a standardised and by far largest trial for MONItoring determinants and trends of CArdiovascular disease) compared in randomly selected middle-aged male representatives of 16 European study populations the plasma antioxidant status with the concurrent age-specific CHD mortality. Thereby, in most, i.e. in 12 study populations, the classical risk factors plasma cholesterol, blood pressure and smoking did not differ significantly and could thus not sufficiently explain the up to six-fold differences in CHD mortality. In contrast, inverse correlations existed between CHD mortality and plasma status of essential antioxidants with the following rank order: vitamin E >> vitamins C and A (6-8). The impressively strong inverse correlation of vitamin E ($r^2 > 0.6$) occurred for both absolute vitamin E (in populations with comparable levels of plasma lipoproteins, i.e. of vitamin E carriers) and lipid-standardised vitamin E (in all study populations). Thereby vitamin E was a stronger predictor of CHD mortality than the classical risk factor hypercholesterolaemia and hypertension. By combination in multivariate analysis of vitamins E and A with the above mentioned classical risk factors the existing CHD mortality could be predicted to 87%, and after inclusion of vitamin C to about 90% (8).

Case-control study in early angina pectoris

In Edinburgh/Scotland, i.e. a community with a traditionally low consumption of fresh fruits and vegetables, a screening of inhabitants identified a considerable percentage of men with angina pectoris which had previously neither been diagnosed nor led to any intentional change of lifestyle. Low plasma levels (quintile 1) of vitamin E, of vitamin C and of carotene were associated with an up to 2.6-fold higher risk of this early stage of CHD as compared to high antioxidant levels (9). Whereas the increased risk of low vitamin C and carotene were confounded by (and most likely mainly due to) cigarette smoking, the statistically significant linear risk attributable to low vitamin E was independent of classical risk factors. Thus in these Scottish individuals essential antioxidants seemed again to have a rank order similar to that in European study populations, i.e. vitamin E >> vitamin A = vitamin C = carotene. As in the cross-cultural comparisons the threshold of "safe", i.e. presumably "optimum" plasma levels of (lipid-standardised) vitamin E may be above 28-30 mmol/l (1).

Prospective data

A preliminary evaluation of the 8-year follow-up of the US Nurses Study (10) showed a significantly lower risk of CHD at the highest intake of either vitamin E or A or carotene (mostly due to self-supplementaiton). A preliminary report on the US Physicians Study states that supplements of ß-carotene (given alternately with aspirin) reduce the CHD risk (11). Correspondingly in the above mentioned Basel Prospective Study the lowest quartile of lipid-standardised plasma carotene or of vitamin A showed (after adjustment for age, cholesterol and smoking) a statistically significant association with an increased subsequent coronary mortality (1). Whereas vitamin E lacked in this study cohort any correlation to CHD as had to be expected from the before mentioned high vitamin E levels (mean 35 mmol/l, i.e. presumably above the critical threshold) it indi-

rectly supports the working hypothesis of CHD-protective potentials of a high plasma status of vitamin E.

Forthcoming intervention trials

Any CHD-preventive potentials of essential antioxidants remain conclusively to be tested by specific supplementation in randomised subjects of high CHD risk and poor antioxidant status - in analogy to current trials on cancer-prevention. The first logical step may be to test a combination of vitamins E, C and ß-carotene (12) - according to the principle of multirisk factor intervention in the multifactorial multistage process of arteriosclerosis.

Conceivable mechanisms of action

Free radical oxidation of low density lipoproteins (LDL) may be involved in atherogenesis (13). In the aqueous phase of plasma the first and major line of antioxidative defence consists of vitamin C (14, 16) whereas within LDL vitamin E has been generally accepted as the principal radical scavenger. After dietary manipulation of the vitamin E level in LDL, the latter is responsible for at least half the antioxidative resistance of isolated LDL (17). Thus, also *in vivo* vitamin E-enriched LDL might be able to resist longer against oxidative modification by free radicals which can be released after transient anoxia ("reperfusion injury") as well as from activated macrophages ("respiratory burst") or from arterial cells, e.g. endothelial cells. Besides the antioxidant protection of LDL by vitamin E other beneficial effects of essential antioxidants might also counteract atherogenesis, i.e. in endothelium, macrophages, smooth muscle cells, blood platelets and/or immune reactions (1).

Prudent intake

Whereas previous dietary guidelines have given general recommendations to lower dietary fat (total and particularly mammalian) but to consume relatively more vegetables/fruits and suitable vegetable oils (as sources of natural antioxidants) an updated prudent diet should more specifically aim for optimal intake of ß-carotene as well as of vitamins E and C in order fully to use their presumable potentials for the prevention of cancer and/or CHD. A prudent intake of vitamin A may be in the range of 1 mg daily (1 RDA), of vitamin C in the range of 60-250 mg (1-3 times the present RDA) whereas for vitamin E a markedly higher dietary intake, i.e. in the range of at least 60-100 IU daily, and for ß-carotene about 15 mg may be advisable to achieve "optimum health" (7, 15).

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Tocopherol and tocotrienols and metabolism of plasma lipoproteins

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Abstract

Vitamin E is found in diets as 8 isomers of α-, β-, ∂- and α-tocopherols and tocotrienols. Although the biological importance of α-tocopherol is generally recognised, the role and function of tocotrienols is poorly understood.

Among current issues concerning tocopherol is whether intake is adequate to protect the circulating lipids from peroxidation, especially the LDL particle involved in atherosclerosis. We examined this issue in humans and monkeys fed diets of different fat saturation. First, human vegetarians were compared with non-vegetarians. Although vegetarians had lower total cholesterol and tocopherol, they had more tocopherol per molecule of cholesterol in their plasma than non-vegetarians. This suggests that vegetarians not only have lower plasma cholesterol associated with high PUFA intake, but their plasma lipids are relatively better protected by tocopherol than those in non-vegetarians.

A second experiment examined the reltive tocopherol status and "atherogenicity" of LDL isolated from monkeys fed three fats which were either saturated (palm oil), monounsaturated (hi-18:1 safflower oil) or polyunsaturated (hi-18:2 safflower oil). The LDL were isolated from plasma and tested in an in vitro atherogenesis assay with endothelial cells and monocytes. No differences in atherogenicity were found between the 3 native LDL. Oxidation of the LDL particles in vitro again rendered them equally atherogenic, but much more than native LDL. The best protective index against atherogenicity in all situation was the α-tocopherol content of the LDL.

A third experiment examined the relationship of tocotrienols to tocopherol. In contrast to α-tocopherol, the tocotrienol content of lipoproteins was essentially undetectable in normal persons and rose to 1/50th the concentration of alpha-tocopherol in supplemented persons.

These data suggest that α-tocopherol is by far the most prevalent antioxidant isomer of vitamin E in plasma lipoproteins. Highly controlled mechanisms apparently regulate its concentration and distribution among lipoproteins to assure proper balance and protection against lipid peroxidation under various circumstances.

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Vitamin A deficiency and child health survival – Indonesian experience

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Introduction

The results of the national xerophthalmia survey in 1978 revealed that the number of blinded children with corneal scarring was much lower than expected. Since the actual number was only 13,830 compared to the expected number of 60,000, as many as 77% might have died.

Even though the cause of death might be multifactorial, it was assumed, at that time, that vitamin A deficiency might perhaps play a significant role in this mortality (1).

A longitudinal observational study in rural areas of West Java at the same time of the national xerophthalmia survey indicated that the mortality of children with ocular signs of mild vitamin A deficiency were higher than their neighbourhood controls. The mortality was directly related to severity of vitamin A deficiency and that poor survival was attributable partly to a high rate of respiratory disease and diarrhoea (2).

After completion of the national xerophthalmia survey, there were three studies on vitamin A interventions, during which the number of deaths among preschoolers and infants could be identified by demographic research teams so that the mortality rate could be known. These studies were: The Aceh Study, fortification, and intervention by giving vitamin A to infants. This paper will show the impact of these vitamin A supplementations on mortality.

Aceh study

The results of the Aceh study had been reported by Sommer *et al.* (3).

The Aceh study was carried out in the Aceh province where the prevalence of active corneal disease was the highest (48.4 per 10,000) based on the results of national xerophthalmia survey 1978. For political and administrative reasons, a cluster sampling scheme was employed. Four hundred and fifty villages with approximately 25,000 preschool children were randomised into two groups after the baseline examination. Standard capsules containing 200,000 IU vitamin A and 40 IU vitamin E were given to every child aged 1 to 5 years in programme villages by trained local volunteers. The first dose was given 1 to 3 months after the baseline examination and the second, 6 to 8 months later.

The prevalence of active xerophthalmia in programme villages declined from 1.9% at baseline to 0.3% at follow-up and that in the control villages, declined from 2.3% to 1.2%. During the follow-up period, 75 preschool children from control villages and 53 from programme villages died,

giving mortality rates of 7.4 and 4.9 per 1000 respectively. The data are presented in Table 1. The relative risk of dying in control versus programme villages was 1.51, equivalent to a reduction in mortality in programme villages of 34%.

Fortification

The results of this study had been reported by Muhilal *et al.* (4). This fortification study was carried out in a rural, traditional rice-eating area in West Java. In programme areas, covering around 5000 preschool children, fortified MSG (3000 IU/g) was marketed through ordinary marketing channels. In control areas, composed of nearby villages, non-fortified MSG was marketed as usual. The average intake of MSG for the children was around 0.23 g/d, therefore, the additional vitamin A ingested from MSG was around 690 IU/child/day. After the marketing of fortified MSG has taken place for 11 months, infant and child deaths were identified by demographic research teams assisted by local field workers. All available families were questioned about infant and preschool (0 - 5 years) child deaths in the previous year. If at the time of the visit, neither the wife nor the husband was at home, the information was sought from the official local neighbourhood leader responsible for every 15 to 20 households.

It was previously reported that the prevalence of Bitot's spots in the programme area declined 85% between baseline and 11 months follow-up (4). The decline of xerophthalmia was parallel with the increase of serum vitamin A (5). No significant changes were observed in the control areas.

The mortality rates of children age 12 - 60 months in programme and control villages are presented in Table 2.

TABLE 1

Mortality during follow-up in programme and control villages

Baseline age (months)	Programme villages		Control villages		RR
	Proportion dying	Rate per 1,000	Proportion dying	Rate per 1,000	
12 - 23	19/1979	9.6	22/1941	11.3	1.17
24 - 35	14/2086	6.7	25/2072	12.1	1.81
36 - 47	11/2274	4.8	8/2016	4.0	0.83
48 - 59	5/1887	2.6	7/1724	4.1	1.58
60 - 71	4/2686	1.5	13/2465	5.3	3.53
Total (1.03-2.28)	53/10917	4.9	75/10230	7.4	1.51

Source: Sommer *et al.*, 1986

TABLE 2

Death rates in programme and control children after fortified MSG had been marketed for 11 months

Age (months)	Programme villages		Control villages		Odds Ratio
	Proportion dying	Rate per 1000	Proportion dying	Rate per 1000	
< 12	109/1199	91/1000	116/1134	102/1000	1.14 (0.87,1.50)
12 – 60	77/4556	17/1000	134/4311	31/1000	1.87 (1.41,2.48)
0 – 60	186/5775	32/1000	250/5445	46/1000	1.45 (1.19,1.76)

Source: Muhilal *et al.*, 1988

Table 2 shows that the mortality rate of children aged 12 - 60 months in programme villages was 77/4556 or 17 per 1000, while that in control villages was 134/4311 or 31 per 1000. The odds ratio of mortality rate of 12 - 60 months age between control and programme villages was 1.87, equivalent to reduction of mortality in programme villages of 45% .

The mortality rates among infants in programme and control villages were 91 per 1000 and 102 per 1000 respectively. The odds ratio of infant mortality rate was 1.14. This lower odds ratio was partly because of the additional vitamin A intake from the breastmilk of mothers consuming fortified MSG and partly from family food for older infants (more than 10 months) introduced to them.

Vitamin A supplementation to infants

In this study, around 3300 newborn babies were divided randomly by village into two groups, (programme and control).

When this study was conducted, there were no guidelines on how to dose vitamin A to young infants aged less than 4 months. The supplementation of vitamin A for infants less than 4 months was through breastmilk of mothers dosed with 2 standard capsules of vitamin A (containing 200,000 IU vitamin A and 40 IU vitamin E each) within 1 2 weeks of birth. When the infants were at 4 months of age, they were dosed with 100,000 IU of vitamin A. A nutritionist visited every infant 1 - 3 days after the dose to collect any complaints based on history by mothers. There was no single report of toxicity symptoms based on what was told by the mothers.

The breastmilk vitamin A concentration of programme areas was significantly higher until 4 months following the dose. This indicated that the infants in the programme area received more vitamin A from the breastmilk than those in the control area. When the breastmilk vitamin A started to decline to a normal level, the infants in the programme area were dosed with vitamin A as mentioned above.

TABLE 3

Infant mortality in programme and control areas

Group	Proportion dying	Rate per 1000	Odds ratio
Programme villages	49/1681	29.1/1000	1
Control villages	77/1624	47.5/1000	1.63

Source: Nutrition Research and Development Centre, 1989.

The infant mortality rates in the two areas are presented in Table 3.

The infant mortality rate in the programme area was 29.1/1000 as compared to 47.5/1000 in the control area. The odds ratio of the infant mortality rate in control area versus programme area was 1.63 or a reduction of 39% .

Discussion

The results of three separate intervention studies revealed that vitamin A supplementation resulted in lower mortality rates among preschool children and infants in Indonesia. However, Vijayaraghavan *et al.* (6) reported that there was no difference in mortality between treatment, who received 200,000 IU vitamin every six months and control groups in their study in Hyderabad, India. This discrepancy might be caused, at least partly, by the fact that in Indonesian children, mild xerophthalmia was associated with increased risk of both diarrhoea and respiratory infection (2), while in Indian children, mild xerophthalmia was associated only with respiratory infection but not diarrhoea (7). In addition, since the cause of death is multifactorial, it is therefore questionable whether vitamin A deficiency is also involved in childhood mortality for other countries or regions, which have different food patterns and are exposed to different environmental conditions.

The data from a recent xerophthalmia survey in some provinces in Indonesia revealed that the prevalence of xerophthalmia, especially Bitot's spot, has declined sharply to a point that it is not a public health problem. In addition to the decline of xerophthalmia, the national figure for preschool child mortality had declined from around 40/1000 in 1978 to around 11/1000 in 1990 (8). Moreover, our study on the impact of vitamin A intervention on immunocompetence revealed that there was an increase in both humoral and cell-mediated immunity.

While all data from Indonesia's experience has supported the important role of vitamin A in decreasing mortality, it is possible that this phenomenon is not applicable to some other areas in the world. This is understandable because the causes of mortality are multifactorial and how high the role of vitamin A depends on the other factors influencing mortality.

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Vitamin and child health

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Introduction

A conservative estimate according to WHO is that today there are 1.5 million children under 16 years of age who are blind, that 0.5 million new cases occur annually, and that 70% of these new cases are due to vitamin A deficiency (VAD) (1). With this incidence of VAD blindness, why does it account for only 4-5% of the total number of blind people in the world (27-35 million)? Tragically, it is because 60-70% of those children who become blind die within a year, and therefore are not present to be counted as blind adults. As a result, VAD blindness does not appear to be competitive for public concern with other causes of blindness. But this estimate does not reflect the true consequences for child health and survival of the problem of VAD. There are 5-10 million additional children with milder clinical ocular signs of VAD who die from infections at least twice the rate of those non-deficient, and another 40-50 million without eye signs whose body supply is depleted to a point where their health, survival and development are also compromised (2).

Review of recent studies of VAD and child health and survival

Using newer techniques for assessing marginal vitamin A deficiency (3), data indicate that in some developing countries with documented inadequate dietary intakes of vitamin A, 40-50% of the preschool-aged children may be subclinically deficient. Their survival is at risk when they contract common and normally not life-threatening, childhood infections such as measles, diarrhoea, and acute respiratory infections. As with blinding malnutrition, those children under 3 years of age are at greatest health-risk. Although it is well recognised that the health effects of VAD are especially pronounced when associated with severe protein-energy malnutrition (PEM), recent data suggest that its most devastating effect on mortality risk occurs among chronically undernourished (stunted) children (4). These are the children who generally come from the most socially and economically deprived homes, the ones least likely to be reached by the usual government health programmes.

Since the landmark study reported from Aceh, Indonesia, claiming more than a 34% reduced risk of mortality by providing a high-dose vitamin A supplement 6-monthly (5), a series of clinical trials has been carried out in several countries to test the replicability and universality of these findings. The results have been variable. Some studies have provided a continuous supply of the vitamin at near physiologic levels through low-dose supplementation (4) or fortified foods, as with fortified MSG (6), to populations of children, where the prevalence of chronic

undernutrition and xerophthalmia is high to moderate, and have reported mortality risk reductions of 30-50%. Other trials have distributed high-dose supplements at 4-6 month intervals and the results range from no significant impact (7,8) to a 30% or greater risk-reduction (9,10). Some trials using high-dose supplements in Asia, Africa and Latin America are still in progress and their results are eagerly awaited (11).

The variable experiences from completed mortality-risk trials emphasise the importance of identifying the existing mix of physiological and socio-economic conditions that appear to be most responsive to vitamin A interventions for the betterment of child health and survival. Recently, a meeting at WHO drew together the principal investigators from 10 studies recently completed or nearing completion to discuss these issues (11). The group reached a consensus that some of the reasons that may explain the variable impacts of vitamin A supplementation on mortality among populations studied include difference in:

(a) severity of the underlying VAD;

(b) severity of the underlying malnutrition and its characteristics, i.e., acute and/or chronic;

(c) exposure to illness and causes of death;

(d) access to health facilities, including immunisation coverage;

(e) socio-economic status, particularly literacy, affecting mothers and their children.

Whereas VAD has been associated directly with a reduced mortality risk, it is more difficult to unambiguously link the problem with morbidity incidence. Controlled clinical trials in field-based settings have failed to make this linkage using the currently available methodologies for determining incidence and severity of illnesses (12,13). A linkage probably exists and is most likely related to severity and lethality, rather than incidence. Institutionally-based studies of severe measles in Africa, clearly link the vitamin to reduced measles mortality (14) and to the duration and severity of measles-related morbidities (15). Verbal autopsies of VAD children associate diarrhoea and respiratory infections with death, but do not link this to incidence. This indicates that vitamin A is no "magic bullet" to child health. Public health programmes that address underlying causes of illness are of critical and concurrent importance.

VAD has health-related effects for children beyond those of ocular health and mortality risk. Studies have also shown that among certain populations, an adequate vitamin A status improves iron utilization and thus reduces the prevalence of iron deficiency (6). Iron deficiency is likely to be even more prevalent and detrimental to child health than that of VAD and the two problems frequently occur together. Programmatic attacks on these two micronutrient deficiencies, therefore, should be considered concurrently.

Some, but not all studies, claim that child growth is enhanced by improved vitamin A status (6,12,16). Growth, of course, is influenced by many factors, including frequency of illnesses and diet. In some circumstances, PEM rather than vitamin A may be more limiting to growth, and in still other situations, additional micronutrients, such as zinc, may also be pivotal.

Programmatic implications for Asia

Because of the complex interactions of the social, ecologic and economic circumstances that contribute to the problem of VAD, simple solutions that are sustainable and can be universally applied are unlikely. Where clinical VAD is

evident, there is no question but that vitamin A supplements are required – this is a medical emergency. But, where a clinical problem is rare, other more locally appropriate, affordable and sustainable strategies should be considered that address not only the lack of vitamin A in the diet, but also the factors contributing to its inefficient utilization and conservation (17). These factors may include the incidence of infectious diseases, some of which could be prevented through broader immunisation coverage and access to health care, and others through programmes to improve environmental sanitation and personal hygiene. Programmes that generate income for women and decrease the prevalence of illiteracy among them can contribute significantly, though indirectly, toward improved nutritional status and child health generally. Such measures will in turn reduce the problem of VAD. Malaysia is one good example, among others in the region, of a country where VAD existed to a significant degree in the past but has been alleviated through economic and social development without the need for programmes directed specifically to VAD.

The recently held meeting in Geneva among principal investigators of large, population-based trials with vitamin A concluded the following:

"There are several possible strategies to ensure and sustain an adequate vitamin A status in all population groups, especially in young children. The choice of intervention is the prerogative of governments and should depend on specific country factors including the severity of the vitamin A problem, the resources available, and national priorities for their utilization (11)."

Conclusions

Countries of South and Southeast Asia house the vast majority of children with clinical and subclinical VAD. It is imperative that the importance of this problem to child health be acknowledged and that sustainable, regionally and locally appropriate strategies for its alleviation be undertaken. Under all circumstances, attention should be given to effective nutrition and health education to achieve changed behaviours to improve the diets of children and improve their health. The technology is available to eliminate VAD as a public health problem and the political will has never been greater, as evidenced in the expressed goals of the UN Agencies' 10- year plans, UNICEF's Summit for Children, the Bellagio Declaration, and other documents that seek to achieve health for all by the year 2000 and the virtual elimination of VAD as a public health problem. The proclamations have been made; it is up to the people, including those of us working with our governments and constituencies, to make it happen.

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Anaemia, rickets and protein-energy malnutrition during the weaning period in a rural community of the People's Republic of China

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Introduction

Surveys carried out by Chinese Health Authorities have shown anaemia and rickets to be the most common nutrition related diseases in childhood in the P.R. China. Through a bilateral development programme of the Chinese and the Italian Governments, a Centre for Child Nutrition was established in Chengdu, the provincial capital of Sichuan; among other activities, a survey was carried out in April 1989 on anaemia and rickets during the weaning period in a rural area of the fertile agricultural plain of Sichuan.

Previous Chinese studies show that the highest prevalence rates of both anaemia and rickets are found in the first year of life, with up to approximately 60% of infants affected in the areas with the highest prevalences; in most cases anaemia and rickets are of a mild degree (1-5). According to some studies the prevalence of anaemia is particularly high during the second semester (1,2,3), a time when also growth falters, as shown by a survey conducted in 10 Chinese provinces (6).

Iron deficiency is considered the main cause of anaemia in childhood, not just due to low iron intake but also to low availability of iron in the Chinese diet: for the majority of Chinese 90% or more of iron intake is from vegetable sources, eggs and milk (7). Low ascorbic acid intake contributes to reduce iron absorption, as shown by studies conducted in kindergarten children in Beijing (1) and, in Jiang Yuan county of Sichuan, in every age group between 6 months and 5 years.

Considering that anaemia and rickets are the most widespread nutrition-related diseases in Chinese infants and that limited data were available for rural Sichuan, it was considered rele-

vant for public health to investigate the prevalence and the main factors associated with anaemia and rickets in rural areas, and during the weaning period, as this tends to be a time of greater nutritional risk for the child.

Subjects and methods

The county of Dujangyan is historically famous for monumental hydraulic engineering works started in the 4th century B.C. to control the water flow and to provide an irrigation system, which is still used today to fertilize the Sichuan plain. The study was conducted in two communes of this county, considered representative of the average living conditions in the Sichuan plain, according to data on infant mortality rate (IMR) and on average income per person obtained from the local Statistical and Health Bureaus. According to 1982 census data, the average IMR of Sichuan is placed in the medium-high range compared to the other Chinese provinces (8).

All infants 5 to 11 months-old living in the two communes of Xu Jia and Chong Yi were included in the study. The diagnosis of anaemia and/or rickets could not be performed on 3 out of 307 subjects, so the number of children with both diagnoses was 304, corresponding to 99% of total. 53% were male and 47% female.

The diagnosis of anaemia was based on values of haemoglobin (Hb) lower than 110 g/l. The level of free erythrocyte protoporphyrin (FEP) was used as indicator of iron deficiency. The FEP:Hb ratio is a reliable and practical indicator of iron deficiency anaemia in infants (9). 3 μg FEP per g of Hb is considered by many authors as the upper limit of normality in infants and young children (10-14). Based on these criteria we adopted the following classification of anaemia and iron deficiency. Normal values: Hb $\geq$ 110 g/l and FEP:Hb $\leq$ 3.0 (μg FEP/g Hb). Iron deficiency (without anaemia) (I.D.): Hb $\geq$ 110 g/l and FEP:Hb > 3.0. Iron deficiency anaemia (I.D.A.): Hb < 110 g/l and FEP:Hb > 3.0 . Anaemia not due to I.D. (N.I.D.A): Hb < 110 g/l and FEP:Hb $\leq$ 3.0.

The diagnosis of early or advanced rickets was based on the presence of at least 2 out of 3 elements: clinical signs of early or advanced rickets, radiological signs of early or advanced rickets from an X-ray of the left wrist, and elevated serum alkaline phosphatase levels (AKP) (15).

The diagnosis of acute and chronic protein-energy malnutrition (PEM) was based on weight-for-length and length-for-age, respectively. Weight-for-age was also used, as a synthetic index of malnutrition, expressing a combination of the information contained in the two other indices. The reference values for weight and height were derived from a study conducted in the rural areas of 10 Chinese provinces in 1985 (16); their use is recommended by the Chinese Ministry of Health. Following WHO recommendations (17), children were classified as malnourished if their weight-for-length, length-for-age and weight-for-age values were lower than the mean minus 2 SD (of the Chinese reference). Values equal to or greater than the mean - 1 SD were considered normal and values between mean - 1 and - 2 SD were considered indicative of moderate malnutrition.

A general physical examination was conducted by a paediatrician. A stool exam was performed on 73% of the children, the ones whose mothers remembered to bring stools to be examined. The presence of parasites which may contribute to cause anaemia, Ancylostoma and Trichuris trichiura, was investigated. Additional information collected by questionnaire included:

(a) Information on the house and family, such as: mother and infant diseases and conditions which may contribute to determine infantile anaemia, rickets or PEM; infant diseases which may occur with greater frequency if anaemia, rickets or PEM are present; socio-economic conditions of the family, based on an assessment of the house characteristics, household assets and of the family's income in the previous year; level of education and occupation of the mother, father and the child-caretaker; total number of family members; type of water source used; daylight available in the rooms used during the day.

(b) Retrospective information in infant feeding since birth.

(c) Retrospective information on exposure of the infant to sunlight since birth.

(d) Mother's or child-caretaker's knowledge of food intake needs and food taboos regarding the infant and the lactating woman.

Finally, a 4-days survey was conducted in each family recording the type and weight of all foods given to the infant and the time spent by the infant outdoors with direct and indirect exposure to sunrays, indicating the part of the body exposed. Both food intake and sunlight exposure records were validated by two health workers with higher education who visited approximately 10% of the households with satisfactory results. All the questionnaires used, together with the procedures for the food intake record and the sunlight exposure records were pretested in a nearby commune in collaboration with health workers from the Dujangyan City Epidemic Prevention Station and from the Sichuan Epidemic Prevention Station.

Results

The total prevalence of anaemia was 43.0%, in 98% of cases of mild degree (i.e. with Hb values between 90 and 109 g/l). The overall prevalence of anaemia is similar to that reported in previous studies. An unexpected finding is that, while it is believed that approximately 80% of cases of anaemia in China are due to iron deficiency (18), only 57% of these anemic infants had IDA (24.3% of the total). There was, however, another 17% of infants who were iron deficient, although their Hb level was $\geq$ 110 g/l. This brings the total prevalence of iron deficiency (with or without anaemia) to 41.3%. The prevalence of rickets was 34%, which is considerably higher than that previously found in two rural counties of Sichuan, but similar to that found in other parts of China. In most cases (75%) rickets was in the early stage. This is also in agreement with previous findings. In the remaining 25%, which corresponds to 8.5% of the total, infants suffered from advanced rickets.

Chronic PEM (LT/AGE < x - 2 SD of the national average) was found in 9.8% of cases, i.e. it is 4 times more frequent than in the national survey of 1985. Acute PEM, instead (WT/LT < x - 2 SD of the Chinese standard) was found in only 1.0% of infants, that is the prevalence is lower than the national average. The prevalence of low WT/AGE values (< x - 2 SD of the Chinese standard) was 4.2% . No statistically significant differences in prevalence of anaemia, rickets or PEM were found between males and females. The same applies to age groups (in months) for anaemia and PEM. The prevalence of rickets, instead, was highest in younger infants (58% at 5 months) and decreased with increasing age, reaching the lowest value of 21% at 11 months ($p = 0.001$). 84% of infants of 7-11 months breastfed for more than 6 months and 25% of the total were exclusively breastfed at the

time of the study. 70% of infants introduced other foods in the first semester, 52% starting in the first month. However, the number of those foods was very limited and satisfied only a small proportion of the infant's requirements. 75% of children received sugar, most of them from the first month. Eggs and meat were given in less than 20% of cases, generally towards the end of the first year; vegetables in less than 40% and fruit in 12% of cases, more often in the second semester; legumes, fish and liver were given only in 1-2% of cases. The intake of vitamin D supplements, which is common in cities like Chengdu, occurred only in 1% of infants in this rural area.

Tables 1-3 summarise the statistically significant associations and significant differences found by univariate analysis, using chi square test, t test and analysis of variance.

Factors associated with rickets are tabulated in Table 1. The fact that the prevalence of rickets decreases sharply as age increases can be explained by the finding that the infant is exposed more to the sun as he grows: this was found for each of the 3 seasons studied retrospectively. We also found that infants affected by rickets had been exposed to sunrays in winter for significantly shorter time than healthy infants. The difference is more highly significant when subjects are divided into two groups, those with face and hands exposed for less than one hour per day and those exposed for longer ($p = 0.002$).

Rural people in this part of China believe that infants should be protected from sunlight and that a baby with light coloured skin is healthy and beautiful. Health education is clearly required to change this belief. (Two examples are shown of how parents protect their children from the sun: a father working outside the home with the child all bundled up, and sitting in the shade. A mother at the market with the child carried in a basket on her back, protected by a black umbrella.) A study conducted in Beijing during September and October indicates that breastfed infants need at least a half hour of direct exposure of the face to sunlight to maintain serum 25-OH-vitamin D above the lower level considered normal (19). Therefore it should be recommended that during winter, when the intensity of UV rays is approximately 3 times less than in autumn, the average time of exposure to sunlight should be at least 3 times longer.

The contribution of diet to rickets is shown by the finding that infants who received both breastmilk and other foods were less affected ($p = 0.01$), particularly if the foods introduced in previous months were 3 or more ($p = 0.002$). The importance of prolonged breastfeeding is shown by the finding that infants who breastfed for more than 6 months were less affected by rickets ($p = 0.05$).

Chronic PEM was found more often in infants with rickets ($p < 0.05$). Infants affected by advanced rickets had a higher incidence of diarrhoeal episodes per month than those with early rickets or free from this disease ($p = 0.03$). It was also found that in houses where the water source was an irrigation canal or a pond the average number of days the infant had diarrhoea in the previous month was more than twice that of infants from the other houses with better water sources ($p = 0.004$). The fact that PEM, IDA, ID and diarrhoea are all more frequent in children with rickets strongly suggests that both inadequate nutrient intake and the loss of nutrients with diarrhoea contribute to determine rickets in these infants. It should be emphasised that the incidence of diarrhoea was high in this survey: 48% of infants suffered from diarrhoea during the 4 weeks before the time of this study.

The homes of infants with advanced rickets received less daylight ($p = 0.02$) and the family income of these households was significantly lower than that of infants with only early rickets or free from this disease ($p = 0.01$).

TABLE 1

Factors associated with rickets

	Level of significance
AGE OF THE INFANT: as age increases, rickets prevalence decreases	X^2=22.3, 6df, p=0.001
EXPOSURE TO SUNLIGHT increases with age:	
in winter	X^2=33.3, 6df, p<0.001
in autumn	X^2=44.7, 5df, p<0.001
in summer	X^2=13.8, 3df, p<0.01
EXPOSURE TO SUNLIGHT IN THE PREVIOUS SEASON (WINTER): higher rickets prevalence when face and hands exposed for <1 hour vs ≥ 1 hour/day)	X^2=9.2, 1df, p=0.002
FEEDING MODE: less rickets in infants receiving both breastmilk and other foods	X^2=9.1, 2df, p=0.001
NO. OF SUPPLEMENTARY FOODS INTRODUCED: less rickets in infants receiving 3-11 vs < 3 supplementary foods	X^2=12.4, 2df, p=0.002
DURATION OF BREASTFEEDING: less rickets in infants breastfeeding for > 6 months	X^2=3.8, 1df, p=0.05
CHRONIC PEM: infants with rickets have WT/LT < x -1SD of reference more frequently than ≥ x -1SD	X^2=7.7, 2df, p<0.05
AVERAGE MONTHLY INCIDENCE OF DIARRHOEA EPISODES SINCE BIRTH: higher in infants with advanced rickets	ANOVA: p=0.03
DAYLIGHT IN THE HOUSE: higher frequency of advanced rickets in homes with scarce daylight	X^2=8.4, 2df, p=0.02
FAMILY INCOME PER PERSON: lower family income in infants with advanced rickets	ANOVA: p=0.01

The study of factors associated with anaemia (Table 2) confirms the importance of the intake of other foods besides breastmilk, for preventing anaemia, similarly to what was found for rickets; in this case however, the infants with the lowest rates of both IDA and NIDA were those who ate only other foods and no breastmilk at the time of the survey ($p = 0.006$). The negative role of prolonged BF without adequate supplementation is confirmed by the finding that both IDA and NIDA were more frequent among infants breastfed for more than 6 months ($p = 0.002$). This also suggests that these lactating mothers probably had nutrient deficiencies leading to anaemia. The analysis of nutrients intake in this survey shows that those infants who were not breastfeeding at the time of the study had the highest iron ($p = 0.0001$) and protein ($p = 0.002$) intakes compared to the infants who practised exclusive breastfeeding (BF) and mixed feeding (MF), and their energy intake was 10% higher. In addition, they suffered from diarrhoea during the previous month and since birth, less than the infants who breastfed in part or exclusively at the time of the study ($p = 0.003$). Intestinal parasites which could contribute to cause anaemia were not found in the stools examined. The incidence of colds since birth was higher in anaemic infants ($p = 0.05$) and the incidence of lower respiratory tract infections was higher in infants with IDA and ID ($p = 0.02$).

Table 3 tabulates the factors associated with PEM. Prolonged BF (for > 6 months) was found to have a positive value for the prevention of PEM, as it did for rickets (but not for anaemia). There is a tendency for infants who ate 2 or more supplementary foods to have a higher prevalence of low WT/AGE values ($p = 0.05$). This tendency is more marked in infants of 7 and 8 months of age ($p = 0.02$), when a considerable increase in the number of supplementary foods takes place; this change in feeding mode is likely to be responsible for the faltering of growth that we observed at this age. The contribution of diarrhoea to chronic PEM is indicated by the higher incidence of diarrhoea episodes since birth found in infants with low LT/AGE (< x - 2 SD of reference values). This indicates the need to prevent microbiological contamination of infant foods by improving hygiene and water quality. The contribution to PEM of inadequate food intake is indicated in Table 3 by the lower intake of energy, protein, vitamins A, C, B1, B2, niacin, calcium as well as by the lower Ca:P ratio which were found in infants with low values for one or more of the indicators of PEM adopted. Infants born with lower birth weight (close to 3,000 g) had more often lower WT/AGE values (< x -1 SD) at the time of this survey than children with birthweight close to 3,400 g ($p = 0.0001$). In addition, families with infants having lower values of these growth indexes were found to have smaller house size, lower income per person and less farm animals.

The investigation on the knowledge of the mother or thechild caretaker about the food intake needs of the infant and the lactating woman shows that only 40% of persons interviewed believed there are foods of particular importance to help the infant grow well, while approximately 50% of mothers think that some foods should be avoided, without scientifically valid reasons. In addition, 23% of mothers think that they should avoid certain foods during lactation, without valid reasons. It also appears that the main source of information on how to feed the infant when sick is the traditional doctor.

Disussion

To conclude, anaemia not due to iron deficiency was found in a higher proportion of infants than expected, i.e.

TABLE 2

Factors associated with anaemia

	Level of significance
FEEDING MODE: anaemia prevalence (both IDA and NIDA) is lowest in infants who received no breastmilk at the time of the study (NBF group) compared to the other 2 groups (BF and MF)	X^2=10.3, 2df, p=0.006
IRON INTAKE is highest in NBF group	ANOVA: p=0.0001
PROTEIN INTAKE is highest in NBF group	ANOVA: p=0.002
ENERGY INTAKE is 10% higher in NBF group	ANOVA: p=0.18
NO. OF DAYS OF DIARRHOEA in the previous month is lowest in NBF group	ANOVA: p=0.003
DURATION OF BREASTFEEDING: prevalence of both IDA and NIDA is higher in infants who breastfed for > 6 months (*)	X^2=15.0, 3df, p=0.002
(*) the opposite is true for the prevalence of RICKETS	
NO. OF COLDS PER MONTH SINCE BIRTH: higher in subjects with anaemia	ANOVA: p=0.05
NO. OF EPISODES OF LOWER RESPIRATORY TRACT INFECTIONS SINCE BIRTH: higher in subjects with IDA and ID	ANOVA: p=0.02

TABLE 3

Factors associated with PEM

	Level of significance
FOOD FACTORS	
BIRTH WEIGHT: lower in infants with low WT/AGE (< x - 1 SD)	ANOVA: p=0.0001
DURATION OF BREASTFEEDING: higher prevalence of PEM in infants breastfed for < 6 months (with WT/AGE and LT/AGE, < x - 1 DS vs ≥ x -1 DS)	WT/AGE: X^2=11.1,1 df, p=0.001 LT/AGE: X^2=7.5, 1 df, p=0.006
NO. OF SUPPLEMENTARY FOODS INTRODUCED: higher prevalence of low WT/AGE values (< x - 1 SD) in infants who introduced 2 or more supplementary foods	X^2=3.9, 1 df, p=0.05
% OF ENERGY REQUIREMENT SATISFIED: lower in infants with WT/LT < x - 1 SD	ANOVA: p=0.03
% OF PROTEIN REQUIREMENT SATISFIED: lower in infants with low WT/AGE, HT/AGE, WT/HT (< x - 1 SD)	ANOVA: p=0.05, p=0.06, p=0.06
% OF VITAMIN A REQUIREMENT SATISFIED: lower in infants with low WT/AGE, LT/AGE, WT/HT (< x - 1 SD)	ANOVA: p=0.0001, p=0.03, p=0.04
% OF VITAMIN C REQUIREMENT SATISFIED: lower in infants with low WT/AGE, LT/AGE, WT/LT (< x - 1 SD)	ANOVA: p=0.0002, p=0.10, p=0.04
% OF THIAMIN REQUIREMENT SATISFIED: lower in infants with low LT/AGE (< x - 1 SD)	ANOVA: p=0.04
% OF RIBOFLAVIN REQUIREMENT SATISFIED: lower in infants with low WT/AGE, LT/AGE, WT/LT (< x - 1 SD)	ANOVA: p=0.05, p=0.06, p=0.07
% OF NIACIN REQUIREMENT SATISFIED: lower in infants with low LT/AGE (< x - 1 SD)	ANOVA: p=0.07

TABLE 3 (continued)

Factors associated with PEM

	Level of significance
% OF CALCIUM REQUIREMENT SATISFIED: lower in infants with low WT/LT (< x - 1 SD)	ANOVA: p=0.10.pa
CALCIUM/POSPHORUS RATIO: lower in infants with low WT/LT (< x - 1 SD)	ANOVA: p=0.02
OTHER FACTORS	
AVERAGE MONTHLY INCIDENCE OF DIARRHOEA EPISODES SINCE BIRTH: LT/AGE < x - 2 SD	ANOVA: p=0.08
HOUSE SIZE (in sq.m./family member): smaller for families with infants having lower LT/AGE, WT/AGE, WT/LT (< x - 1 SD)	ANOVA: p=0.05, p=0.09, p=0.11
FAMILY INCOME PER PERSON: lower for families with infants having low WT/AGE (< x - 2 SD), LT/AGE (< x - 1 SD)	ANOVA: p=0.09, p=0.09
AVAILABILITY OF FARM ANIMALS: lower for families with infants having lower WT/LT (< x - 1 SD)	ANOVA: p<0.03

in 43% instead of 20% of cases of anaemia. In China, NIDA is considered to be mainly due to folic acid and copper deficiencies (18). Hereditary anaemias have been estimated to affect 2.5% of children. Although anaemia was only of a mild degree in 98% of cases, its prevention should lead to a reduced incidence of acute respiratory infections in the first year of life, as these occurred more frequently among anaemic infants.

The analysis of factors associated with anaemia, rickets and PEM suggests some recommendations, indicated in Table 4, for preventing these conditions in infants born in this part of Sichuan. Among the risk factors for rickets the vitamin D status of pregnant women and newborns should also be investigated, as neonatal rickets was found in 8% of 316 newborns born in winter in Beijing, with low levels of 25-OH-D in both mothers and newborns (20).

TABLE 4

Recommendations for preventing anaemia, rickets and PEM in the Sichuan Plain

Recommendations	*Rationale*
(1) BREASTFEED THROUGHOUT THE SECOND SEMESTER	1.1 The highest prevalence of PEM was found in the NBF group, whereas the lowest prevalence of PEM was found in the BF group. 1.2 Infants who breastfed for > 6 months were less affected by rickets and by PEM.
(2) PROMOTE EARLIER INTRODUCTION OF SUPPLEMENTARY FOODS OF HIGH NUTRITIONAL VALUE; IMPROVE THE DIET OF LACTATING WOMEN INVOLVE TRADITIONAL DOCTORS IN IMPROVING FEEDING PRACTICES FOR THE SICK INFANT	2.1 The supplementary food most commonly consumed is sugar; foods such as eggs, meat vegetables and fruit are given only in small quantity and in a minority of cases. 2.2 About 50% of mothers believes that certain foods should be avoided in infancy, without scientifically valid reasons. 2.3 23% of mothers think they should avoid certain foods during lactation, without valid reasons. 2.4 Traditional doctors appear to be the main source of information on feeding practices in the sick infant.
(3) INCREASE EXPOSURE TO SUNLIGHT AND PART OF BODY EXPOSED STARTING FROM THE FIRST MONTHS (AT LEAST 90 MINUTES OF DIRECT EXPOSURE TO SUNLIGHT DURING WINTER WITH FACE AND HANDS EXPOSED)	3.1 With age increasing from 5 to 11 months exposure to sunlight also increased while rickets prevalence decreased. 3.2 Infants who were more exposed to sunlight in the previous (winter) months had a lower prevalence of rickets.

TABLE 4 (continued)

Recommendations for preventing anaemia, rickets and PEM in the Sichuan Plain

Recommendations	*Rationale*
	3.3 Infants living in houses with scarce daylight had higher prevalence of advanced rickets.
(4) DEVELOP SIMPLE METHODS OF ADMINISTRATION OF VITAMIN D TO INFANTS IN THE FIRST SIX MONTHS, ACCEPTABLE TO LOCAL CUSTOMS	The intake of vitamin D supplements occurred in only 1% of infants in these communes.
(5) DEDICATE SPECIAL PRIMARY HEALTH CARE ASSISTANCE TO INFANTS WITH:	Between 5 and 11 months of age these infants were found to have:
- BIRTH WEIGHT $\leq$ 3,000 g	- lower WT/AGE.
SMALLER HOUSE SIZE, LOWER INCOME PER PERSON, LESS FARM ANIMALS	- lower WT/AGE and/or LT/AGE, WT/LT; higher prevalence of rickets in families with lower income.
(6) PROMOTE HYGIENE IN FOOD HANDLING AND IMPROVE QUALITY OF WATER SOURCES TO PREVENT MICROBIOLOGICAL CONTAMINATION OF FOODS IN THE HOUSEHOLD	6.1 48% of infants had diarrhoea during the 4 weeks before the survey. 6.2 In households using as water source irrigation canals or ponds the average number of days of diarrhoea per month in infants was more than twice that of other households. 6.3 The number of episodes of diarrhoea per month since birth was about two times higher in infants with advanced rickets than in other infants. 6.4 Infants with chronic PEM suffered a higher number of episodes of diarrhoea since birth compared to other infants.

TABLE·4 (continued)

Recommendations for preventing anaemia, rickets and PEM in the Sichuan Plain

Recommendations	*Rationale*
(7) INVESTIGATE ANAEMIA AND MICRONUTRIENT STATUS IN LACTATING WOMEN	7.1 Both IDA and NIDA were more frequent among infants breastfed for > 6 months.
(8) INVESTIGATE ON A LARGER SAMPLE THE CHARACTERISTICS OF THE NBF GROUP OF INFANTS (10% OF TOTAL), WHO APPEAR TO BE "POSITIVE DEVIANTS" FOR ANAEMIA	8.1 Infants who were not breastfeeding at the time of the study had the lowest rate of anaemia and the highest esti mated intake of iron and protein; their energy intake was 10% higher, and they suffered from diarrhoe less than infants who were breastfed in part or totally.

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Nutritional responsibilities of the food industry

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Introduction

The food processing and packaging industry and the retail food industry take very seriously their responsibility for providing consumers with good quality wholesome food, adequately labelled, as free as possible from contamination.

The industry has been successful in supplying, to consumers, an ever widening range of wholesome foods, with a longer shelf life than ever before. In recent years, however, there has been increasing criticism of the food supply in many countries. Malaysia does not yet suffer from all the excesses of other countries. Nordin and Nasir (4) surveyed the growing franchised food outlets in Malaysia and concluded that the nutritional implications of the growth of fast foods was minimal, and that `taken in moderation' the foods offered are of reasonable nutritional quality.

The term `taken in moderation', is the key to understanding the responsibility of the food industry towards the consuming public. Criticisms of the nutritional quality of some foods, which is the subject of this paper, must be taken in the context of a mixed diet where a wide range of wholesome foods can be safely consumed.

Food consumption and health have always been inextricably linked. In many countries, in recent years, the traditional concern about undernutrition has been replaced by worries about the diseases of affluence related to over-consumption and/or unbalanced food consumption patterns.

Roie of consumers, government and health related professionals

The responsibility for food consumption patterns in any country is shared by consumers, the government, health professionals and the food industry. The primary responsibility rests, of course, with consumers theselves. They can be influenced by customs, regulations, religion, advertising, packaging, prices, presentation and information from many sources but ultimately most will insist on making up their own minds about what they eat, the foods they consume.

The other players in this game, the government, health professionals and the food industry all acknowledge this and all try to influence the consumers' decisions, one way or the other.

Governments have a responsibility to set standards for food composition, quality, safety, labelling and even retail outlets. They then monitor these standards. In many cases they also advise consumers on what constitutes a healthy diet as part of a healthy lifestyle. Sometimes they influence consumers' choices by raising or lowering the price of specific food items by price control, tariffs, import restric-

tions and of course the many non-tariff barriers to trade.

Governments can also be regarded as a source of authoritative information and advice to consumers. However their primary role is to set standards. Any food which is unsafe to consume in reasonable quantities should not be sold. However if it is safe, then it should be permitted. There are no junk foods, only junk diets.

Nutritionists, dietitians and the medical profession have an important position in influencing consumers about what constitutes a balanced diet. They should give advice to consumers and where necessary, recommend changes in dietary intakes. For example, a dietitian may recommend eliminating soy sauce and added salt in the diet of a client suffering from hypertension, or recommend eliminating wheat products from the diet of a client suffering from coeliac disease. However these are not reasons for placing any restriction on the sale of soy sauce, salt or bread to the population at large.

At the same time, it places no obligation on the food processing and packaging industry to restrict the sale of soy sauce, salt or bread. It does not even demonstrate a need for nutrient labelling of prescribed foods. If the government standards specify that soy sauce shall contain 20-25% sodium chloride, table salt is almost pure sodium chloride and bread is made from wheat flour, then consumers can be aware of what they are consuming.

Likewise, health professionals may recommend decreasing excessive intakes of food, fats in general, saturated fats in particular, un saturated fats, or salt. However it is unreasonable to blame the palm oil industry of the fast food industry for unbalanced consumption patterns resulting in excessive intake of a particular food ingredient in the diet.

Ingredient labelling

The last 20 years has seen a dramatic rise in consumer interest in labelling of foods, including nutritional information and the listing of ingredients. In the United Kingdom, this has been attributed to a rising interest in diet and health as well as to the success of the media and consumer groups in convincing people that they should have more information.

One result of this trend, unforeseen by many of its proponents, is that the more detail that is required of the food processing industry, the more it will favour the large multinational companies with strong technical back-up, and the greater will be the demand for governments to step up policing to enforce the new codes, and the more it will inevitably cost the consumer. In an industry like food processing in Asia, where so many manufacturers are small operators, this will be a major concern.

The Australian experience has been that the introduction of ingredient labelling has been useful to consumers, in spite of the cost, by helping to educate them about health and food concepts. But whether ingredient labelling is compulsory or only voluntary, it is an important way for the food industry to contribute to the education of consumers about nutrition and health matters.

Many people are uneasy about extending labelling to allow health claims on any particular food item and the food industry is apprehensive about controls on the use of specific words on food labels. Such controls are difficult enough where everyone speaks the same language but could be a nightmare in a country where several languages are used.

New foods

In western countries, concern about intakes of fat, refined sugar, salt

and dietary fibre have led to the development of new foods with modified levels of these ingredients. Supermarkets now carry a range of foods labelled `low salt', `low fat', `lite', `high fibre', `no added sugar', etc. These new formulations will only survive if they are commercially and technologically successful. There is no point in marketing foods which consumers do not consume. The old adage applies that "The nutritive value of a food which is not eaten is nil". Nevertheless, the food industry has been innovative and will continue to help consumers meet dietary goals through improved formulations by both (a) developing "healthier" formulations of existing products, and (b) developing completely new formulations and products. For example, reduced fat sausages, milk, yoghurt, spreads and cheese; high-fibre ready-to-eat cereals and breads; low-sodium soups, processed meats, canned vegetables, and bakery goods; reduced calorie soft drinks and beer; and low-sugar jams and preserved fruits. In some cases, however, the changes in formulation will not significantly alter the dietary intake of the target ingredient.

For example, low-salt margarine and low-fat spreads are marketed in Australia, both with National Heart Foundation logos on the packet endorsing them as low salt and/or low-fat products. In fact the salt content of regular margarine is only about 2%, and low-salt margarine is just under 1%. Considering the modest amount of margarine which is consumed by most people, there is going to be very little contribution to salt intake from either type of margarine. Nevertheless, the food industry has shown that it is willing and able to market such new food formulations which have perceived nutritional advantages.

Salt-free bread and salt-free soup have also been marketed from time to time, `as a concession to health interests, but inevitably they bomb' (2). McBride attributes this to "bread without salt being unacceptable, the epitome of blandness, like eating cotton wool"

However salt-reduced canned foods are widely marketed. The Heinz company in Australia markets salt-reduced tuna, baked beans, spaghetti, tomato soup, tomato sauce and a few other products. Each contains 30-40% of the salt content of the regular product and commands a market share of about 20-25% of the market for the regular product. This is what McBride would call a concession to the health interests. Another such `concession' was the removal of added salt from all Heinz baby foods in cans and jars. This was done gradually, over a period of 12 years between 1970 and 1982.

The salt content of `regular' products are also modified from time to time and from country to country. The Heinz company relies on consumer surveys to establish the most desirable level of salt in it canned foods. As a result, over the last 15-20 years, the salt content of their Australian range of soups has decreased over 40%, from 1.1-1.2% to only 0.7% now.

In other products, it is not so easy. Significant decreases in the level of salt in soy sauce, fish sauce or salted fish will lead to spoilage problems because the salt acts as a preservative in the traditional method of manufacture. Likewise, in natural cheddar cheese manufacture, adequate salt is essential for the growth of the correct microorganisms, to expel moisture and for the development of the characteristic body, texture and flavour (3).

However the use of sugar substitutes provides a different picture. The use of intense sweeteners in soft drinks, and in some other products, has increased remarkably in recent years. Sugar free `diet' soft drinks with good shelf life and a stable sweet

flavour are widely available at competitive prices (4). In the USA, diet soft drinks have experienced remarkable growth. The almost negligible market segment of the early 1970's rose to 29% in 1990 and is expanding at the rate of about 2% per annum, although the total soft drink market is growing at only 1-2% p.a. A similar trend is seen in all developed countries.

In other cases, there are technological barriers to the marketing of some foods when they are made "healthier". For example, some years ago in the Philippines it was decreed that all retailers of milled rice had to also offer for sale. Brown unmilled rice which, of course, contains more of the vitamin B complex and dietary fibre. The problem was that brown rice also had a shorter shelf life, so the Philippines presidential decree had to be withdrawn.

The surface of the rice grain which is removed during milling is packed with essential nutrients. It contains about 14% protein, 20% oil and 27% dietary fibre, compared to the milled rice which contains only about 7% protein, 1% dietary fibre. Putting it another way, brown rice compared to white rice contains 0.6% more protein, 1.6% more fat and 3% more dietary fibre. However the keeping quality of brown unmilled rice is not as good as that of polished white rice.

The bottom line is that the food industry, in the long term, can only produce foods and formulations which are commercially successful. It must meet consumers' nutritional needs and government regulations, but without compromising other needs such as keeping quality and price. Products will reach consumers consistently, only if all these requirements are satisfied.

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The food industry role in health promotion

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Abstract

The World Health Organisation (WHO) has called for a population-wide approach to prevention of diet related chronic disease (Diet, Nutrition and the Prevention of Chronic Diseases, WHO, 1991). As WHO sees it, "intervention on a mass scale is needed to shift dietary patterns....". While public health agencies have made great progress in influencing consumer knowledge of diet and health issues, the active involvement of the privte sector is essential to achieving recommended behaviour change.

Food companies contribute to improvements in dietary habits by developing products consistent with dietary guidelines, educating consumers about the elements of a healthy diet and the role fo their products in that diet, and by providing easy access to information consumers need to make wise food choices

The author will outline nutrition policies of the Kellogg Company, the world's leading cereal company, and describe innovative approaches to promoting good nutrition in the U.S., Canada, Japan, U.K., France and other countries.

Programmes cited promote the importance of a healthy diet, specifically breakfast nutrition, and address three major nutrition issues: (1) Increasing consumption of dietary fiber, (2) Decreasing consumption of fat and cholesterol, and (3) Managing diabetes.

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Nutritional supplements and their role in health promotion: an industry viewpoint

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Introduction

One of the strongest health messages to emerge in the last two decades is that of personal responsibility for one's health. In this spirit of self-responsibility, many individuals have chosen to use nutritional supplements. This raises a number of questions. Are vitamin and mineral supplements necessary? What is the supplement industry doing to promote health? Do supplements offer any benefits in terms of disease prevention and health promotion?

The need for supplementation

Dietitians, doctors, and other health professionals typically instruct their patients that nutritional supplements are not necessary. Essential vitamins and minerals should be obtained from foods, rather than from supplements. However, there are some circumstances where supplements may be indicated: during pregnancy and breastfeeding, in women with excessive menstrual bleeding, for people on very low-calorie diets, for strict vegetarians, and in certain medical conditions or treatments (1).

Ideally, everybody would choose a well-balanced diet and eat a wide variety of foods. Realistically, people eat whatever they like! Taste, convenience, and speed often take precedence over good nutrition. As a result, many people in Western societies fail to meet the dietary recommendations designed to protect their health.

In the United States, the Surgeon General's Report on Nutrition and Health and the National Research Council's Diet & Health Report provide specific dietary guidelines which are believed to have the potential for reducing the risk of chronic diseases (2, 3). But the typical American diet does not come close to meeting these guidelines.

Instead of eating 5 or more servings of fruits and vegetables each day, Americans eat about 1.3 servings. Three out of four eat **no** beta-carotene or vitamin C-rich fruits or vegetables on any given day (4). Less than 25% of teenagers and adult females consume the recommended amounts of calcium (1). And fewer than one out of five Americans eats any breads, cereals, or legumes which are rich in dietary fibre (4).

These examples demonstrate that having a safe, abundant, and affordable food supply does not guarantee that individuals will choose the right foods to meet their nutrient needs. For those who cannot or will not select a proper diet, nutritional supplements are a convenient way to replace the vitamins, minerals, and fibre which may be missing. This does not imply

that supplementation is an excuse for eating a poor diet!

The supplement industry and health promotion

No responsible member of the supplement industry would argue that pills alone can correct the nutritional problems that exist in modern societies. Nor would anyone claim that supplements promote health in the absence of other lifestyle modifications. Supplementation should properly be viewed as one of several components of a health promotion strategy.

Nutrilite Products, Inc., a subsidiary of the Amway Corporation, has been manufacturing nutritional supplements products, exercise equipment, smoking cessation and weight control programmes into one broad Health & Fitness programme to meet the needs of its customers and employees. Customers select the products which best meet their needs, based on their individual lifestyles and health habits.

As a whole, the supplement industry has performed a valuable service by making people more aware that what they eat, or don't eat, directly affects their health. Responsible manufacturers and suppliers are committed to using sound science to formulate and market their products, and they are striving to increase their creditability within the scientific community.

Potential benefits of supplementation

The relationship between the intake of certain nutrients and the incidence of cancer, heart disease, and other chronic diseases is topic of great interest. Epidemiological evidence suggests that low intakes of the antioxidant nutrients (vitamin C, vitamin E, β-carotene, and selenium) are associated with higher rates of disease (5).

In dozens of clinical trials around the world, human subjects are swallowing vitamin, meneral, or fibre supplements to evaluate their effectiveness in preventing or slowing the development of chronic diseases (6). Some researchers have stated that there is no reason to wait until the trials are completed to consider supplementation, given the potential benefits and the absence of risk from moderate dosages (7, 8).

Conclusion

The future looks exciting for the science of nutrition. Genetic predispositions to chronic disease may be discovered early in life and susceptible individuals treated with very specific diets. Perhaps the purpose of the Recommended Dietary Allowances will be expanded beyond prevention of nutrient deficiencies to include promotion of health (8). Supplements, fortified foods, and dietary manipulation may play a greater role not only in increasing the lifespan, but enhancing the quality of life.

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Improving the iron fortification of foods

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Four major factors govern the amount of iron absorbed from an iron fortified food. These are the iron fortification compound used, the amount of iron added, the presence of enhancers or inhibitors of iron absorption in the meal, and the iron status of the consumer. The best prospects for improving the absorption of fortification iron are the optimisation of the iron fortifiation compound used, the addition of absorption enhancers, and the removal of absorption inhibitors.

Iron Compounds

Iron absosrption by human subjects from different fortification compounds can vary considerably. Table 1 shows the major iron compounds used in food fortification. They can be divided into 3 groups: (a) those that are freely water soluble, (b) those that are poorly water soluble but readily soluble in dilute acids and (c) those that are insoluble in water and poorly soluble in dilute acids. As the absorption of fortification iron depends firstly on its solubility in the gastric juice, those freely water soluble compounds, such as ferrous sulphate and ferrous gluconate, and those compounds that are readily soluble in dilute acids, such as ferrous fumarate and ferrous succinate, are better absorbed than the compounds which are poorly soluble in dilute acids, such as elemental iron powders and the iron phosphates. Ferrous sulphate dissolves instantaneously in the gastric juice whereas some elemental iron powders may never dissolve completely.

Bioavailability however is ony one of the criteria used to select an iron compound for food fortification. Possible adverse organoleptic changes are another major consideration in the food industry. There is unfortunately a strong relationship between bioavailability and adverse organoleptic changes and those freely water soluble compounds which are the most bioavailable often cause unacceptable colour and flavour changes. The more insoluble compounds are usually inert organoleptically but poorly absorbed.

Food manufacturers are obliged to fortify foods with inert iron compounds (1). Infant cereals are most commonly fortified with elemental iron, ferric pyrophosphate and ferrous fumarate. Some European companies occasionally use ferric orthophospate and ferric sacccharate. Chololate drink powders contain iron fortificants such as ferric pyrophosphate, ferric saccharate and ferrous fumarate. Wheat flour, other grain flours, and breakfast cereals usually contain elemental iron powders. Ferric pyrophosphate has been used to fortify rice and ferric orthophosphate has been added to salt.

Many studies have been made in rats and some in man to evaluate the

TABLE 1

Iron compounds used in food fortification (compiled from references 2-5)

Iron compound		Relative bioavailability		Commonly fortified foodstuff
		Rat	Man	
(a)	*Freely water soluble*			
	Ferrous sulphate	100	100	Infant Formula
	Ferrous gluconate	97	89	–
	Ferric ammonium citrate	107	–	–
(b)	*Poorly water soluble/ soluble in dilute acids*			
	Ferrouss fumarate	95	100	Infant Cereal
	Ferrous succinate	113	92	–
	Ferric saccharate	92	74	Infant Cereal, Chocolate drink powders
(c)	*Water insoluble/poorly soluble in dilute acids*			
	Ferric pyrophospate	45	21,39,74	Infant cereals, Chocolate drink powders
	Ferric orthophosphate	6-46	25,31	Infant cereals, salt
	Elemental Iron	8-76	5-90	Wheat flour, breakfast cereal, infant cereal

relative bioavailability of iron compounds (Table 1). As the absolute absorption of a single compound in man can vary from less than 1% to almost 100%, depending on the iron status of the consumer and the presence of absorption inhibitors and enhancers, bioavailability is usually measured relative to ferrous sulphate which have designated a relative bioavailability (RBV) of 100. It has recently been demonstrated that the haemoglobin repletion test in rat is a good predictor of the RBV of fortification iron compounds in man (2). All freely water soluble compounds have RBV values in rat and man at or around 100. Those iron compounds readily soluble in dilute acid have RBV values from 75-100, whereas those compounds poorly soluble in dilute acids normally have RBV values less than 50 but more importantly they give very variable RBV values. Elemental iron powders for instance have given RBV values from 5-90 in man.

Using radiolabelled compounds, ferrous fumarate has recently been shown to be as well absorbed as ferrous sulphate from infant cereals (3). In the same study, ferrous succinate had an RBV of 92, ferric saccharate an

RBV of 74 and ferric pyrophosphate an RBV of 39. Fortification of infant cereals can thus be improved by changing from ferric pyrophosphate to any of these alternative iron compounds which can be added to standard cereals without causisng organoleptic problems. Unfortunatley, ferrous fumarate does cause colour problems in some infant cereals (e.g. with banana) and it cannot be used to fortify wheat flour as it provokes fat oxidation during storage.

Improving the absorption of fortification iron

Despite the high RBV of ferrous sulphate and ferrous fumarate, the absolute absorption of these compounds is only around 4-5% by infants receiving iron fortified formulas or cereals (6, 7) due to the presence of inhibitors. Absorption of fortification iron can be increased in infant foods and other fortified foodstuffs by either using "protected" iron compounds, adding ascorbic acid, or removing the absorption inhibitors.

Protected iron compounds

The most promising compound is NaFe EDTA (8). Although iron is less well absorbed from this compound than from ferrous sulphate in food containing few inhibitors of absorption, it is 2-4 fold better absorbed from foods containing strong absorption inhibitors such as cereals (9). Several pilot fortification trials with this compound have resulted in an improvement in iron status (10). EDTA is a strong chelator, however, and there are some concerns over its influence on the metabolism of other minerals such as Zn, Cu and Ca. A small fraction of EDTA (0.5%) is absorbed and excreted in the urine, while the majority passes through to the stools (11). Sodium iron EDTA would seem a particularly useful compound to fortify cereals and other foods in developing countries where iron deficiency is widespread. A major obstacle to its use, however, is legislation. While sodium EDTA is an accepted additive in many countries such as the USA, NaFe EDTA is not. This is, not because of fears for its safety, but because the intake of EDTA is already close to the permitted acceptable daily intake (2.5mg/kg/day). This is of no concern to developing countries.

Ascorbic acid

The most effective way of improving the iron fortification is by adding ascorbic acid. This substance increases the absorption of all fortifcation iron compounds in a dose dependent fashion (12), including the more insoluble compounds such as ferric pyrophosphate (12), elemental iron and feric orthophospate (2). Adding increasing amounts of ascorbic acid to a milk-based infant formula containing 15mg iron as ferrous sulphate increased iron absorption by human infants almost 3-fold (13). It should be noted that ascorbic acid can be considerably destroyed during preparation of the food (14) and during prolonged storage.

Removal of inhibitors

Phytic acid is the major inhibitor of iron absorption present in cereals and legumes and its removal would substantially increase iron absorption from these foods (24,25). Hallberg and co-workers (24) reported that a bread roll containing white wheat flour and bran gave an iron absorption in man of 4.2% with ordinary bran, and 23.9% with dephytinized bran. We have recently prepared phytate-free soy protein isolate than with a normal isolate (25). Fermentation is a more traditional way to remove phytate from cereals and legumes (26). Phytases are now available commercially and the production of phytate-free soy formulas and infant cereals would seem to be technically possible.

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Food labelling, health claims and the law

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Introduction

To set the stage, it is essential to make it clear what we are actually talking about today. First, I will be reviewing nutritionally-related aspects of food labelling. The core of such aspects is nutrition labelling which specifically involve nutritional matters, including ingredient labelling, adjectival descriptors such as "low calorie", labelling of foods for special dietary uses such as infant formulas, warning labelling, and last but not least, so-called "health claims" or "health messages". These latter label statements are in fact disease-specific claims, referring to reduction of risk of such disease states as heart disease, hypertension, and osteoporosis. The second part of my talk will focus on these types of claims. Throughout the talk, I will try to weave in the implications of law, both in the U.S. and briefly in international terms.

Before getting into the details of my specific topics, a bit of history might prove useful. Originally, the concept of nutrition-specific labelling got a huge boost from the introduction of nutrition labelling in the U.S. in 1971. i.e., 20 years ago. The original purposes were two-fold: (a) to provide the consuming public with information on the nutritional characteristics of packaged food; and (b) to stimulate the "nutrition conscience" of the food processing industry. Both worked. The public rapidly became familiar with the existence of nutrition labelling, even if some of the information was too complex for many to understand with precision. In the U.S. today, about two-thirds of packaged foods bear such labelling, the majority on a voluntary basis by industry. Major food processors indeed did develop a "nutrition conscience" and over the years have made great strides in improving the nutritional quality of thousands of different foods, and in instituting quality assurance programmes to be sure that the claimed nutritional quality is consistently maintained.

However, the basic purpose has changed to some extent during the last decade with the introduction of **Dietary Guidelines for Americans**. These first appeared in 1980, and have now been revised twice in 1985 and 1990. In a recently passed law, U.S Congress now requires that these Guidelines be updated every 5 years. In today's world, the fundamental purpose of nutrition-related labelling is to support the Dietary Guidelines—no longer simply a matter of describing the nutritional characteristics of individual foods. All of the Guidelines are for purposes of maintaining good nutritional health and of reducing risk of chronic, diet-related degenerative diseases. The 1990 Guidelines are as follows:

1. Eat a variety of foods
2. Maintain healthy weight

3. Choose a diet low in fat, saturated fat, and cholesterol
4. Choose a diet with plenty of vegetables, fruits, and grain products
5. Use sugars only in moderation
6. Use salt and sodium only in moderation
7. If you drink alcoholic beverages, do so in moderation

In 1990, Canada issued its first Guidelines for Healthy Eating which are as follows:

1. Eat a variety of foods
2. Emphasise cereals, breads, other grain products, vegetables and fruits
3. Choose low-fat dairy products, lean meats, and foods prepared with little or no fat
4. Achieve and maintain a healthy body weight by enjoying regular physical activity and healthy eating
5. Limit salt, alcohol and caffeine

Nutrition labelling

Now, I would like to focus on nutrition labelling itself. The original U.S. proposal was published in 1971, and industry could implement such labelling at that time. The final regulations are still in effect, but will change by 1992 to comply with the most significant nutritionally-related legislation ever passed - The Nutrition Labelling and Education Act of 1990, signed into law by President Bush. Current nutrition labelling is voluntary unless nutrients are added to the food or specific nutrition claims are made. About 60% of existing labelling is voluntary; 40% mandatory because of fortication or claims. If the food is labelled, it must contain all of the following information (except as noted):

Heading: Nutrition Information

Serving size: in ordinary household measures, or per unit (such as a slice)

Servings per container:
Macronutrients per serving:
calories
protein (grams)
carbohydrate (grams)
fat (grams)
fatty acids (optional- in grams as saturated & polyunsaturated)
cholesterol (optional-mg.)
fibre (optional-grams)

Micronutrients per serving (all as % of the USRDA):
vitamin A
vitamin C
thiamin
riboflavin
niacin
calcium
iron
other vitamin & minerals (optional)

The new law changes things substantially, the emphasis shifting from nutrition parameters intended to minimise risk of deficiency diseases to reduction of risk of degenerative diseases. In addition, nutrition labelling as of 1992 becomes mandatory for all packaged foods, except meat and poultry products, regulated by the United States Department of Agriculture (USDA), and spices and flavourings. The mandatory content of the new labels is as follows:

1. Total calories and calories derived from fat
2. The amount of the following nutrients:
   total fat (grams)
   saturated fat (grams)
   cholesterol (mg)
   sodium (mg)
   total carbohydrates (grams)
   complex carbohydrates (grams)
   sugars (grams)
   dietary fibre (grams)
   total protein (grams)
3. Any vitamin, mineral or other nutrient as determined by the Secretary of Health and Human Services (HHS)

Some may argue that this is excessive and that the science base for some of the required declarations is not solid, e.g., the requirement for sugar declaration. But, the law is the law, and it must be implemented and enforced. I might add that changing a law in the U.S. is extraordinarily difficult, so we will have this type of labelling for a long time. One other problem with the law is that it puts the U.S. out of step with most of the rest of the world to one degree or the other. This is going to create problems for the worldwide effort towards free trade. I suppose, with difficulty, we will get around this problem somehow.

As I'm sure most of you are aware, the Joint FAO/WHO Codex Alimentarius Commision (the "Codex") has a Committee on Food Labelling, chaired by Canada. In 1985, this Committee completed development of the Codex Guidelines on Nutrition Labelling, and the Guidelines were approved by the Codex Commission. Hence, under international agreement, we are all obliged to consider these Guidelines, which are as follows:

1. Content (per 100 grams or serving):

   energy value; protein; available carbohydrate; fat

   other nutrients deemed important nationally or when claims are made

2. Should be mandatory if claims are made; otherwise voluntary

3. Should list nutrients only if present in significant amounts (>5% RDI/serving) (vitamins and minerals listed in metric units or % RDI)

The discrepancies between the elaborate U.S. scheme and the Codex approach are obvious. The U.S. Food and Drug Administration (FDA) currently is frantically trying to draft and publish regulatory proposals to implement the new law—all of which is supposed to be completed by 1992. The task is virtually overwhelming, and I have enormous sympathy for my former staff in nutrition at FDA. I guess I was lucky to decide to retire two years ago.

One final part of nutrition labelling per se in the U.S. is the 1991 proposal by USDA for labelling of meat and poultry products. In the past, USDA has permitted an abbreviated form of FDA-type labelling for such products, and about one-third are so labelled in the marketplace. Although USDA is not directly affected by the Nutrition Labelling and Education Act of 1990, their new proposal is basically in response to the Act and public interest in more labelling. This proposal is as follows:

1. Similar to FDA's proposal
2. Would require:

   macronutrients: calories; calories from fat;

   total protein; total carbohydrates.

   micronutrients: sodium; calcium; iron; vitamin A;

   vitamin C
3. USDA questions the appropriateness of the following and

   requests comments:

   complex carbohydrates

   sugars

   fibre

It is worthy of note that the National Advisory Committee on Meat and Poultry Inspection advised USDA in June 1991 that it does not seem necessary for labelling of meat and poultry products to be required to declare the amounts of complex carbohydrates and sugars, fibre, and vitamin C, largely because such products usually contain little or none of these components. The Committee also felt that it was not in the public interest to declare total saturated fatty acid content, because the scientific base for lumping all the saturated fatty acids

together as if they were one metabolic entity lacked a firm, consensus in light of recent research on such fatty acids as stearic and palmitic acids. This is in spite of the mandatory provisions for these declarations for FDA-regulated products found in the recent Congressional Act.

Before turning to other nutritionally-related aspects of food labelling, it would seem appropriate to briefly describe the rather curious "separation of powers" that we have in this regard in the U.S. FDA has legal responsibility for labelling of all foods except meat and poultry, and FDA's basic philosophy is based on public health needs and scientific consensus. USDA has legal responsibility for promotion of agricultural products from the farm to ultimate consumer consumption, including exports. In a sense, USDA has two bosses, i.e., the general public and the industry. FDA has no promotional responsibilities for the industries which it regulates. Lastly, and most curiously, the Federal Trade Commission (FTC) has legal responsibility for all food advertising in the U.S., and its basic philosophy is quite different, focusing on fair trade practices. In addition, FTC does not require scientific consensus to exist for nutrition-related claims to be made, so long as there is some kind of substantiation for the claim. This obviously creates a degree of inconsistency between what the consuming public find on food labels as contrasted with what they read in newspapers or see on the television.

Ingredient labelling

Ingredient labelling is important to consumers from a nutrition point of view. For example, many individuals read the ingredient statement to figure out if there is a significant amount of sugar or salt in the food because of their desire to minimise such consumption. As you will recall, moderation of intake of these ingredients is explicitly called for in the Dietary Guidelines. There are four key points worth mentioning:

1. The 1990 Act requires full ingredient labelling of all foods regulated by FDA except for spices and flavourings. This means that all standardised foods must now bear such labelling in addition to non-standardised foods as has been required in the past. This overturns an old regulation which stated that mandatory ingredients in standardised foods did not have to be declared, e.g., flour in bread or eggs in mayonnaise. This is a good provision of the new Act.

2. FDA's 1991 labelling proposal retains the somewhat controversial provision to allow so-called "and/or" labelling of fats and oils. This practice permits the manufacturer to label "vegetables oils (may contain soybean oil, corn oil, palm oil, and/or coconut oil)" or similar statements. It is allowed because manufacturers very frequently change the mixture of oils used to attain specific technical properties in the finished food, depending primarily on market price. If this type of labelling were not permitted, manufacturers would have to change labels very often, the ultimate cost being borne by the consumer with little or no health benefit.

3. All ingredients are listed in descending order of predominance. However, FDA developed a policy in 1989 which permits ingredients at the end of the list that are present in very small amounts to be lumped together as each being present at <2% by weight. This has the advantage of highlighting the major ingredients as well as making it clear that the minor ingredients are in fact minor.

4. FDA will probably propose in 1991 that the ingredient list be preceded by the statement "from most to least". This would be helpful

because many consumers do not know that the list is in descending order of predominance.

Adjectival descriptors

Adjectival descriptors are the most important component of nutrition-related labelling. The most important element is that they be clearly and quantitatively defined on a sound scientific and public health basis. In the U.S., we are about half-way in establishing such definitions by regulation. Definitions are already on the books for calories ("low" and "reduced") and sodium (low"; "very low", "reduced"; and "free"). With luck, by the end of 1991, FDA will finalise its proposal for cholesterol ("low"; "reduced"; and "free). The biggest problem ahead is defining the meanings of "low" and "reduced" fat and saturated fat. This is very controversial, particularly at the industry level. To illustrate the problem, there have been individual definitions for "low fat" dairy products for many years. However, if one applies these definitions to meats, virtually none would qualify. A possible alternative for meat and poultry products is to develop a different set of definitions that would describe degrees of leanness, and simply not use "low" or similar terms on these products. This issue is further compounded by the fact that the new Act requires that FDA develop regulations to define a whole series of definitions applicable to a whole range of nutrients and other food components, including definitions of "free"; "low"; "light" or "lite"; "reduced"; "less"; and "high". The definition of "high" is particularly troublesome, e.g., from a biomedical point of view, how much fibre and what kind of fibre could be stated to be "high" in labelling? It is also worthy of note that there is considerable interest internationally in these adjectival descriptors, particularly in the Codex Committee on Food Labelling and the Codex Committee on Nutrition and Foods for Special Dietary Uses. It seems to me that there has to be some sort of international agreement on these definitions to facilitate world trade in packaged foods.

Foods for special dietary use require highly specialised labelling, and I do not intend to go into detail on this aspect. I simply want to bring to your attention two basic points. In the biomedical field, laws are often very difficult to deal with, if for no other reason than the science base changes rapidly. Foods for special dietary use are no exception. With the passage of the two Infant Formula Acts of 1980 and 1986, FDA has now promulgated 23 regulations to date to implement the law, about a third of which relate to labelling, and the task is not completed yet. There remain to be completed regulations that, for example, relate to microbiological safety criteria. A curious related matter in the U.S. is the complete absence of any regulations for medical foods, which are very similar as life support systems to infant formulas. I am delighted however with the positive steps taken by the Codex Alimentarius wherein at their July 1991 meeting they approved as final the Standard for Foods for Special Medical Purposes developed by the Codex Committee on Nutrition and Foods for Special Dietary Uses over the past 6 years. This is basically a labelling standard which should stimulate the U.S. and other countries to develop their own regulations based on the Codex Standard.

Warning labelling

Warning labelling is another type of labelling that relates to nutrition in some instances. In the U.S., there are only 5 warning or alert-type labelling regulations, 3 of which concern nutritional health. The Congress decided over a decade ago that, rather than ban saccharin as a possible human

carcinogen, foods containing saccharin must bear a warning label alerting the consumer that saccharin has been shown to cause cancer in some laboratory animals. After a number of deaths in the late 1970's in obese individuals consuming protein-based very low calorie diets for extended periods (i.e., diets providing less than 400 kcal/day), FDA finalized a regulation requiring warning labelling on such products, alerting the consumer to the need for strict medical supervision when such diets are used. The exact mechanism of deaths has not been established, but the deaths themselves were due to sudden ventricular tachycardia. Lastly, when aspartame was approved as a sweetener, it was essential to warn patients with phenylketonuria and their families that the sweetener contains phenylalanine, the intakes of which must be kept to a minimum in such patients. This is accomplished by a simple warning statement on all aspartame-containing foods. The only other warning labels present on foods are: (1) for foods containing sulfites (specifically canned and dehydrated fruits and vegetables; wines; and a pending proposal to ban use of sulfites on fresh potato products) because of a series of precipitious deaths from anaphylactic shock in exquisitely sensitive individuals; and (2) a label statement to alert consumers that a food has been exposed to ionizing radiation. Such foods are perfectly safe, but the consuming public still has a fear of radiation generally, so they have a right to know that a food has in fact been radiation-exposed. In reality, virtually no such products exist in the U.S. presently, but my prediction is that such foods will slowly enter the marketplace in the years ahead, because there are so many potential advantages for prolongation of shelf-life.

Before turning to the last major topic of this presentation concerning health claims in labelling, I would like briefly to describe FDA proposals issued in 1990 that are directly concerned with nutrition labelling, but are independent of the requirements of the 1990 Congressional Act. The U.S. Recommended Daily Allowances (USRDA's) were created in 1971 as part of the original nutrition labelling regulation as a simplified version of the Recommended Dietary Allowances (RDA's), specifically for labelling purposes. FDA has now proposed two new types of reference values for labelling:

1. To replace the USRDA's:

   Reference Daily Intakes (RDI's) - to directly replace the USRDA's

   Daily Reference Values (DRV's) - to replace "Estimated Safe and

   Adequate Daily Dietary Intakes" (which

   were a set of ranges for such nutrients as

   sodium, biotin, and molybdenum)

   It is virtually impossible to deal with nutrients in terms of ranges on labels, so these new DRV's will be most helpful if finalized by FDA as proposed.

2. Standardised serving sizes for all common foods. Although this sounds simple on the surface of it, this proposal is proving to be very controversial, primarily because industry does not want to be "locked in" to such standardised serving sizes. To me, they are making a mountain out of a mole hill. It seems to me that they can declare any serving size they want so long as the nutritional content is expressed in terms of a standardised quantity of the food. It also makes sense to me to declare nutritional content in terms of some reasonable amount usually consumed by individuals rather than per 100 grams for everything, which seems to be preferred by

many countries for reasons I have never understood.

Health claims

Finally, let me turn to the matter of disease-specific claims and the law. Relative to labelling, the Federal Food, Drug and Cosmetic Act (FD&CA) remained little changed over the years since 1938 until passage of the Nutrition Labelling And Education Act in 1990. Nevertheless, the FD&CA has been reinterpreted significantly from time to time. Prior to 1970, FDA prohibited any form of nutrition-related claim in food labelling (except for foods for special dietary use). The White House Conference on Food, Nutrition and Health organized by President Richard Nixon in 1969 substantially changed this status quo, and we entered the era of "implicit health claims" consisting primarily of nutrition labelling and the use of adjectival descriptors such as "reduced calorie". Still, there was no mention of specific diseases, because it was generally accepted that disease-specific claims would render the product a drug.

Then, the food labelling world precipitously changed in October 1984 when the Kellogg Company, in cooperation with the National Cancer Institute (NCI) of the National Institutes of Health (NIH), made on its own initiative specific claims on several high fibre cereals inferring a link between high fibre intakes and reduction of risk of certain cancers. It is fair to say that this caught the Government off guard, and the basic question arose as to whether we should practice preventive medicine on the back of the cereal box or elsewhere in labelling. Soon afterwards, numerous other firms entered the disease-specific labelling arena and the subjects expanded to include calcium and osteoporosis, fat and heart disease, sodium and hypertension, etc. A perception arose to the effect that FDA wasn't going to do much about it. Much public debate surfaced, and in 1987, FDA issued an "Advance Notice of Proposed Rulemaking" concerning "health messages". This laid out a number of options for public comment. Finally, in February 1990, FDA issued a Reproposed Rule on "health messages". This proposed a number of criteria which must be met to avoid false or misleading claims, e.g., "The label statement is consistent with generally recognised medical and nutritional principles for a sound total dietary pattern". This proposal also laid out a multicomponent and rather complex scheme on how to reach a satisfactory consensus on what would be appropriate for label claims. The proposal specifically identified six topics deemed appropriate for possible labeling claims: (1) calcium and osteoporosis; (2) dietary fibre and cancer; (3) lipids and cardiovascular disease; (4) lipids and cancer; (5) sodium and hypertension; and (6) dietary fibre and cardiovascular disease.

Then, somewhat unexpectedly, Congress passed and President George Bush signed into law the Nutrition Labelling and Education Act of 1990 in November 1990, to which I have referred earlier. The provisions of the law as they relate to disease-specific claims are as follows:

1. The Act significantly modifies most of the FDA proposals made earlier in 1990, requiring reconsideration of many specific topics by FDA.

2. The Act retains the original six disease-specific topics, and adds four more:
   (a) folic acid and neural tube defects
   (b) antioxidant vitamins and cancer (such as ß-carotene and vitamin E)
   (c) zinc and immune function in the elderly
   (d) omega-3 fatty acids and heart disease

3. The Act requires the Secretary of Health and Human Services (HHS) to consider separate rules for "health claims" for dietary supplements of vitamins, minerals, herbs or other similar substances.
4. The Act requires establishment of a formal public petition process for issuing regulations for "health claims" for other new topic areas.
5. The Act establishes very rigid time requirements for FDA to propose and finalise all of the implementing regulations—a task which for practical purposes must be completed by the end of 1992.

I have no idea where this is all going to end up. One way or the other, there will be some form of disease-specific claims on food labels in the future that has the blessing of the Government, but the nature and depth of such claims is unclear. On the one hand, the Act implies quite strict control by FDA and the Department of HHS over any disease-specific claims. On the other hand, it adds four more topics most of which can be considered to be in the area of continuing biomedical research without solid consensus. In addition, it implies a looser control over dietary supplements—an area which has been most troublesome for FDA for many years. All of this, including the other areas discussed earlier, is taxing FDA resources virtually to the breaking point, and the tight time constraints for proposals and final orders is most difficult to attain, given the complexity of public rulemaking. FDA has contracted with the Life Sciences Research Office (LSRO) of the Federation of American Societies for Experimental Biology (FASEB) to prepare reviews of the total of 10 disease-specific areas stipulated in the law. This too will take substantial time, although they are progressing well at present. FDA currently plans to issue its proposal for disease-specific claims in late 1991. Both the earlier FDA proposals and the new Act have made industry more cautious about making disease-specific claims for the moment, but it remains to be seen how long this will last. It is also reasonable to anticipate that efforts by FDA and the Department to finalize these rules will be contested in Federal courts. Hence, the decade of the 1990's will be a controversial one relative to the use of the label of conventional foods as a means of giving advice to the public on dietary means of reducing risk of degenerative and other diet-related diseases.

I realise this has been a rather detailed presentation on the nutrition-related aspects of food labelling, health claims and the law. It is a complex set of topics, and it seems to me that providing a reasonable amount of detail is the only way to make the topics make sense.

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Response of the Australian meat industry to changing nutrition issues

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Abstract

Beef and lamb have long played a part in Australia's history. Since the arrival of the First Fleet in 1988, they have remained prominent foods in the developing food culture. In the late 1970's nutrition issues came to the forefront of pressional, media and consumer interest, particularly the issues regarding excess fat consumption. Australians being high red meat consumers, beef, lamb and mutton became a scapegoat for criticisms about their fat intake. The industry was hampered in its activities to curb such criticisms, as up-to-date compositional data for Australian meat was unavailable. Also any attempt by an industry organisation to provide factual information supporting its product is usually received with extreme cynicism. With these problems being recognised, the meat industry has confronted the nutritional problem across a comprehensive front. This paper outlines the industry's response, led by the marketing activities of the Australian Meat and Live-stock Corportion, to address these changing social and nutritional issues. Today, beef and lamb are seen by Australians as modern, innovative