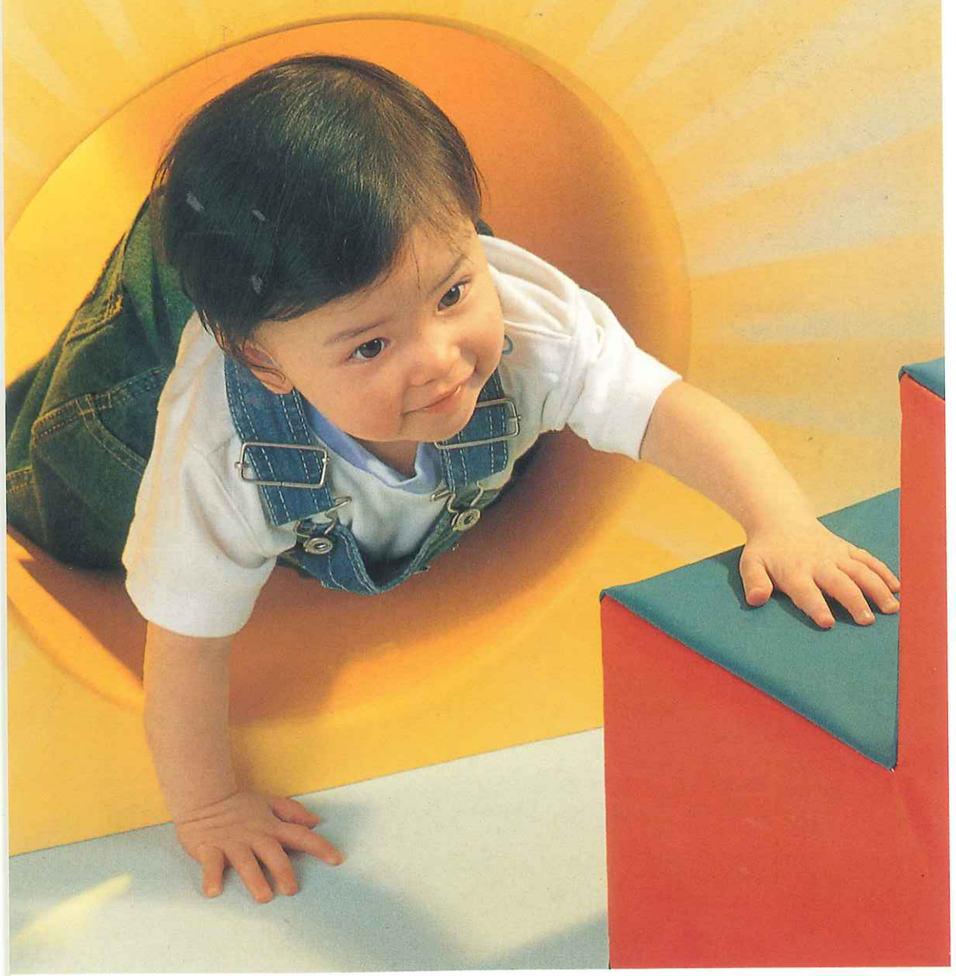






THE SINGAPORE JOURNAL OF

# Nutrition & Dietetics

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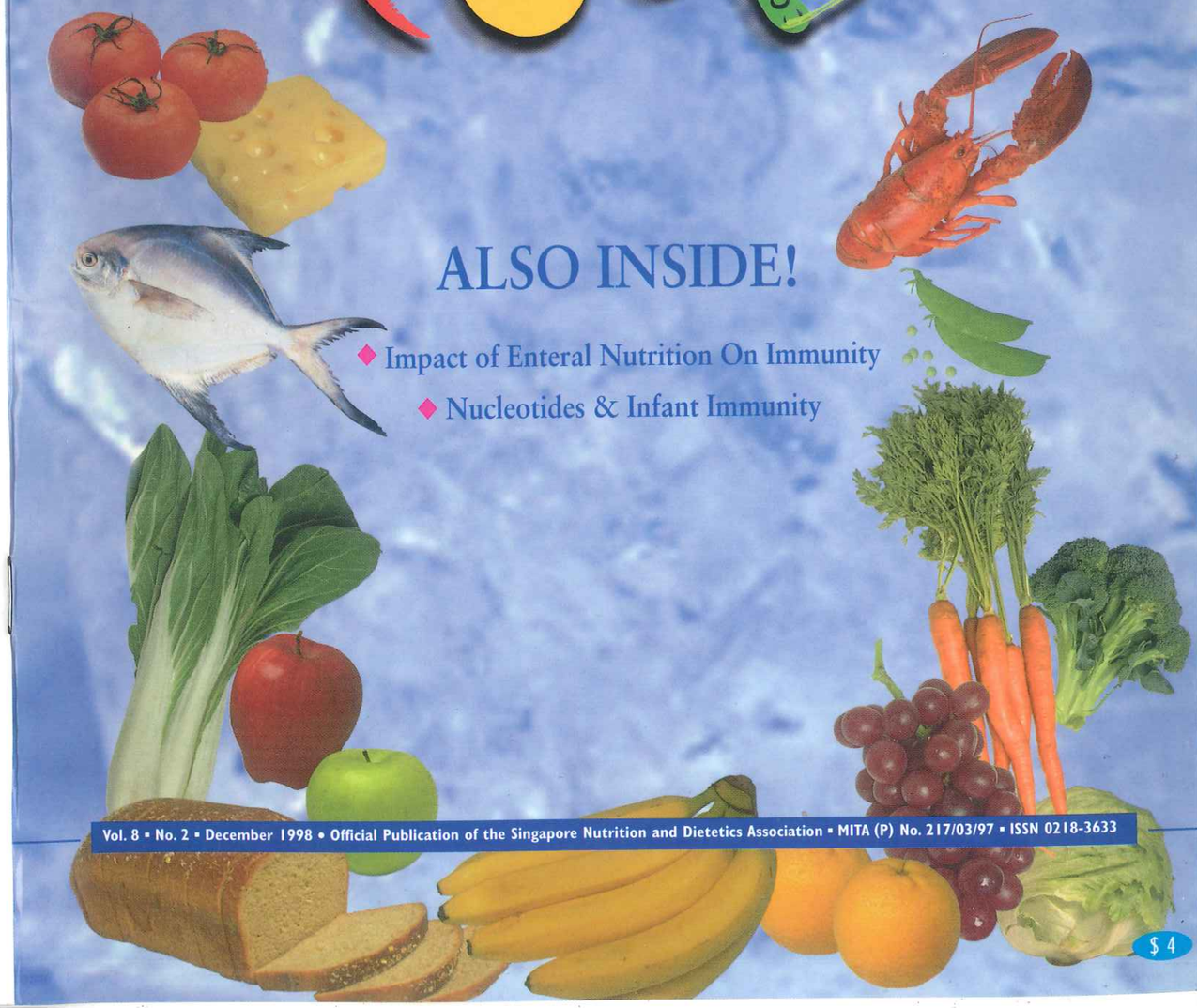
## FUN WITH FOOD



## ALSO INSIDE!

- Impact of Enteral Nutrition On Immunity
- Nucleotides & Infant Immunity

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# Editorial

Functionality of foods is gaining importance. The race to identify the functional ingredients in food, their action and efficiency is on. The information generated present challenges to regulators and health professionals. Nutrition professionals are pressed to keep up with new information, evaluate the outcomes and harness the benefits in a responsible manner.

This bumper issue of the annual Singapore Journal of Nutrition and Dietetics comes to you packed with 'cutting edge' nutrition news. Three articles focus on the immune-enhancing properties of nucleotides in two population groups – the young infant and the severely ill. Also included is a road map of the changes in the US RDA to date with easy summary tables for your reference and a brief announcement of the new soy protein health claim that will hit the consumer market soon.

To keep you updated with news on the home front is the Nutrition News and Abstracts Sections. Reports on two landmark nutrition conferences near home: The Asian Congress of Dietetics and The Asian Conference on Early and Childhood Nutrition will give you a snapshot of the events.

Hope you enjoy this Journal brought to you by the kind support of our sponsors: Nestle Singapore Pte. Ltd, Novartis Nutrition Singapore Pte. Ltd and Abbott Laboratories Singapore Pte Ltd Input, feedback and support from readers will be greatly appreciated.

On behalf of the Editorial Team, I take this opportunity to wish all readers a happy, prosperous and professionally rewarding New Year ahead.

*The Editor, Leow Sooi Mee*
*& The Editorial Committee*




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FEATURE ARTICLE

# A PROSPECTIVE, RANDOMIZED, DOUBLE-BLIND, CONTROLLED CLINICAL TRIAL OF ENTERAL IMMUNONUTRITION IN THE CRITICALLY ILL

Simon Atkinson, FRCS; Edith Sieffert, RN; David Bihari, FRACP;
on behalf of the Guy's Hospital Intensive Care Group*

*Objective:* To assess the effects of enteral immunonutrition (IMN) on hospital mortality and length of stay in a heterogeneous group of critically ill patients.

*Design:* Prospective, randomized, double-blind, controlled clinical trial with an *a priori* subgroup analysis according to the volume of feed delivered in the first 72 hrs of intensive care unit (ICU) admission.

*Setting:* A 13-bed adult general ICU in a London teaching hospital.

*Patients:* A total of 398 patients were enrolled and data from 390 patients (IMN = 193, control = 197) were used for an intention-to-treat analysis. There were 369 patients (IMN = 184, control = 185) who actually received some enteral nutrition, of whom 101 patients (IMN = 50, control = 51) received >2.5 L within 72 hrs of ICU admission. This latter group was defined as the successful "early enteral nutrition" group.

*Interventions:* Within 48 hrs of ICU admission, patients were randomized to receive either the IMN Impact® (Novartis Nutrition), an enteral feed supplemented with arginine, purine nucleotides and ω-3 fatty acids, or an isocaloric, isonitrogenous control enteral feed.

*Measurements and Results:* There was no significant difference in hospital mortality rate between the two groups on an intention-to-treat analysis (Impact group 48%, control group 44%) nor in any other predefined subgroup analysis. However, patients randomized to receive the IMN had higher Acute Physiology and Chronic Health Evaluation II scores (20.1 ± 7.1 vs. 18.7 ± 7.1 [$p = .07$] intention-to-treat [n = 390]; 20.1 ± 7.2 vs. 18.5 ± 7.1 [$p = .04$] received feed [n = 369]). Of the 101 patients achieving early enteral nutrition, those patients fed with the IMN had a significant reduction in their requirement for mechanical ventilation compared with controls (median duration of ventilation 6.0 and 10.5 days, respectively, $p = .007$) with an associated reduction in the length of hospital stay (medians 15.5 and 20 days, respectively, $p = .03$).

*Conclusion:* While the administration of enteral IMN to a general, critically ill population did not affect mortality, those patients in whom it was possible to achieve early enteral nutrition with Impact had a significant reduction in the morbidity of their critical illness. (Crit Care Med 1998; 26:1164–1172)

KEY WORDS: immunonutrition; arginine; purine nucleotides; omega-3 fatty acids; Impact®, early enteral nutrition; ICU outcome; duration of ventilation; systemic inflammatory response syndrome; length of hospital stay

While it is generally accepted that the nutritional requirements of the critically ill are best provided by the enteral route (1–3), controversy surrounds the benefits associated with the various formulations available. In particular, in some groups of critically ill patients, additional amounts of compounds normally found in the diet are claimed to have beneficial effects on immune function that result in detectable differences in clinical outcome (4–6). A study (7) in a relatively homogeneous group of patients requiring intensive care suggested that supplementation of enteral feeds with three specific immunonutrients may have beneficial effects. These ingredients—arginine, purine nucleotides (in the form of yeast RNA), and ω-3 polyunsaturated fatty acids—were chosen because of their well-established effects on *in vitro* and *in vivo* markers of immune function. These effects include the promotion of T-cell blastogenesis (8, 9), enhancement of cellular immunity (10, 11), and increased concentrations of the trienoic eicosanoids (12, 13), respectively, but the exact mechanism of action of the combination remains unknown. Recently, these three immunonutrients have been combined into a single, commercially available enteral feed (Impact®, Novartis Nutrition, Berne, Switzerland) with the aim of appropriate immune modulation in those patients in whom sepsis is considered likely.

The potential benefits of such immunonutrition on outcome, in comparison with an isocaloric, isonitrogenous "control" feed that is similar in composition but without the specific immunomodulatory ingredients, has only undergone limited assessment in the general intensive care unit (ICU) population (6, 14, 15). The aim of this study was to compare predefined measures of ICU and hospital outcome in a general population of critically ill patients fed enterally with either Impact or an appropriate control enteral feed.

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Supported, in part, by Novartis Nutrition, Berne, Switzerland.

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## MATERIALS AND METHODS

A prospective, randomized, double-blind, single-center, controlled clinical trial of the use of two formulations of enteral nutrition was conducted in a 13-bed, adult, general ICU in Guy's Hospital, London. The primary end point was all-cause inhospital mortality, stratified *a priori* by the volume of enteral feed delivered. Successful early enteral nutrition was defined as >2.5 L of enteral nutrition in the first 72 hrs after ICU admission. Secondary outcome measures included the following: a) duration of ventilation; b) duration of the systemic inflammatory response syndrome (SIRS) (16) (ICU days of SIRS per patient); c) postrandomization intensive care and hospital length of stay; and d) the requirement for therapeutic intervention within the ICU, which was quantified using daily Therapeutic Intervention Scoring System (TISS) scores (17).

Patients were considered eligible for the study if they were expected to stay for ≥3 days in the ICU and had no contraindications to the use of enteral nutrition. To assess the expected ICU stay, we used an admission Acute Physiology and Chronic Health Evaluation [APACHE] II score of >10, TISS score of >20, and clinical assessment by the attending intensive care specialist. The study reflects a patient population from July 1992 to December 1994. Within 48 hrs of ICU admission, they were randomized to receive either the immunonutrition Impact (Novartis Nutrition), supplemented with the immunonutrients L-arginine, RNA, and ω-3 fatty acids, or a specially manufactured, isocaloric (1 kcal/mL), isonitrogenous (16.55 g of nitrogen per 1500 mL) control feed (Novartis Nutrition) identical to Impact in its vitamin and trace element profiles (Table 1) and in its appearance. To render the control feed isonitrogenous, it was itself supplemented with the amino acids L-serine, glycine, L-alanine, and L-proline. Exclusions to the study included age of <16 yrs, pregnancy, absence of informed consent from patient or relatives, or a contraindication to enteral nutrition. Rates of nutritional delivery were determined by a feeding protocol (Fig. 1) and were gradually increased, titrated to the volume of nasogastric aspirates, and the individual patient's ideal body weight (according to their age, gender, and height). The target rate of delivery in all cases was 32 total kcal/kg/day (25 nonprotein kcal/kg/day: 32 mL/kg) and 1.8 g of protein/kg/day. The use of the trial feeds was continued until ICU discharge. Routes of delivery of enteral nutrition were individually assessed for each patient, but the majority (97.2%) of patients were fed via a nasogastric tube. Other routes included nasojejunal and surgical jejunostomy feeding tubes but no patient received parenteral nutritional supplements. Data collection included volume of enteral nutrition, together with daily physiologic measurements and laboratory results to calculate APACHE II scores (18) and the presence of SIRS. The study protocol was approved by the Lewisham and North Southwark Committee on Medical Ethics.

*Statistics.* Given an expected mortality rate of 35% in the control group (based on inhouse historical data), the power $(1 - \theta)$ of the trial was set at 0.80 to detect a reduction in mortality rate of 30% in the treatment group at the $p < .05$ level. This approach mandated the inclusion of 180 patients in each group. The intention-to-treat analysis included all patients correctly randomized, irrespective of the volume of feed delivered. Stratification thereafter included all patients who received any feed (the received feed group, n = 369) and those patients achieving successful early enteral nutrition (n = 101).

The data are expressed as mean ± SD values or medians with ranges according to their distribution. Univariate comparison analyses used parametric and nonparametric tests as

**Table 1.** Composition of the trial enteral feedings

| | Impact® | Control |
|---|---|---|
| Energy (kcal/mL) | 1.0 | 1.0 |
| Energy distribution (% protein/fat/carbohydrate) | 22:25:53 | 22:25:53 |
| Carbohydrate (g/100 mL) | 13.4 | 13.4 |
| Protein (g/100 mL) | 5.58 | 5.58 |
| Nitrogen (g/1500 mL) | 16.55 | 16.55 |
| L-arginine (g/100 mL) | 1.25 | 0 |
| L-serine (g/100 mL) | 0 | 0.93 |
| Glycine (g/100 mL) | 0 | 0.77 |
| L-alanine (g/100 mL) | 0 | 0.51 |
| L-proline (g/100 mL) | 0 | 0.45 |
| Fat (g/100 mL) | 2.78 | 2.78 |
| % Fatty Acids Polyunsaturated | | |
| Omega-3 | 10.5 | 0 |
| Omega-6 | 8.3 | 24.1 |
| Lactose (%) | <0.02 | <0.02 |
| RNA (mg/100 mL) | 123 | 0 |
| Osmolality (mOsmol/kg) | 350 | 580 |
| pH | 6.6 | 6.8 |
| Sodium (mg/100 mL) | 106 | 106 |
| Potassium (mg/100 mL) | 134 | 134 |
| Calcium (mg/100 mL) | 80 | 80 |
| Magnesium (mg/100 mL) | 26.6 | 26.6 |
| Iron (mg/100 mL) | 1.2 | 1.2 |
| Copper (mg/100 mL) | 0.17 | 0.17 |
| Manganese (mg/100 mL) | 0.2 | 0.2 |
| Zinc (mg/100 mL) | 1.5 | 1.5 |
| Selenium (μg/100 mL) | 4.6 | 4.6 |
| Vitamin C (mg/100 mL) | 6.7 | 6.7 |
| Vitamin E (mg/100 mL) | 1.4 | 1.4 |

Impact®, Novartis Nutrition, Berne, Switzerland.

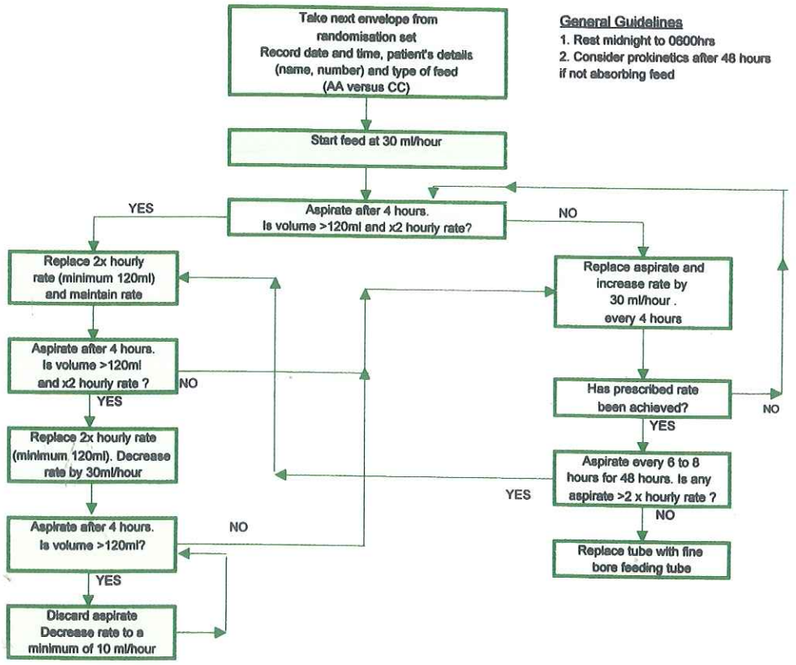


**Figure 1.** Flow diagram of the protocol used to establish enteral nutrition.

appropriate, and categorical data were compared using the chi-square test. Survival comparisons used the log-rank test and the Kaplan-Meier method for censored observations. Time to discharge from the ICU or hospital was further compared using the log-rank test; data from patients who died during the study period were censored (19). The multiple linear regression model was developed with stepwise selection using the method of least squares.

## RESULTS

During the study period (July 1992 to December 1994), 2,935 patients were admitted to the ICU with an overall hospital mortality rate of 16% and a standardized mortality ratio (observed mortality/APACHE II expected mortality) of 1.03. Only 634 (15%) patients received nutritional support: 19 patients received total parenteral nutrition alone; 73 patients required nutritional support with a combination of parenteral and enteral nutrition; and 542 (85%) patients were fed entirely by the enteral route. Of the last group, 398 (73%) patients were eligible for study and were randomized into the trial. The intention-to-treat analysis used data from 390 patients, with eight patients (five Impact, three control) being excluded because of errors in feed allocation after randomization. Twenty-one other patients were randomized but did not receive any enteral nutrition (nine early deaths, with 12 patients withdrawn from the study) and were excluded from the 369 received feed cohort.

The case-mix was heterogeneous (Table 2) but similar between the two feed groups, with a high proportion of tertiary referrals (36% overall, Table 3). Results of randomization on intention-to-treat-analysis and by *a priori* stratification are shown in Table 4. Overall, the trial cohort had a hospital mortality rate of 46% (180/390) and the two groups were well matched (Tables 3 through 5) for age and gender. In contrast, severity of illness on ICU admission, as measured using the first 24-hr APACHE II score and risk of hospital death (Table 4), tended to be greater in the Impact group compared with the control group for both the intention-to-treat and the received feed cohorts (APACHE II scores 20.1 ± 7.1 vs. 18.7 ± 7.1 [$p$ = .07] and 20.1 ± 7.2 vs. 18.5 ± 7.1 [$p$ = .04], respectively). No such statistically significant difference was observed in the early enteral nutrition group.

Duration of enteral nutrition, and therefore total volumes of feed delivered, ranged widely from no delivery at all to a maximum of 164 days of enteral feed. Rates of daily delivery adjusted for ideal body weight were considerably less than the target rate (Impact group median 14 [range 0 to 32] total kcal/kg/day; control group median 13 [range 0 to 32] total kcal/kg/day). When patients who did not attain the specified "therapeutic" delivery target (>2.5 L in 72 hrs after ICU admission) were excluded (persisting high nasogastric aspirates resulting in the slower institution of full enteral nutrition), rates of delivery were closer to target rates (50 Impact patients receiving a median of 17 [range 9 to 31] total kcal/kg/day; 51 control patients receiving a median of 19 [range 7 to 32] total kcal/kg/day). There was no difference between the two groups in the frequency of side effects of enteral nutrition, particularly in the frequency of diarrhea.



**Table 2.** Acute Physiology and Chronic Health Evaluation II specific diagnostic categories of 390 patients analyzed on an intention-to-treat basis

| Nonoperative Diagnostic Categories | Impact® | Control | Operative Diagnostic Categories | Impact® | Control |
|---|---|---|---|---|---|
| Asthma | 1 | 3 | Multiple trauma | 2 | 1 |
| Chronic pulmonary edema | 1 | 2 | | | |
| Noncardiogenic pulmonary edema | 1 | 2 | Chronic cardiovascular disease (coronary artery surgery) | 17 | 22 |
| After respiratory arrest | 10 | 6 | Peripheral vascular disease (aortic surgery) | 8 | 3 |
| Aspiration/poisoning/toxic | 1 | — | Heart valve surgery | 9 | 3 |
| Pulmonary embolism | 2 | 1 | Thoracic surgery for neoplasm | 1 | — |
| Respiratory failure: infection | 19 | 18 | | | |
| Respiratory failure: neoplasm | — | 2 | | | |
| CVS failure (hypertensive) | — | 1 | Craniotomy for neoplasm | 1 | — |
| CVS failure (dysrhythmia) | — | 2 | Head trauma | 1 | 1 |
| Congestive cardiac failure | 2 | 1 | Craniotomy for ICH/SDH/SAH | — | 1 |
| CVS failure (hemorrhagic/ hypovolemic shock) | — | 1 | Laminectomy or other spinal cord surgery | — | — |
| CVS failure (ischemia) | 2 | — | | | |
| CVS failure (septic) | 18 | 18 | Renal surgery for neoplasm | — | 1 |
| CVS failure (after cardiac arrest) | 17 | 16 | Renal transplant | — | — |
| CVS failure (cardiogenic shock) | 4 | 11 | | | |
| CVS failure: aortic dissection | 4 | 1 | Hemorrhagic shock, GI bleeding | 1 3 | 3 — |
| Multiple trauma | 9 | 6 | GI surgery for neoplasm | 5 | 4 |
| Head trauma | 4 | 6 | GI perforation/obstruction | 5 | 2 |
| Neurologic seizure disorder | 1 | 3 | | | |
| Neurologic ICH/SDH/SAH | 4 | 5 | Respiratory insufficiency | 3 | — |
| Drug overdose | — | 1 | Neurologic | — | — |
| Diabetic ketoacidosis | — | — | Cardiovascular | 2 | 3 |
| GI bleeding | 4 | 2 | GI | 4 | 1 |
| Metabolic/renal | 14 | 17 | Metabolic/renal | 1 | 2 |
| Respiratory | 8 | 5 | Sepsis | — | — |
| Neurologic | 5 | 8 | Cardiac arrest | — | 3 |
| Cardiovascular | 2 | 2 | | | |
| GI | 1 | 3 | | | |
| Total | 134 | 143 | Total | 63 | 50 |

CVS, cardiovascular system; ICH/SDH/SAH, intracerebral hemorrhage, subdural hemorrhage, subarachnoid hemorrhage; GI, gastrointestinal; —, none.

Impact®, Novartis Nutrition, Berne, Switzerland.

While the death rates were higher in all Impact groups (Table 4; Fig. 2 [*top*] intention-to-treat; Fig. 2 [*bottom*] early enteral nutrition), these differences were not statistically significant. Postrandomization ICU and hospital stay with the measures of ICU intervention are given in Table 5. In the intention-to-treat and received feed groups, there was no difference between the two feeds for any measured variable. Yet, in the early enteral nutrition group (Table 5), both duration of mechanical ventilation and postrandomization length of hospital stay were significantly reduced in those patients receiving Impact (duration of ventilation: Impact group 6 [1 to 40] days, control group 10.5 [1 to 204] days, $p$ = .007; length of hospital stay: Impact group 15.5 [3 to 111] days, control group 20 [2 to 289] days, $p$ = .03). In addition, ICU stay, total TISS points accrued during ICU stay, and the numbers of days during which the criteria for the diagnosis of SIRS were fulfilled were significantly reduced in the group receiving Impact (Table 5). Taking into account the small nonsignificant difference in death rate between the two arms of the early enteral nutrition cohort, when lengths of stay of patients who died were censored, the difference remained but did not achieve statistical significance ($p$ = .08, log-rank test).

For the early enteral nutrition subgroup, a multiple linear regression model was developed to assess the effects of hospital outcome, formulation of feed, APACHE II score, risk of death in the first 24 hrs of ICU admission, and therapeutic intervention (mean daily TISS) on postrandomization length of hospital stay. A log transformation of length of stay produced a better model. Stepwise analysis excluded the APACHE II score and risk of death as having any effect. However, formulation of feed was retained, and it had an independent statistically significant effect in the model: log (length of hospital stay) = 2.13 – 0.29 (hospital outcome [$p$ < .001]) – 0.16 (formulation of feed [$p$ < .05]) – 0.006 (TISS [$p$ < .05]).

## DISCUSSION

The interpretation of controlled clinical trials performed in the ICU is fraught with difficulty, primarily because of the heterogeneity of the patient population and our study is no

**Table 3.** Case-mix of the three study cohorts by specialty and source of admission

| | Intention To Treat | | Received Feed | | Early Enteral Nutrition | |
|---|---|---|---|---|---|---|
| | Impact® (n = 197) | Control (n = 193) | Impact® (n = 184) | Control (n = 185) | Impact® (n = 50) | Control (n = 51) |
| Trauma | 18 (9)[a] | 18 (9) | 18 (10) | 18 (10) | 7 (14) | 6 (12) |
| Medical | 109 (55) | 113 (59) | 100 (54) | 107 (58) | 32 (64) | 38 (75) |
| Surgical[b] | 70 (36) | 62 (32) | 66 (36) | 60 (32) | 11 (22) | 7 (13) |
| Number of patients requiring MV | 194 | 191 | 182 | 183 | 50 | 51 |
| Postoperative Admissions From Within Guy's Hospital | | | | | | |
| Elective | 37 (19) | 36 (19) | 34 (19) | 35 (19) | 5 (10) | 3 (6) |
| Emergency | 26 (13) | 14 (7) | 25 (14) | 14 (8) | 2 (4) | 2 (4) |
| Emergency transfers from wards within Guy's | 48 (24) | 49 (25) | 43 (23) | 47 (25) | 12 (24) | 18 (35) |
| Transfers from the Accident and Emergency Department | 15 (8) | 25 (13) | 14 (8) | 22 (12) | 4 (8) | 6 (12) |
| Emergency transfers from other hospitals | 71 (36) | 69 (36) | 68 (36) | 67 (36) | 27 (54) | 22 (43) |

MV, mechanical ventilation.
[a]Values in parentheses indicate percent; [b]some patients classified as "surgical" were not admitted from the operating room and are therefore classified within the "nonoperative" Acute Physiology and Chronic Health Evaluation II specific diagnostic categories.
Impact®, Novartis Nutrition, Berne, Switzerland.

**Table 4.** Clinical features, severity of illness, and mortality of the three study cohorts

| | Intention To Treat | | Received Feed | | Early Enteral Nutrition | |
|---|---|---|---|---|---|---|
| | Impact® (n = 197) | Control (n = 193) | Impact® (n = 184) | Control (n = 185) | Impact® (n = 50) | Control (n = 51) |
| Age, yr (median) with range) | 63 (18–99) | 62 (18–87) | 63 (18–99) | 62 (18–87) | 58 (18–53) | 62 (18–76) |
| Males (%) | 125 (63%) | 126 (65%) | 116 (63%) | 122 (66%) | 30 (60%) | 28 (55%) |
| APACHE II scores (mean ± SD) | 20.1 ± 7.1 | 18.7 ± 7.1[a] | 20.1 ± 7.2 | 18.5 ± 7.1[b] | 19.5 ± 7.5 | 18.0 ± 7.3 |
| APACHE II risk of death (%) (mean ± SD) | 33 ± 24 | 30 ± 21 | 33 ± 24 | 29 ± 21 | 33 ± 25 | 31 ± 22 |
| ICU mortality (deaths/total number) | 41% 80/197 | 38% 74/193 | 40% 74/184 | 38% 70/185 | 36% 18/50 | 28% 14/51 |
| Hospital mortality (deaths/total numbers) | 48% 95/197 | 44% 85/193 | 48% 88/184 | 43% 80/185 | 42% 21/50 | 37% 19/51 |

APACHE, Acute Physiology and Chronic Health Evaluation; ICU, intensive care unit.
[a]$p = .07$; [b]$p = .04$ vs. Impact groups (95% confidence intervals for differences being –0.12 to 2.72 and 0.1 to 3.02, respectively).
Impact®, Novartis Nutrition, Berne, Switzerland.

exception. Traditionally, attempts to overcome this problem have depended on the inclusion of large numbers of patients in multiple centers, followed by their stratification into predefined subgroups of interest together with some adjustment for differences in severity of illness (20, 21). In the case of the few randomized, prospective trials of enteral nutrition that have been published, the most severely ill ICU patients have been excluded. Moreover, the majority (1, 3, 7, 15) of studies have focused on relatively young, good-prognosis patients with multiple trauma. In contrast, our study was designed to assess the efficacy of the widespread use of immunonutrition in the critically ill, with an expected hospital mortality rate of >35%. Our entry criteria were established to allow the randomization within a single center of a large number of patients with a broad range of diagnoses and risk of hospital death, thus more closely resembling usual clinical practice. Our study design addressed the necessity of an intention-to-treat analysis. Correctly randomized patients who did not receive any trial agent (early ICU deaths or trial withdrawals) were included in the analysis. However, we also created *a priori* two specific cohorts of interest: a) those patients who received some enteral nutrition; and b) patients who received reasonable volumes of feed early on in their ICU course (>2.5 L within 72 hrs of ICU admission). If efficacy is related to dose, the latter cohort would be more important. Using this approach, while we were unable to show any benefit of immunonutrition on overall outcome in our intention-to-treat analysis, our study demonstrated that in those patients who tolerated early enteral nutrition, and were fed with Impact, there was a significant reduction in their requirement for mechanical ventilation,



**Table 5.** Secondary end points of the trial in the three study cohorts

| | Intention To Treat | | Received Feed | | Early Enteral Nutrition | |
|---|---|---|---|---|---|---|
| | Impact® (n = 197) | Control (n = 193) | Impact® (n = 184) | Control (n = 185) | Impact® (n = 50) | Control (n = 51) |
| Days of ventilation | 4 (0–101) | 4 (0–204) | 4 (0–101) | 4 (0–204) | 6 (1–40) | 10.5 (1–204)[a] |
| Days of SIRS | 2 (0–63) | 3 (0–40) | 2 (0–63) | 3 (0–40) | 3 (0–38) | 6 (0–40)[b] |
| Total TISS points per admission | 204 (0–4565) | 221 (0–5622) | 218 (0–4565) | 221 (0–4565) | 265 (50–1670) | 380 (41–5622)[c] |
| Length of ICU stay[d] (days) | 6 (0–103) | 6 (0–282) | 6 (1–103) | 6 (0–282) | 7.5 (3–50) | 12 (2–282)[e] |
| Length of hospital stay[d] (days) | 12 (0–187) | 13 (0–289) | 12 (0–187) | 13 (0–289) | 15.5 (3–111) | 20 (2–289)[b] |
| Days of renal support in the ICU[f] | 3 (1–58) | 4 (1–47) | 3.5 (1–58) | 4 (1–47) | 5.5 (1–21) | 5 (1–47) |

SIRS, systemic inflammatory response syndrome; TISS, Therapeutic Intervention Scoring System; ICU, intensive care unit.
Values in parentheses indicate range.
[a]$p = .007$, [b]$p = .03$, [c]$p = .01$, [e]$p = .02$ compared with the Impact group; [d]postrandomization length of stay; [f]renal support was continuous venovenous hemodiafiltration using a polyacrylonitrile (AN69, Hospal, Lyons, France) membrane.
Impact®, Novartis Nutrition, Berne, Switzerland.

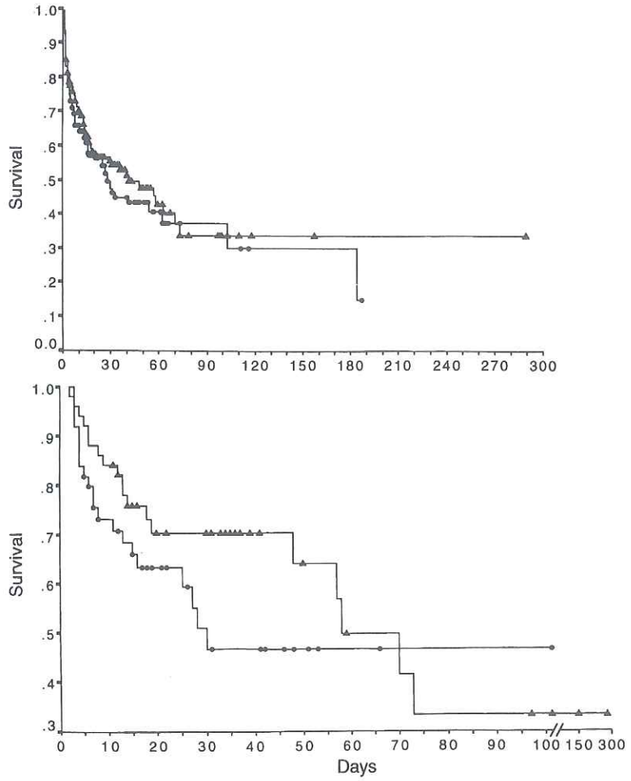


**Figure 2.** *Top:* Kaplan-Meier analysis of survival in the "intention-to-treat" cohort ($p = .36$, log rank). There were 197 patients with 95 hospital deaths in the Impact® group (*circles*) and 193 patients with 85 hospital deaths in the control group (*triangles*). *Bottom:* Kaplan-Meier analysis of survival in "early enteral nutrition" cohort ($p = .16$, log rank). There were 50 patients with 21 hospital deaths in the Impact group (*circles*) and 51 patients with 19 deaths in the control group (*triangles*).

with an associated, significant reduction in postrandomization hospital length of stay. If these differences in outcome really did arise directly from the intervention studied (i.e., enteral immunonutrition)—and our multiple linear regression model suggests that they did—then our trial provides additional evidence that it is not only important to achieve early enteral nutrition in the general ICU population but also, more specifically, to achieve this goal with an "immune-modulating" feed.

The manipulation of the immune system of critically ill patients in a way that improves their outcome is the subject of extensive investigation at the present time. The hypothesis that this is achievable through appropriate nutritional supplementation is attractive for many reasons, not least in its simplicity but also in so far as it lends support to the naturalistic idea that it is the quality and not the quantity of nutrition that counts. After all, "we are what we eat" (22). While the various animal studies of immunonutrition (11–13, 23, 24) provide good evidence of a beneficial effect of specific nutrients on immune function and have enabled the development of regimens such as Impact, "Immun Aid®" (McGaw, Irvine, CA) (15), and the "modular tube feed" (Shriner's Burns Institute, Cincinnati, OH), the situation is far from straightforward in the general ICU. Nevertheless, there are now several

*Our study demonstrated that in those patients who tolerated early enteral nutrition, and were fed with Impact, there was a significant reduction in their requirement for mechanical ventilation, with an associated, significant reduction in postrandomization hospital length of stay.*

published studies (5–7, 14, 15, 25, 26) demonstrating both immunologic and clinical benefits of Impact and "Immun Aid" in a variety of clinical settings. Presently, it is not clear whether it is the combination of immunonutrients which is crucial rather than any one in particular, and our trial did not address that issue. A recently published study (27) in postoperative patients with cancer used an enteral formula enriched only with fish oil and medium-chain triglyceride, and reported some small, apparently beneficial effects. These effects included reductions in the number of gastrointestinal complications and infections, with improvements in liver and renal function. However, the differences barely achieved statistical significance or clinical importance. In contrast, combination immunonutrition seems to be more powerful (6). Nitrogen balance and lymphocyte mitogenesis were better maintained in patients with upper gastrointestinal malignancies fed with combination immunonutrition (Impact) after surgery compared with controls. This result was associated with a lower rate of infections, wound complications, and length of hospital stay. A similar group of patients, studied in Germany (14) and fed after surgery with Impact, were found to have better preserved T-lymphocyte function and higher immunoglobulin concentrations compared with patients given an isocaloric and isonitrogenous control diet identical to that used in our study. Modulation of cytokine production and their receptor expression represent at least two other possible mechanisms by which this form of immunonutrition might have its effects (28, 29). Finally, the North American multicenter study (7) of 326 patients demonstrated that in a subgroup of 89 septic patients, there was a significant reduction in length of hospital stay in the 44 patients fed with Impact compared with 45 controls fed with a standard feed (Osmolite HN®, Ross Laboratories, Columbus, OH). Again, this trial had many subgroups, and even more exclusion criteria, so that the majority of patients included were young (mean age 40 yrs) and had suffered an episode of multiple trauma (84% of 279 enterally fed eligible patients), which gave a relatively low hospital mortality (33 deaths in total). Moreover, the two feeds studied were not matched for nitrogen content nor vitamins (specifically vitamins A and E) and trace elements (particularly selenium) so that the immunonutrition patients received greater daily intakes of these nutrients. These difference, by themselves, could have contributed to the apparent improvements in outcome.

While our results in the early enteral nutrition group are surprisingly similar to the results in this North American multicenter study (7) (particularly the multiple regression analysis of the effect of Impact on length of hospital stay), our study design and patient case mix were different. The overall mortality rate of 46% reflected our lack of exclusion criteria; 73% of all patients receiving enteral nutrition in our ICU were entered into the trial and very few patients were nourished with total parenteral nutrition during the study period. We also included a large group of patients transferred to Guy's Hospital from other hospitals' ICUs with already established organ failure. These tertiary referrals, in combination with late referrals from the wards, probably accounted for the higher than expected death rate (observed hospital mortality vs. APACHE II expected hospital mortality – overall standardized mortality ratio of 1.48) through the process of "lead time bias" (30, 31). The greater severity of illness and the higher mortality had the disadvantage of reducing the numbers of patients who not only actually received the feed but in whom it was also possible to achieve early enteral nutrition. Early death accounted for nine of the 21 randomized patients not receiving any feed, and there was a suggestion of a greater severity of illness in the immunonutrition groups, both in the intention-to-treat and received feed cohorts. These differences, (which only reached statistical significance for the APACHE II scores in the received feed group) were not so evident in the early enteral nutrition groups, perhaps making this cohort better matched so that differences related to the intervention, enteral immunonutrition, could be distinguished. We did not attempt to document episodes of ICU-acquired infection because of the difficulties surrounding their diagnosis, particularly that of the most frequent—ventilator-associated pneumonia. We preferred to rely on the readily obtainable objective criteria for SIRS, which are sensitive but not specific for infection (32), as a surrogate measure of continued inflammation. Those patients receiving immunonutrition in the early enteral nutrition group had fewer ICU days of SIRS compared with the control group. This finding provides some explanation of the mechanism leading to the reduced length of hospital stay in the early enteral nutrition group.

Another issue surrounds the adequate provision of energy in our patients, since the average daily intake was only 14 total kcal/kg, much less than our relatively high target of 32 kcal/kg/day. While energy requirements in catabolic patients are still disputed, and no detrimental effects of the use of enteral nutrition (which tends to be hypocaloric) have been reported (33), it is conceivable that persistent underfeeding could mask any beneficial effects of immunonutrition. Daily energy intake was closer to the target rate in the early enteral nutrition group, again supporting the notion that if immunonutrition was going to have an effect, it would be more obvious in this group. A final consideration concerns the control feed, which was rendered isonitrogenous by its supplementation with additional amino acids, albeit small amounts. One of the amino acids used, glycine, has been described as minimizing the hepatic reperfusion injury in a rat liver ischemia-reperfusion model (34) and improving survival in rats after endotoxin shock (35). This may have added an advantage to the control feed, in addition to the relatively (for enteral feeds) high nitrogen content, with the result that any specific immunonutrient effect of Impact was masked. These two factors—the tendency toward a greater severity of illness in the immunonutrition groups and the possible beneficial effects of the control feed—might well be an explanation for the lack of any difference in outcome in our intention-to-treat and received feed analyses.

It is fashionable to emphasize end points other than a reduction in mortality in the randomized, controlled, clinical trials taking place in the ICU (e.g., outcomes such as reductions in morbidity, duration of ventilation, and length of stay) (36). However, these other end points become more difficult to interpret when there are differing death rates (although statistically insignificant) in the two groups of interest (37). One explanation for the reduction in length of stay in the immunonutrition group of early enteral nutrition patients might be that more patients died early on in their ICU course and so contributed less to the accumulation of ventilator, ICU, and hospital days in the study. We attempted to correct for this bias by censoring the effect of deaths on length of stay and developing our multiple linear regression model. Using the first approach, the difference in length of stay remained but became nonsignificant at the 5% level ($p$ = .08). In contrast, the multiple linear regression model retained the nature of the feed as a significant determinant of hospital length of stay along with hospital outcome, suggesting there was a genuine effect of the feed.

In conclusion, given all of these difficulties in interpretation, it seems likely that the differences demonstrated in the early enteral nutrition group were real, albeit small. That this difference could only be demonstrated in 25% of the patients randomized (the early enteral nutrition group) is probably the consequence of the overall severity of illness of the patients studied. Administration of an immunonutrient feed may only affect that group of patients in between those patients who are highly likely to die whatever the intervention and those patients who will survive irrespective of the route or type of nutritional support. Perhaps the earlier use of prokinetics (cisapride, erythromycin) or routine nasojejunal access might increase the numbers of patients successfully absorbing the critical volume of the immunonutrition early on in their ICU course (38). However, before we can recommend a wholesale change to an immune-modulating formulation such as Impact, a careful cost-benefit analysis is required to assess whether or not the widespread, early use of the more expensive immunonutrition is cost effective in the setting of a general ICU. Such an evaluation, based on the clinical outcome differences observed in this study, is presently ongoing.

## ACKNOWLEDGMENTS

We are grateful to all physicians and surgeons at Guy's Hospital for allowing us to study their patients. We thank Dr. Heinz Schneider and Miss Valerie Streichenberg of Novartis Nutrition for their considerable help with this project. We are also indebted to Dr. Frank Cerra for his thoughtful advice.

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# FUN WITH FOOD



Mrs Chan-Yam Yoke Yin
*BSc (Hons), MSc, PG CE, PostgDipNutr*

Children begin learning about food from birth. Good nutrition is essential for normal childhood development and for lifelong health. Parents are primarily responsible for their child's nutrition but healthcare workers and child educators can contribute to it. Scientific evidence shows that food habits are largely acquired and preferences for most foods, taste and textures are learnt early in life.

The pre-school years are critical for inculcating positive attitudes and practices related to healthy eating. Today, pre-schoolers in Singapore spend three hours a day, five days a week, for two to three years in kindergartens. Besides serving nutritious snacks that contribute significantly to young children's total nutrient intake, kindergartens also provide opportunities for pre-schoolers to learn about food in interesting ways.

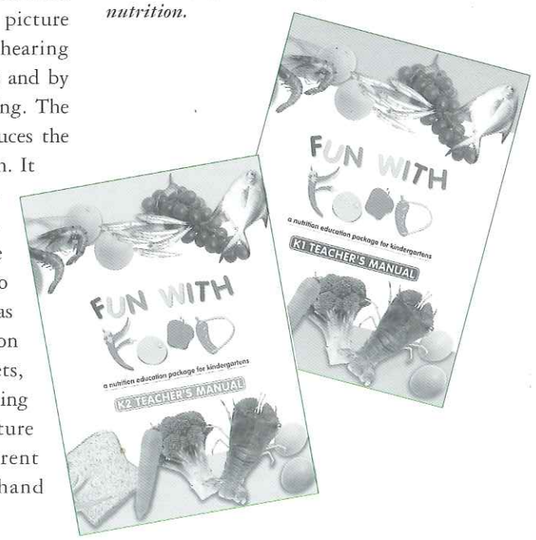
However, in Singapore, formal lessons on nutrition begin only at the age of six with the primary school health education curriculum. As increasing evidence shows that early eating habits influence future health, there is a need to provide nutrition education for kindergarten children. Children may learn about food through snacks, field trips and food preparation. However, their parents, teachers and peers influence their attitude towards food.

FUN with FOOD, a nutrition education package, has been developed to serve as a tool for kindergarten teachers to teach pre-school children about food and nutrition. The package aims to increase children's familiarity with a wide range of foods, to promote positive attitudes towards food and food preparation and to introduce the relationship between food and health. The package was pilot tested in July 1998 and it was officially launched through a series of seminars at which 530 teachers from 344 kindergartens attended. Evaluation on the usage of the package will be conducted in 1999 using a structured questionnaire.

The package consists of two components: the K1 Teacher's Manual and the K2 Teacher's Manual. The K1 Teacher's Manual aids in familiarizing children with food and it includes ten lessons, each with activities that encourage children to use their senses to learn about food. The children learn by seeing through posters, picture cards, and worksheets; by hearing discussion, stories and songs and by touching, smelling and tasting. The K2 Teacher's Manual introduces the link between food and health. It includes ten lessons, each with activities that link across the curriculum, from language skills (describing taste) to mathematics (counting bananas for a milkshake). Each lesson contains students' worksheets, full colour posters and supporting materials such as food picture cards (60 local foods), parent information sheets and hand puppet designs.

The package was pilot tested in 20 kindergartens involving 94 teachers and 2000 children across Singapore. Teachers consistently rated the discussions, activities and worksheets as suitable (i.e., neither too difficult nor too easy) and children's reaction to the programme as enjoyable. More than 90% of the teachers stated that the lessons met the learning objectives. Some 71% indicated that they would use the package as part of their resources while 44% would build the lessons into the curriculum.

*Mrs Chan-Yam Yoke Yin is the Head of Education and Training Section of the Department of Nutrition, Ministry of Health. She has more than 15 years of experience at the Ministry of Health and has special interest in community nutrition, particularly childhood nutrition.*



# VALIDATION OF A SHORT FOOD FREQUENCY QUESTIONNAIRE

## To Assess Consumption Of Cereal Foods, Fruit And Vegetables In Chinese Singaporeans

AMC Ling, C Horwath and W Parnell
*Department of Human Nutrition, University of Otago, P O Box 56, Dunedin, New Zealand*

**Objective:** To assess the ability of a 16-item food frequency questionnaire (FFQ) to measure consumption of cereal foods, fruit and vegetables in Chinese Singaporeans.

**Design:** Subjects completed the questionnaire twice, at the beginning and end of a six-week period during which they also provided three 24h diet recalls. Estimates of intake from the questionnaire were compared with those from diet recalls.

**Subjects:** Subjects were recruited from a range of occupational groups through random sampling across divisions in the headquarters of the Singapore Ministry of Health. Of the 81 subjects initially recruited, three failed to complete the diet recalls, one was excluded due to changes in diet, and seven did not return the second questionnaire.

**Results:** Mean difference in food group consumption estimated by the two methods did not differ significantly from zero for fruit (0.00 serving, s.d. = 0.54, 95% CI = -0.13, +0.12, P = 0.95) or vegetables (-0.05, s.d. = 0.29, 95% CI = -0.12, +0.02, P = 0.13). For cereal foods, the mean difference was small, but significantly different from zero only in women (-0.32 servings, s.d. = 0.92, 95% CI = -0.59, -0.06, P = 0.02). At an individual level, cereal food intake as measured by the FFQ may be 37% below or 59% above the diet recall values; and values for total fruit and vegetables may be half or double the recall values. Among subjects whose intake was classified into the lowest quartiles by diet recalls, 78% and 94% respectively, fell into the lowest two questionnaire quartiles for cereal foods, and total fruit and vegetables. The ability of the questionnaire to predict those having inadequate intake based on recall data was more than 90% for the three food groups.

**Conclusion:** The short questionnaire cannot replace the three-day recalls in intake assessment for individuals, but it could be used to screen for low consumers in intervention programmes, to assess mean food group intake in population groups, and to rank individuals into broad categories of food group intake.

**Sponsorship:** International Life Sciences Institute, South East Asia.

**Descriptors:** Cereals; fruit; food frequency questionnaire

# PILOT STUDY ON CONSUMER AWARENESS, KNOWLEDGE OF AND ACCEPTANCE OF GENETICALLY MODIFIED PLANT FOODS (GMP) IN SINGAPORE.

## (Final Year Project (Industry) Year 3 Students, Diploma in Applied Food Science and Nutrition, School of Information Technology and Applied Science, Temasek Polytechnic)

**Students:** Aliza Bte Mohammed Shariff, Melina Lau Shu Hui, Tan Yoke Yen

**Industry Supervisors:** Mrs. Anna Jacob (Food and Nutrition Specialists Pte Ltd)

**Supervisor:** Mrs. Sudha Vasudevan

A pilot test on the awareness, knowledge and acceptance of GMP foods among 150 Singaporean shoppers (18 years of age and over) was done. They were randomly selected from 2 popular supermarkets. This pilot study was also aimed to establish Singaporean consumers' desire for more knowledge and the choice of medium of information. This study involved the development of a questionnaire consisting of ten questions and a face to face interview.

It was evident in this study that the awareness of GMP foods in Singapore is very low. Less than 20% of the subjects interviewed had any awareness of GMP foods, despite media information in the local press. About 64% of consumers' information on GMP foods came from newspapers followed by television. Despite being reassured that GMP foods are 'substantially equivalent' to natural foods, 92% of the subjects wanted GMP foods to be labelled. Fifty percent of the subjects said that they would be persuaded to buy these foods if a reliable authority certified them as safe. After highlighting the potential benefits to consumers, 61% would accept this technology on plants. With regards to genetic modification of animals for food, it registered a sharp drop in acceptance. This acceptance increases marginally when the concept of the use of gene technology on animals for the production of medicine.

Majority of the subjects, (80%) wanted to know more about GMP foods. Education of the consumers should go hand-in-hand with development and research. With effective education, majority of the consumers can be persuaded to accept GMP foods. This would maximise the efforts of scientists in bringing out the full potential benefits of this technology to the consumers.

*In Partial Fulfillment of the Requirements for the Diploma in Applied Food Science and Nutrition.*





# PROFESSOR WIJA VAN STAVEREN

Professor Wija started her career as a Clinical Dietician in Amsterdam and worked in the Research Institute. She had much experience in her hands when she went to Surinam in Latin America for a few years. There she was responsible for nutrition in developing countries and carried out dietary surveys on the nutritional status of pre-school children. She then went on to Queen Elizabeth College to pursue a Masters degree in Nutrition and a PhD with Waageningen Agricultural University. Presently, she is Professor in Nutrition and Gerontology at Waageningen Agricultural University. Her hobbies include playing the flute, singing in the choir, listening to music and cycling in Europe.

***Professor Wija, what are your current research interests in nutrition?***

Currently, I work at the Waageningen Agricultural University Research Centre in the Department of Nutrition and Epidemiology. My areas of interest include nutrition and gerontology. I am involved in the 'The SENECA study' and am interested in the nutrition of elderly living in nursing homes. The other major area of interest is dietary surveys. In January 1998, I was also involved with the University Hospital dieticians to do clinical research. My emphasis was on the importance of evidence-based treatment, as scientifically correct data will help patients in their recovery. Good nutrition reduces the period of illness and improves the quality of life.

***Professor Wija Van Staveren, what brings you to Singapore?***

The Department of Nutrition, Ministry of Health, invited me to Singapore on a consultancy assignment. In addition, I conducted a course, lectures, and workshops for Department of Nutrition (DON) staff on several aspects of nutritional epidemiology. This course covered the role of nutritional policies, the Food Information and Nutrient Database (FIND), dietary goals and targets, gaps in research and evaluation of programs for implementation in nutritional policies.

***What do you think of the nutrient database being developed by the DON, Ministry of Health?***

The DON has put in a lot of effort into the development of FIND. The work on the software is fine but the nutrient database has to be kept up-to-date. There is a need to source for help from other related organisation such as institutes in neighbouring countries and different agencies of the food industry to keep up to date with different data sets.

***Should Asian countries have a common or different set of RDAs?***

It is very important for all nutrition and dietetics professionals to read the article on Southeast Asian RDAs in the 1997 Nutrition Reviews. Recently, there is a change in approach to the setting of RDAs, especially as populations are moving from nutrition-deficiency problems to nutrition-related chronic diseases. Originally, the RDAs were used to combat nutrition-related deficient diseases. Therefore, it is important that various expert committees come together to discuss what is applicable for each respective country. Having a common set of RDAs for Southeast Asia would be better but it is prudent to conduct a good literature research on the current data to justify the proposed RDAs. It would be most helpful if this exercise was also was done regionally to identify commonalties and differences, so that the RDAs truly reflect population needs.

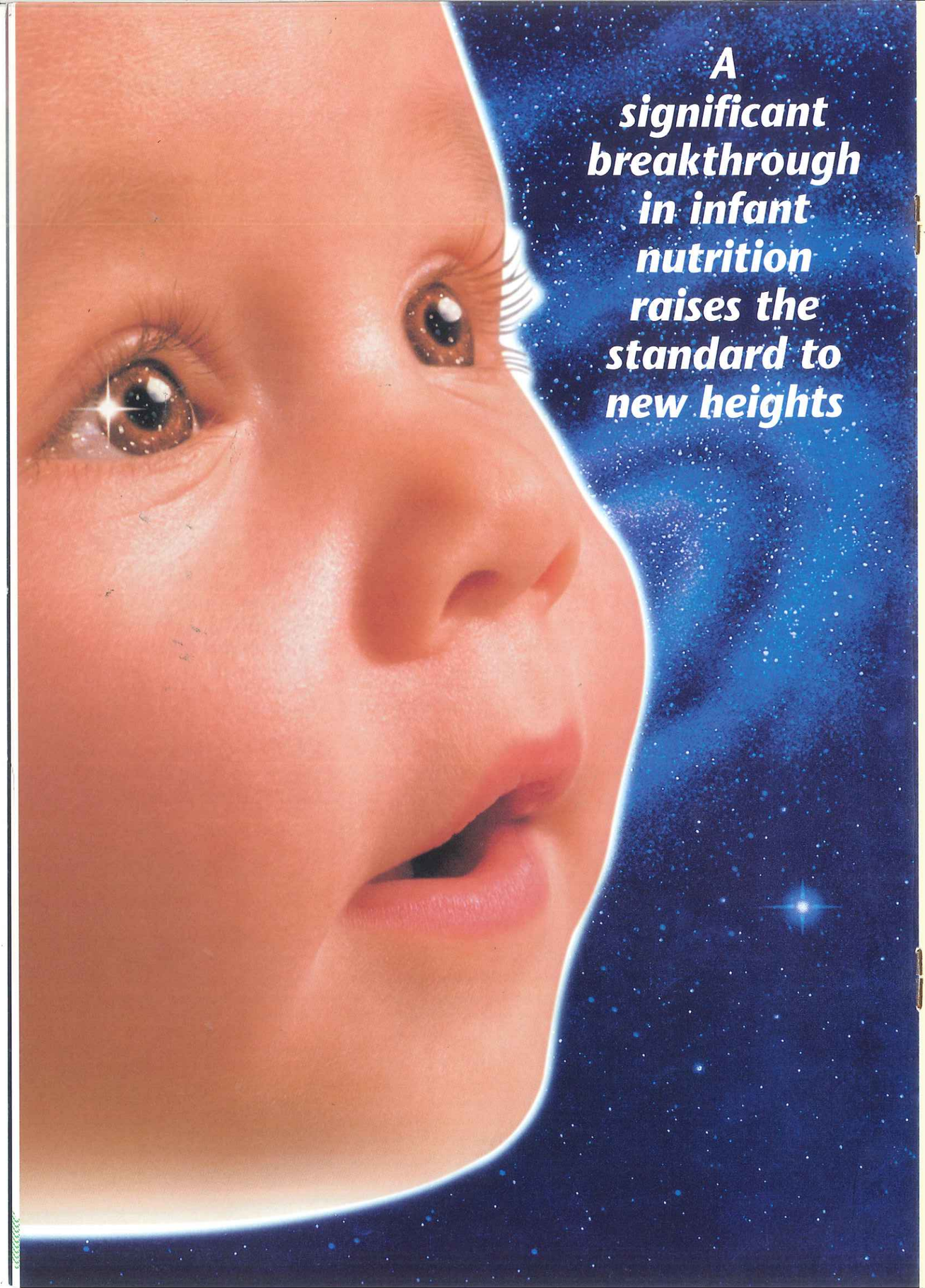
***Do you have any advice for dieticians in Singapore?***

Generally, my advice is that dieticians should come together to study the importance of evidence-based treatment on patients and in public health so that we can show that nutrition does matter for the health and well-being of the patient. More dieticians should be involved in research as the evaluation component is often missing.

***What in your opinion, are the differences in the roles of a Nutritionist and a Dietician?***

A Nutritionist is equipped in research methodologies and is often involved in management and planning. On the other hand, a Dietician is better trained for clinical work and consultancies. Both health professionals should work hand in hand in order to deliver the best healthcare possible.

*Ms Leow Sooi Mee and Ms Sherlyn Quek interviewed Professor Wija van Stavern in August 1998. Ms Leow currently is working as a Dietician and Ms Sherlyn is a Nutritionist at the Department of Nutrition, Ministry of Health Singapore.*



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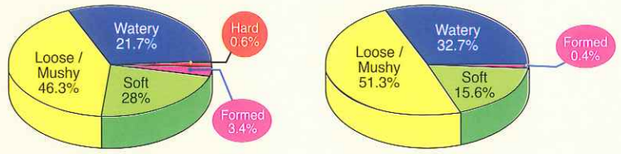


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# NUCLEOTIDES AND INFANT IMMUNITY

It is widely accepted that breast-feeding is best for mums and babies alike. One of the many reasons for this is that breast milk decreases the risks of allergies and upper respiratory tract infections. Researchers have put this down to substances in breast milk, which have been found to stimulate the immune system. These substances, known as nucleotides, are known to play important roles in metabolism and are the building blocks of RNA and DNA.

*Dr Jane Carver from the Division of Neonatology, Department of Paediatrics, University of South Florida College of Medicine visited Singapore in April 1998. Mrs Yashna Harjani interviewed Dr. Jane Carver, about the role of nucleotides in an infant's diet.*

**YH: What are the benefits of breast-feeding?**

**Dr. JC:** Breast-feeding confers many benefits to both the mother and the infant. The baby's suckling causes a mother's uterus to contract, decreases postpartum blood loss and helps the uterus to return to its pre-pregnant state more quickly. Breast-feeding women also tend to lose weight more easily, have improved bone mineralisation and a lower incidence of breast and ovarian cancer.

Breast-feeding clearly provides important benefits to the infant. Breast-fed infants have fewer gastrointestinal and respiratory illnesses, fewer ear infections and are less likely to develop allergies. There is also increasing evidence that breast-feeding protects against SIDS and the development of allergies, chronic digestive disease and diabetes. In addition, several studies suggest that the neuro-development of breast-fed infants is enhanced.

**YH: What are the main reasons that women cite for stopping breast-feeding?**

**Dr. JC:** Lack of support during the immediate post-natal period is a significant contributor to unsuccessful breast-feeding. Health care professionals who are well trained and supportive can have an enormous impact on the initiation and subsequent success of breast-feeding. However, these professionals are often not available. Other obstacles include insufficient education of the parents and hospital policies, which offer bottles to infants of breast-feeding mothers and working mothers.

**YH: What are nucleotides and why are they important for infants?**

**Dr. JC:** Nucleotides play many important roles in metabolism and are the building blocks of DNA and RNA. They are found in human milk at levels considerably higher than in cow milk and cow's milk based infant formulas, which are not supplemented with nucleotides. Numerous studies suggest that nucleotides may be one of the components of human milk that contributes to the superior clinical performance of the breast-fed infant. While the human body can make them, nucleotides are considered to be 'conditionally essential' nutrients. That is, they may become essential when the body's supply is insufficient for optimum function. The conditions under which they may be important include disease states like diarrhoea, periods of limited nutrient intake, rapid growth spurts or immaturity of metabolic systems. It takes lot of energy for the infant to synthesise nucleotides. During periods of increased demand, the baby's system may be unable to handle this load or manufacture enough nucleotides to meet the increased demand. At this time, infant formulas containing additional nucleotides may be necessary for formula-fed infants. Also, during gastrointestinal disturbance, the intestinal tract is inflamed due to infection and this may result in decreased absorption of nucleotides and subsequently increased requirement.

**YH: If an infant is not breast-fed, are infant formulae with added nucleotide suitable?**

**Dr. JC:** If an infant is not breast-fed for whatever reason, an infant formula should be used as a substitute for the first year of the infant's life. The breast-fed infant is used as the ideal model against which all formula-fed infants are measured with respect to growth, health, and development. While much work has been put into trying to produce a formula as similar as possible to breast milk, this work is far from complete. Adding nucleotides to infant formula takes it one step closer in composition to human milk.

Most international agencies and regulatory bodies worldwide have approved the addition of nucleotides to infant formulas. The nucleotides added to infant formula are easily absorbed and have been shown to improve immune function.

*Yashna Harjani is a Consultant Dietitian with Food and Nutrition Specialists Pte Ltd. She is a regular nutrition feature writer for several local magazines as well as a popular public speaker. In addition, Mrs Harjani provides consultancy services to several hospitals and nursing homes in Singapore.*



REVIEW

# IMMUNE-ENHANCING ENTERAL DIETS: WHERE'S THE BEEF?

Infection is a major problem in critically ill patients, contributing to increased morbidity, mortality, and healthcare costs. Thus, researchers and clinicians constantly seek new methods for decreasing infections. Starvation is a potent suppressor of immune function and predisposes to infection. Feeding reverses immune depression, decreases infection rates, and improves outcome in malnourished patients. Because feeding reverses malnutrition-induced immune depression, investigators sought to identify the specific components of the diet that were responsible for the reversal of immune depression. To date, numerous dietary compounds have been identified that possess immune-enhancing actions. Dietary peptides (derived from casein, soy, and other proteins), arginine, glutamine, nucleic acids, vitamin C, vitamin E, and vitamin A have been found to enhance immune function. In addition, the ratio of ω-3 to ω-6 long-chain polyunsaturated fatty acids has been found to alter plasma membrane composition and fluidity, ion-channel flux, cell-signaling mechanisms, eicosanoid responses, cytokine release, and immune cell responses. Based on animal studies, several enteral nutritional formulas were developed to augment the human immune system and reduce infections in critically ill patients.

These immune-enhancing formulas improve immune response in animal models of injury (such as burn and infection) and in humans admitted to intensive care units (ICUs). Experimental evidence also indicates that these formulas can have a favorable effect on morbidity and mortality in animals. Based on these responses, the immune-enhancing formulas were evaluated for their ability to improve outcome (decrease morbidity and mortality) in critically ill patients. Efficacy of the immune-enhancing formulas has been assessed in 12 prospective, randomized, clinical trials (Table 1) (1–12). The majority of these trials used a formula containing intact protein, added arginine, RNA, and a mixture of ω-3 and ω-6 polyunsaturated fatty acids. However, a variety of formulas were used in the trials, and results are similar using different immune-enhancing formulas. Given that early enteral feeding is beneficial (13), patients were fed early after injury or illness. Recent trials (7–14) matched calories and protein intake when comparing the immune formulas with control formulas. However, some of the early trials (2, 4–6) did not match protein intake. The results of both recent and earlier trials do not appear to differ as a result of protein intake. In general, the control formulas consisted of standard intact protein- or amino acid-based formulas. Most of the studies were performed in burn, trauma, or surgical patients. The results of all of the studies support an outcome advantage (i.e., reductions in infections, total complications, or length of stay) for the immune-enhancing formulas (Table 1).

In this issue of *Critical Care Medicine*, Dr. Atkinson and colleagues (14) add to the existing literature on immune-enhancing formulas in critically ill patients. Their study evaluated both medical and surgical ICU patients and was performed using a prospective, randomized, double-blind, controlled design, making it the most rigorously designed study to date. Importantly, the design matched calories and protein intake, and *a priori* evaluated a subgroup of patients who received a minimal quantity of formula during the first 72 hrs of ICU hospitalization. Since immune-enhancing formulas take some time (usually days) to produce their immune effects and only patients who receive a critical amount of formula would be expected to benefit, it is important to feed all patients in a study the critical amount or to *a priori* design the study to evaluate only patients receiving a specified amount of formula. One must also ensure that study groups are comparable. This issue is extremely important since we would not expect antibiotics and other drugs to work in patients who fail to receive them or fail to receive adequate doses. Dr. Atkinson and colleagues (Table 1) report that successful early feeding with the immune-enhancing formula reduced mechanical ventilation time, ICU stay, hospital length of stay, and the duration of the systemic inflammatory response syndrome.

To date, 12 of the 13 prospective, randomized, clinical trials comparing an immune enteral formula with a standard formula report improved outcome (i.e., reduced complications, infections, or length of stay). Overall, mortality does not appear to be affected. However, reduced morbidity and length of stay have been reported by a number of investigators to result in lower hospitalization charges and presumably lower hospitalization costs (8, 10). Thus, the majority of the available data supports the use of an immune formula in most critically ill patients. It remains unclear which immune-enhancing formula is the best. Multiple immune-enhancing formulas have been used in the trials, and all appear to be efficacious. Only one published study (15) compared two immune-enhancing formulas. Saffle et al. (15) compared an immune-enhancing formula containing added arginine, RNA, and ω-3 polyunsaturated fatty acids with a formula containing high protein and added ω-3 polyunsaturated fats. The second formula was higher in glutamine, glutamic acid, cysteine, branch-chain amino acids, β-carotene, vitamin C, and fiber concentrations. This study of two immune-enhancing formulas reported no differences between formula groups for mortality, length of hospitalization, hospitalization charges, or frequency of complications. Additional studies comparing immune-enhancing formulas are underway, and results should be available within the next year.

In evaluating the available data, it is important to acknowledge the fact

Key Words: infection; immune-enhancing enteral diets; enteral feeding; nutrition; length of hospital stay; ICU outcome



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that every study has some flaws. For example, in some studies, protein intake was not matched between study formulas. More recent studies and current thinking support the premise that the slight differences in protein intake are not clinically important for the reported effects. Many of the early studies were designed to reproduce clinical practice in which clinicians used the formulas directly from their containers and tapered the formula to clinical effect. Formulas with supplemental arginine would have higher protein concentrations and patients receiving these formulas would receive more protein. These early studies using the formulas "as is" better reflect clinical practice than the newer studies, which supplement protein so as to match protein intake. The outcome benefits of the immune-enhancing formulas are found only in patients receiving critical amounts of formula. This scenario makes scientific sense, since patients who do not receive enough formula are unlikely to receive the benefits (as with drug administration). Thus, I believe that the analysis of the subgroups who received critical amounts of formula are valid. Intention-to-treat analysis is less valid since it would also fail to demonstrate the beneficial effects of drugs in patients who fail to receive adequate amounts. However, subgroup analyses should be considered before starting a study. This point is unclear in some of the studies.

The present enteral formulas represent first-generation immune-modulating formulas. Current research is aimed at evaluating the immune effects of individual nutrients, isolation and study of the pharmacologic effects of new immune nutrients, and investigation of the mechanism of action of immune-modulating dietary compounds. New-generation formulas, based on better knowledge of nutrient pharmacology, are on the horizon.

In summary, a critical review of prospective, randomized, clinical trials, comparing early enteral feeding with immune-enhancing vs. standard

**Table 1.** Prospective, randomized, clinical trials of immune-enhancing versus standard enteral formulas

| Reference | Patients | Isocaloric and Isonitrogenous | Results | Improved Outcome? |
|---|---|---|---|---|
| Gottschlich et al. (1) | Burn; n = 50 | Yes | IMF reduced wound infections (75%) and LOS (31%) ($p < .05$); IMF decreased total infections ($p < .07$) | Yes |
| Daly et al. (2) | Gastrointestinal surgery; n = 77 | No; less protein in STD group | IMF reduced infections and wound complications (70%; $p < .05$); IMF reduced LOS (22%; $p < .05$) | Yes |
| Chlebowski et al. (3) | HIV; n = 56 | Yes | IMF reduced hospital admissions ($p = .02$) | Yes |
| Brown et al. (4) | Trauma; n = 37 | No; similar protein intake; IMF group received more calories | IMF reduced infections by 71% ($p < .05$) | Yes |
| Moore et al. (5) | Trauma; n = 98 | No; similar caloric intake; IMF group received more protein | IMF reduced abdominal abscesses ($p = .023$) and multiple organ failures ($p = .023$); IMF group had decrease in ventilator days, ICU days (5.3 vs. 8.6), and hospital days (14.6 vs. 17.2) (NS) | Yes |
| Bower et al. (6) | Trauma, surgery, sepsis; n = 296 | No; IMF group received more protein | All patients: IMF group had 24% less infections and decreased LOS (21 vs. 26 days) (NS); IMF decreased LOS in septic patients (18 vs. 28 days) ($p < .05$)<br><br>Patients meeting feeding parameters (n = 85): IMF reduced LOS (21 vs. 29 days) ($p < .05$) | Yes |

IMF, immune-enhancing formula; LOS, length of stay; STD, standard formula; ICU, intensive care unit; ARDS, adult respiratory distress syndrome; SIRS, systemic inflammatory response syndrome; NS, not significant.



**Table 1.** *(cont'd)*

| Reference | Patients | Isocaloric and Isonitrogenous | Results | Improved Outcome? |
|---|---|---|---|---|
| Daly et al. (7) | Gastrointestinal surgery; n = 60 | Yes | IMF group developed fewer infections and wound complications (10% vs. 42%) ($p < .005$); IMF group had shorter LOS (16 vs. 22 days) ($p = .02$) | Yes |
| Kudsk et al. (8) | Trauma; n = 35 | Yes | IMF reduced major infections (6% vs. 41%) ($p = .02$); IMF group had shorter LOS (18 vs. 33 days) ($p = .03$); IMF group had lower hospital charges ($80,000 vs. $110,000) ($p = .10$) | Yes |
| Mendez et al. (9) | Trauma; n = 43 | Yes | More ARDS in IMF group before entry into study (32% vs. 14%)<br><br>IMF patients remained on ventilator longer and had longer LOS (NS); IMF group had more infections (86% vs. 57%) (NS) | No |
| Senkal et al. (10) | Gastrointestinal surgery; n = 154 | Yes | Total complications lower in IMF group (22% vs. 31%, NS); Late infections (after postop day 5) lower in IMF group (6% vs. 17%; $p < .05$); lower cost in IMF group; LOS similar | Yes |
| Braga et al. (11) | Gastrointestinal surgery; n = 110 | Yes | Infections (16% vs. 24%), sepsis score (4 vs. 6.5), and LOS (14 vs. 16 days) lower in IMF group (NS) | Trend toward yes |
| Galban et al. (12) | Sepsis; n = 176 | Yes | Mortality (19% vs. 32%; $p < .05$) and infections (7% vs. 20%; $p < .05$) lower in IMF group | Yes |
| Atkinson et al. (14) | Mixed medical and surgical ICU patients; n = 101 | Yes | Successful early enteral feeding with IMF resulted in reduced requirement for mechanical ventilation (6 vs. 10.5 days), reduced LOS (15.5 vs. 20 days), reduced ICU stay (7.5 vs. 12 days), reduced SIRS (3 vs. 6 days) (all $p < .05$) | Yes |

IMF, immune-enhancing formula; LOS, length of stay; STD, standard formula; ICU, intensive care unit; ARDS, adult respiratoy distress syndrome; SIRS, systemic inflammatory response syndrome; NS, not significant.

enteral formulas, indicates that these formulas are highly likely to improve outcome and reduce hospitalization costs. Using an evidence-based approach, the use of immune-enhancing formulas in critically ill patients represents a level I recommendation.

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# EVENTS TO LOOK FORWARD TO IN 1999

**January**

*Singapore Medical Association*
Saturday, 23 January, 1999
30th National Medical Council: Staying Healthy in the Golden Years
Topic: Healthy Dietary Habits for the Elderly
Venue: IRAS Auditorium
English Forum
*Time: 2.00 – 3.30 p.m.*
*Speaker: Ms Tanya Footman*
Mandarin Forum
*Time: 4.00 – 5.30 p.m.*
*Speaker: Mrs. Chan Yam Yoke Yin*

**February**

*Singapore National Heart Association (SNHA)*
Food Industry Seminar

**March & April**

*SNHA*
Talks and Briefings to health professionals, home economics teachers and schools

**June**

*SNHA*
Launch of Healthier Choice website

**July**

*ILSI Southeast Asia*
Regional Workshop on Nutrition and Aging

**August**

*SNHA*
Contest for "Healthier Choice" symbol

**September**

National Healthy Lifestyle Campaign

*SNHA*
Public Exhibition at National Healthy Lifestyle Campaign

World Osteoporosis Day

**October**

*ILSI Southeast Asia*
Regional Workshop on Biomarkers for Functional Foods

*Singapore Cancer Society*
World Cancer Awareness Day
Terry Fox Run
Cancer Awareness Fair

Diabetes Awareness Day

**December**

*SNHA*
Supermarket Tour Program

*Diabetes Society of Singapore*
3 – 6 December
Annual Diabetes Camp for Children



REPORT

# ASIAN CONFERENCE ON EARLY AND CHILDHOOD NUTRITION

## November 1–4, 1998
## Kuala Lumpur, Malaysia

The Asian Conference on Early and Childhood Nutrition: Growth, Health and Economics was held in Kuala Lumpur, Malaysia, from November 1 - 4, 1998. It was organized by ILSI Southeast Asia together with UNICEF, Ministry of Health Malaysia, and the Nutrition Society of Malaysia, in collaboration with the Food and Agriculture Organization of the United Nations (FAO) and the Federation of Asian Nutrition Societies (FANS). The conference was attended by almost 300 experts and participants from the region and elsewhere.

In the keynote address, **Dr. Joseph Hunt** of the Asian Development Bank, stressed the enormous cost of neglecting early and childhood nutrition arising from losses in preventable deaths, illness, poor psychomotor and cognitive development, poor achievement in school, reduced earnings and work productivity, and lower life expectancy. **Dr. Fernando Monckeberg**, President of the Chilean Nutrition Foundation, highlighted the impact of economic crisis on food security which may range from minimal and transient to disastrous and long-lasting, depending on the level of socio-economic development of the country. Dr. Monckeberg stressed that the economic crisis could be an opportunity to develop and implement long-range programs to attack the root causes of poverty and malnutrition. **Dr. Rudolf Knippenberg** of UNICEF EAPRO, summarized that most of the countries in the region recognize protein-energy malnutrition (PEM) and micronutrient deficiencies notably vitamin A deficiency (VAD), iron deficiency anemia (IDA) and iodine deficiency disorders (IDD), as the major problems.

In the plenary session, "From Mother to Child: Issues and Options", **Dr. Lindsay Allen** of the University of California, Davis, USA, stressed that achieving optimum weight gain during pregnancy is an important goal because of the close association of weight gain with the infant's birth weight. She reviewed the value of vitamin A/beta carotene, iron, zinc and folic acid supplementation in women, citing the benefits to both mother and child. Dr. Allen recommended improving the nutritional quality of pregnant women's diet with animal products, micronutrient-dense foods and multiple micronutrient supplementation.

In the session on "Preventing Growth Faltering: The Challenges", **Dr. Ray Yip** of UNICEF pointed out that the process of growth faltering starts from 6 months of age and is completed by 2 years of age. He called for a refocus of attention on children less than 2 years of age. Dr. Yip also explained that it is necessary to include the entire malnourished population in nutrition strategy and not just the severely or moderately malnourished. **Dr. Dennis M. Bier**, Children's Nutrition Research Center, Houston, Texas, USA, reviewed the recent revision in energy and macronutrient requirements by the UNU International Dietary Energy Consultancy Group in 1996. **Dr. Sandra Hoffman** of the Academy for Educational Development, Washington, D.C., USA, discussed strategies to improve exclusive breast-feeding and complementary feeding. She said that complementary feeding could be improved with age-appropriate, energy-dense foods, frequent feedings, and 'interactive feeding' techniques such as feeding the child directly, encouraging the child to eat and talking to the child during feeding. **Dr. Budi Utomo** of the University of Indonesia presented the results of a recent survey that showed that absence of exclusive breast-feeding, delayed breast-feeding initiation, prelacteal feeding, discarding colustrum, and early introduction of supplementary feeding were common practices in Indonesia.

**Dr. R. A. Gibson** of the Child Nutrition Research Center, North Adelaide, Australia discussed the value of long-chain poly-unsaturated fatty acids (LCPUFA), particularly docosahexaenoic acid (DHA), and their possible role in infant's neurodevelopment. The benefits of DHA are likely to be greater in preterm infants than term infants. **Dr. David Hill** of the Royal Children's Hospital in Melbourne, Australia, said that food protein hypersensitivity affects 5-8 % of children in the first 3 years of life. Reactions range from immediate to intermediate to late, in the form of cutaneous, gastrointestinal, respiratory or mixed. He enumerated some of the common food allergens in infants such as fish, shellfish, eggs, and milk, but stressed that breast milk is virtually non-allergenic. **Dr. Peter Aggett** of the University of Central Lancashire, UK, reviewed epidemiological evidence showing challenging association

between sub-optimal intrauterine growth and development of chronic disease in later life. The progression of atherosclerotic lesions, dyslipedemia, raised blood pressure, and impaired glucose tolerance, can be tracked from early childhood to adulthood.

In the Session on 'Improving Micronutrient Status: Development and Progress', **Dr. Martin Bloem**, Asia Regional Director of Hellen Keller Institute, cited the results of meta-analysis of studies on the effect of vitamin A supplementation that reduced mortality in children. Dr. Bloem recommended dietary diversification and continuing high-dose vitamin A supplementation. Maternal mortality was also reduced by 30-50% after supplementation with low dose vitamin A. **Dr. Ray Yip** highlighted that IDA results in significant developmental delay, and part of the impact is not reversible. Dr. Yip recommended the promotion of iron-rich food items that are already acceptable and affordable. He emphasized food fortification for populations already consuming industry-produced complementary food with single or multiple micronutrients, for example, with iron, zinc and vitamin A. During the same session, **Dr. Lindsay Allen** said that zinc deficiency may be a widespread problem in areas with low intake of animal products. Zinc supplementation studies have shown that such intervention may improve linear growth, reduce prevalence, incidence duration and persistency of diarrhea, respiratory infections and risk of malaria. Zinc supplementation may also improve dark adaptation and neurobehavioral function in zinc deficient children.

In the Session 'Nutrition and Physical Activity in Children: The Asian Picture', **Dr. Rodolfo Florentino** of the Philippine Association of Nutrition, **Dr. Soekirman** of the Bogor Agricultural University in Indonesia, and **Dr. Tee E-Siong** of the Institute of Medical Research, Malaysia, summarized the results of the ILSI SEA coordinated study on nutrition, dietary and physical activity pattern of 8-10 yr old school children in three Asian cities. The study showed that high prevalence of underweight and stunting is still the main nutritional problem in public schools. On the other hand, signs of the emerging problem of overweight, particularly in private schools and in boys were seen in all three cities. The study also highlighted methodological problems in using the WHO guidelines for assessing under- and overweight among this age group of children.

**Dr. Motoko Sakamoto** of Wayo Women's University, Japan, traced the growth of Japanese children from before the last World War to the present. The rapid increase in height after the war may have been related to improvement in the diet, including increases in dietary energy, protein and fat intakes. Similarly, **Dr. Jin Shuigao** of the Chinese Academy of Preventive Medicine, showed that in China, increases in per capita intakes of dietary energy and protein starting from the late 70s, were accompanied by very significant drop in the proportion of underweight children especially in the urban areas. In fact, the prevalence of overweight appears to be increasing in urban areas.

Examining the impact of economic crisis on nutrition, **Dr. Martin Bloem** presented preliminary data of four provinces in Indonesia. It showed a significant decrease in the consumption of foods from animal sources resulting in an increase in the prevalence of wasting especially in girls and increase in prevalence of micronutrient deficiencies. In Chile, **Dr. Fernando Monckeberg** said that the rapid improvement in nutritional status of children even during periods when economic status of the country were unstable, could be attributed largely to long-range programs and interventions. According to **Dr. Kraisid Tontisirin** of Institute of Nutrition, Thailand, the present economic crisis affecting the region has not shown any severe effect on food security due partly to 'food safety nets' of the government and NGOs.

In the Panel Discussion that followed, **Dr. Lindsay Allen** pointed out that based on what we now know, the greatest benefit in investment in nutrition lies in improving nutrition during pregnancy and infancy to prevent stunting and wasting; in promoting breast-feeding and improving complementary feeding; and in micronutrient intervention. **Dr. Krishna Belbase** of UNICEF, USA, explained that information should be assessed for its relevance, analyzed in its usefulness, and translated to action at all levels of planning and implementation. **Dr. Kraisid Tontisirin** enumerated important success factors related to nutrition programs: creation of public awareness. **Ms. Ma. Bernardita Flores** of the National Nutrition Council of the Philippines, recommended that the partnership among government, NGOs and industry should be a relationship of equals anchored in respect, mutual trust, honesty and openness. Stereotypes of government, academe, NGOs and industry must be broken; similarities and differences recognized to achieve a win-win arrangement. Finally, **Dr. David Yeung** of HJ Heinz Co., Canada, said that given the commitment of the industry to produce nutritious foods, governments should get the food industry involved and responsible in nutrition promotion.





# 2ND ASIAN CONGRESS OF DIETETICS

The 2nd Asian Congress of Dietetics was held in Seoul, Korea from 9th to 12th August 1998. Three members from the Singapore Nutrition and Dietetics Association attended the Congress which was held at Lotte World, Seoul. The Congress was hosted by the Korean Dietetic Association and it attracted representatives from over 14 countries. Approximately 3000 representatives were from Korea itself.

The 1st Asian Congress of Dietetics was hosted by the Indonesian Dietetic Association in Jakarta in 1984.

The Congress consisted of 10 plenary lectures, 58 symposia, 6 workshops, 7 free communication posters and 120 oral poster presentations. There were also nutrition products, instruments, equipment and books on display.

The theme of this year's Congress was "Networks and New Ventures", presented by Ms. Sook He Kim, Vice President, The International Union of Nutritional Sciences. She stressed the importance of forming a new vision and pursuit by solving dietetic problems in the region.

Among the outstanding plenary lectures and symposia presented, some of the more interesting ones are as follows:

## Dietitians' Role in Preventive Medicine

*Sunard Taechangam (Thailand)*

Dietetics and nutrition have become increasingly important as interest in health promotion and the prevention of disease and medical nutrition therapy gain momentum. Changes in lifestyles, occupation patterns and environment induced by ongoing developmental transition have brought about changes in the traditional dietary practices. Dietetic professionals in all areas of practice assume more responsibility to meet the challenges and needs of preventive dietetics. In Thailand, rural Thais are still facing nutrient deficiency diseases, whereas affluent urban Thais are encountering diet related chronic diseases. Food safety is becoming an important issue. The dietitian is responsible for carrying out all three levels of preventive measures provided for individuals including health promotion and disease prevention, risk appraisal and reduction, and treatment and rehabilitation. The paper addresses major areas of activities for dietitians involved in preventive medicine. The activities promise to make the greatest contribution to optimal nutrition that can promote health and reduce the risk of chronic disease.

## Computerised Nutrition Screening and Length of Hospital Stay (LOS)

*Younghae, Kim Park (Korea)*

It has been well documented that malnutrition is prevalent among hospitalised patients and is associated with extended LOS, higher costs, and increased mortality and morbidity. We carried out a prospective study of 2022 patients in the Asan Medical Centre to determine 1) the prevalence of malnutrition at the time of admission and 2) any relationship between nutritional status and LOS. All patient information was obtained from the Order Communication System database. The nutrition screening sheet shows the most current values for serum albumin and TLC. Within 72 hours of admission, the nutritional status was screened. Patients were classified as malnourished if serum albumin was less than 3.3g/dl, and/or TLC was less than 1500/mm$^3$. Malnutrition existed in all diagnostic areas, with the highest prevalence in oncology (52.7%). 37% of all patients were malnourished at the time of

admission. Either serum albumin or TLC was subnormal (malnourished I) in 29% of the patients, and both were subnormal (malnourished II) in 8% of the patients. The LOS (in days) was significantly higher in the malnourished group I than in the well nourished group [16.6 (22.9 versus 12.7 (3.01, p (0.01)], and in the malnourished group II than in the malnourished group (23.7(30.68 vs 16.6(22.9, P(0.01) with large individual variations. The mortality rate was 4.6 times higher in malnourished group I (21.2% Vs 0.47%), and 17 times higher in the malnourished group II (8.07% Vs 0.47%) compared to the well nourished group.

**Conclusion:** A patient's nutritional status upon admission has serious effects on LOS and mortality. Computerised nutritional screening is a simple and cost-effective way of prioritizing patients who need nutrition intervention.

## Maternal Weight Gain and Pregnancy Outcome

*Hyeon-Sook Lim (Korea)*

Gestational weight gain has been a concern of maternal and foetal health care workers for a long time. However, the focus has shifted from achieving appropriate infant birth weight and preventing low birth weight to prevention of high birth weight and subsequent maternal obesity in developed countries. Thus, the Institute of Medicine (IOM), in 1990, established recommended ranges for maternal total weight gain during pregnancy according to pre-pregnancy maternal body mass index. Several studies tried to validate the ranges for women who have different ethnic background, especially for Black and White, but the results were inconclusive. There were a few reports for women who have smaller body size in South East Asia compared to western countries. Since body mass of reproductive women has increased and the IDM's 1990 guidelines are higher than those previously recommended, there is a growing concern about postpartum weight retention. However, pregnancy and maternal body weight development are intertwined complicated matters.

## Nutrient Intake and Growth of Infants by Feeding Practices

*Hong Seok Ahn (Korea)*

The purpose of this study was to evaluate the nutritional status and growth of Korean infants, who were treated in community clinics in low-income areas, by estimating anthropometric measurements and dietary intakes. Dietary intake and growth were compared among 143 infants, who were at the age of 1 to 9 months, by different feeding patterns.

The overall mean nutrient intake in this study was below the current recommendations except for calcium intake at the age of 7 to 9 months. At 1 to 3 months, the average calorie and protein intake showed no significant difference in each group; however, calcium, zinc and iron intake in the formula-fed infants (FF) were higher than in breast-fed infants (BF) and mixed-fed infants (MF). At the age of 4 to 6 months, nutrient intake was shown to be higher in breast-fed groups given supplementary foods (BSF) and formula-fed ones given supplementary foods (FSF).

All the subjects of this study showed large Z-score. The growth of infants up to the age of 6 months showed no significant difference by the feeding pattern, however, after 7 months the growth of the BSF group was significantly lower than that of the FSF group.

As a result, the average status of nutrient intakes of infants in this area were lower than the RDA. However, the growth pattern was fairly good. Although breast-milk is beneficial for infants, mothers should be aware of the importance of supplemental food and its practice to support good nutrition.

*By Nehal Kamdar*
*Dietitian, Kendang Kerbau Women's & Children's Hospital, Singapore*

*The author would like to thank SNDA and the other sponsors for making this trip possible.*





# ASIAN FOOD INFORMATION CENTRE –

## A New Resource for Nutrition and Food Safety Matters

New research is reported almost daily in the dynamic area of nutrition and food safety. The sheer volume of information and its technical nature can make it difficult for health professionals and the media to keep abreast of latest developments in this area. In addition, new findings often appear to conflict with previous findings making interpretation of the research difficult.

Asian consumers have become more aware of the relationship between diet and health. They are actively searching for information on nutrition and food safety matters. Confusion and misperceptions on what constitutes a healthy diet and lifestyle are common.

A new organisation has been established in Asia to assist all of these parties by communicating science-based information on nutrition and food safety in a readable format. The Asian Food Information Centre (AFIC) opened its first office in Singapore in July this year. AFIC is a non-profit organisation covering the entire Asian region. Its mission is to serve as a link in relaying information between the scientific community, health professionals, government agencies, food manufacturers and the media.

AFIC works in partnership with key scientific associations in Asian countries to provide the latest and most accurate scientific information. Supported by a broad mix of food, beverage and agricultural companies, AFIC employs a team of scientific, nutrition and communications professionals to manage its programmes. A loose association is also maintained between AFIC and similar food information organisations around the world

The programmes developed by AFIC vary by region according to local needs. One program which is undertaken Asia-wide is the distribution of Food Facts Asia, a newsletter examining current topics in food safety and nutrition that is distributed quarterly. In addition to this, AFIC produces a variety of brochures and background papers on nutrition and food safety topics.

An AFIC website is currently under development and is expected to be operational by December this year.

The AFIC office also serves as an information resource for the media and other interested parties in identifying scientists and other expert sources on food topics and providing referrals to additional sources of information on food issues.

In addition, AFIC holds educational programmes, such as workshops and seminars, in various Asian countries, on nutrition and food-related issues.

The AFIC office can be reached at 8 Temasek Boulevard, #42-01 Suntec Tower Three, Singapore 038988. Tel: 832 7637 Fax: 832 7638.

# NEW HEALTH CLAIM PROPOSED FOR RELATIONSHIP OF SOY PROTEIN AND CORONARY HEART DISEASE

FDA has proposed allowing health claims about the role soy protein may have in reducing the risk of coronary heart disease (CHD) on the labels and labelling of foods containing soy protein. This proposal is based on the agency's determination that soy protein, as part of a diet low in saturated fat and cholesterol, may reduce the risk of CHD.

CHD is the most common, most frequently reported, and most serious form of cardiovascular disease, and is the number one cause of death in the United States. Despite the decline in deaths from CHD over the past 30 years, this disease still causes more than 500,000 deaths annually, and contributes to another 250,000 deaths. High blood total cholesterol and high low-density lipoprotein (LDL) cholesterol levels are proven risk factors for CHD.

In proposing this health claim, FDA concluded that foods containing protein from the soybean as part of a diet low in saturated fat and cholesterol may reduce the risk of heart disease by lowering blood total cholesterol and LDL-cholesterol. The amino acid content in soy protein is different from animal and most other vegetable proteins, and appears to alter the synthesis and metabolism of cholesterol in the liver.

Foods containing soy protein include soy milk, tofu, meat substitutes (such as vegetable burgers) and baked goods made with soy flour. Because soy protein occurs in or can be added to a wide variety of foods and beverages, it is possible to eat soy protein-containing products as many as 4 times a day (3 meals and a snack).

Studies show 25 grams of soy protein per day have a cholesterol-lowering effect. Therefore, for a food to qualify for the health claim, each serving of the food must contain at least 6.25 grams of soy protein, or one-fourth of the 25-gram amount shown to have a cholesterol-lowering effect.

An example of a claim using this food-disease relationship is:

"Diets low in saturated fat and cholesterol that include 25 grams of soy protein per day may reduce the risk of heart disease. One serving of (name of food) supplies ____ grams of soy protein."

FEATURE ARTICLE

# THE US RDA — BEING REVAMPED

## BACKGROUND

The US Recommended Dietary Allowance (RDA) has been around since 1941. The RDAs were intended to evaluate nutrient adequacy of the diets of groups. Periodic revisions since then provided the state-of-the-artknowledge for planning and assessing diets of healthy populations. Designed to provide for 97 percent of a healthy population, there was no scientific basis that RDAs would meet the needs of every individual. And, most important, RDAs were set to prevent deficiency diseases.

## NEED FOR REVAMP

Since the RDAs were the only reference tools available for the practicing Nutritionist and Dietitian, they were used to evaluate the diets of individual patients and even to develop special food products to meet the needs of individuals. Further, the science of nutrition has over the last few decades, pointed to the emerging facts of the role of nutrients in the prevention of chronic diseases. The RDAs needed to reflect this new science.

## A MAMMOTH TASK BEGUN

The Food and Nutrition Board (FNB) initiated the process of changing the RDA in 1993. The overall project is a comprehensive effort undertaken by the Standing Committee on the Scientific Evaluation of Dietary Reference Intake (DRI) of the FNB, Institute of Medicine, National Academy of Sciences, and Health Canada.

## KEY FEATURES

- Standardized reference values for two countries – The United States and Canada;
- Clear set of documentation for the derivation of each value;
- Inclusion of the concept of the promotion of nutrient function and biologic-physical well-being;
- Consideration of evidence of prevention of diseases and developmental disorders; and
- Examination of data about selected food components that have not been considered as essential nutrients, such as phytoestrogens, phytochemicals and fibre.

## ACHIEVEMENTS TO DATE

In 1995, seven expert group panels were set up to review major nutrients, vitamins, minerals, antioxidants, electrolytes and other food components. In 1997, the first DRI report in calcium, phosphorus, magnesium, vitamin D and fluoride were released. In 1998, the report on thiamin, riboflavin, niacin, vitamin B6, folate, vitamin B12, pantothenic acid, biotin and choline was released.

## DRI'S TAKE OVER

The RDAs have now been replaced by the Dietary Reference Intakes (DRIs). Unlike its predecessor, the DRIs are no longer a single set of values. DRIs include the following: Estimated Average Requirement (EAR), Recommended Dietary Allowance (RDA), Adequate Intake (AI) and Tolerable Upper Limit (UL).

## WHAT'S IN THE NAME?

- *Estimated Average Requirement (EAR):* EAR is the nutrient value that is estimated to meet the requirement of 50 percent of the individuals in each life-stage and gender group. It is expressed as a daily value averaged over time, for most nutrients at least one week. It also includes an adjustment for an assumed bioavailability of the nutrient. The EAR is used to set the RDA. It is to be used to assess the nutritional adequacy of intakes and planning diets of groups.

- *Recommended Dietary Allowance (RDA):* The RDA is the daily dietary intake level that is sufficient to meet the nutrient requirements of nearly all (97 to 98%) individuals in the life stage and gender group. The RDA is to be used in a prescriptive sense, as a goal for dietary intake by individuals. It is not intended to be used for assessing the diets of either individuals or groups or for planning diets for groups.

The EAR serves as the foundation of the RDA. The RDA is set at 2 SDs above the EAR. If sufficient data is not available to calculate standard deviation, a coefficient of variation of 10% is used.

$$RDA = EAR + 2\,SD_{EAR}$$
Or
$$RDA = 1.2\ EAR$$

- *Adequate Intake (AI):* The AI is based on observed or experimentally determined approximations of the average nutrient intake, by a defined population or subgroup that appears to sustain defined nutritional state such as normal circulating nutrient values or growth. In the absence of EAR and RDA, the AI may be used as a goal for nutrient intake of individuals.

- *Tolerable Upper Limit (UL):* UL is the maximal level of nutrient intake that is unlikely to pose risks of adverse health effects to almost all individuals in the target group. The UL is not intended as a recommended level of intake. The need for ULS grew out of the increase in the practice of fortifying foods with nutrients and in the use of dietary supplements by people and in larger doses. As intake increases above the UL, the risk of adverse effects increases.



## Uses of Dietary Reference Intakes

| Suggested Uses of DRI | | | | |
|---|---|---|---|---|
| Type of Use | Individual | | Group | |
| Assessment | EAR | Of limited use without clinical, biochemical and anthropometric data | EAR | Use with data on the group's distribution of intake, adjusted for day to day variation in intake |
| | AI | | | |
| | UL | | | |
| Planning | RDA | Aim for this intake | EAR | Use with data on the group's distribution of intake |
| | AI | Use as a guide in the absence of RDA | AI | Use for formulation of tentative goals for mean intake of the population |
| | UL | Use as a guide that higher amounts increase risk | | |

The FNB will be releasing a manual for the users of the DRIs. This guide is aimed at health professionals, nutrition policy planners, dietitians and nutritionists to ensure appropriate use of the DRIs.

## INTERNATIONAL USES OF THE DRI

The FNB cautions against the use of the DRIs outside the US and Canada, until more is known about the prevalence of chronic disease risk and habitual nutrient intakes in other countries.

## IN THE FUTURE

1999 will see the release of the reports on vitamins C, E, beta-carotene and other antioxidants. Reports of trace elements vitamin A, K, electrolytes, fluids, energy, macronutrients and functional food components are expected in the next millennium.

# PLATE WASTAGE AND NUTRITIONAL ASSESSMENT OF RESIDENTS AT THONG TECK HOME (98NC7)

### Final Year Project (Industry), Year 3 Students
### Diploma in Applied Food Science and Nutrition

**Students:** Sri Devi d/o Arunagiri, Tan Leng Leng, Mohamed Hisham Bin Salim

**Industry Supervisors:** Mrs. Anna Jacob, Ms. Pauline Chan (Food and Nutrition Specialists Pte Ltd)

**Supervisor:** Mrs. Sudha Vasudevan

nutritional assessment on the residents at Thong Teck Home, a lacto-vegetarian nursing home and a study of its food service operation was conducted. The nutritional assessment involving anthropometric measures and dietary history was carried out on 52 residents comprising of twenty-six males and twenty-six females. Assessment of plate wastage was done randomly. A study of the food service operation was made and an analysis of the Home's menu for nutritional content was carried out.

The results showed that certain factors such as body mass index (BMI), height and weight status, patterns on food consumption, appetite, emotions, medical conditions, food intolerance and the type of diet influenced the nutritional status of the residents. High plate wastage was also observed and this was due to poor timing of meals, inconsistent serving size of meal items, poor spacing and planning in the menu and meal fatigue. The high plate wastage could be reduced by regularly monitoring the standard of meals provided. A variety of meals were present in the diet of the residents but more planning should be incorporated in the meals to prevent repetition of meals.

'The amount of energy available in the diet meets 71.9% of the RDDA for males and 83.9% of the RDDA for females. Carbohydrates in the menus provide 71.2% of the total energy, protein 13.1% and fat 15.7% of the total energy. Availability of nutrients such as energy, fat, vitamin A, vitamin C, fibre, cholesterol and folate are adequate with the exception of protein, calcium, potassium, zinc, vitamin B6 and B12. Recommendations such as increasing the level of protein by including more legumes and incorporation more soybean mock meat into recipes.

The food service operation was an efficient one but better utilization of equipment cleanliness, hygiene and flow of the food production may be the area to be improved. Incorporation of a stock rotation form and a schedule for cleaning may further improve the effectiveness and efficiency of the food service operation.

*In Partial Fulfillment of the Requirements for the Diploma in Applied Food Science and Nutrition.*

# SNHA MAKES HEALTHY FOOD CHOICES A BREEZE

Making healthier food choices will soon be quite a breeze, as the Healthier Choice Label Programme launched by the Singapore National Heart Association (SNHA) gathers momentum.

Unveiled by the Minister for Health, Mr Yeo Cheok Tong on 30 August 1998, the Healthier Choice Symbol will be displayed on pre-packaged foods in Singapore. Interested companies with healthy products may apply for the annual licence, which permits them to display the Symbol on products that meet the guidelines set by the Food Labelling Committee of the SNHA. Evaluation of food products is done on a case by case basis and looks closely at the fat, saturated fat, sodium and dietary fibre contents, as well as the contribution it makes to a healthy, well balanced diet.

Healthier Choice
SINGAPORE NATIONAL HEART ASSOCIATION
Eat In Moderation

The Healthier Choice Symbol consists of a four-layered pyramid in bright red, to represent the Healthy Diet Pyramid. The Symbol is accompanied by a cautionary message "Eat In Moderation" to ensure that consumers do not assume that the approved foods can be eaten in excessive amounts or in exclusion of all other foods.

The earliest line of approved products to hit the supermarket shelves were the low fat diary products, notably Anlene, Nespray, Klim and Milkmaid. Consumers get to hear more about the Symbol through series of advertisements launched by the SNHA recently. Companies are also permitted to include the Symbol in their product advertisements.

The programme is implemented on a phased basis. Consumers will see the symbol on other food products as more food categories are included in the programme.

A product without the Healthier Choice Symbol does not necessarily mean that it does not qualify for the Healthier Choice Symbol. A company may choose not to participate in this voluntary programme. However, consumers can load up their trolleys with the products labeled with Healthier Choice Symbol with greater confidence that they are the *healthier choices*.

SNHA plans a series of public education programmes to help health professionals, food industry and consumers use the symbol better. Two public forums will be held in conjunction with the Department of Nutrition of the Ministry of Health in January 1999 to educate the general public on reading food labels and understanding the Healthier Choice Symbol. Health practitioners will be briefed in a series of seminars. Dialogue sessions will be conducted to update food industry throughout the year.

For more information, you can contact Ms Chew Pei Gee at Tel: 5340018.

*By CHEW PEI GEE*
*Nutritionist*
*Singapore National Heart Association*
*and ANNA JACOB*
*Food Labelling Committee*
*Singapore National Heart Association*



# APPLICATION FOR MEMBERSHIP

## [ Singapore Nutrition and Dietetics Association ]

The SNDA welcomes all dietitians and nutritionists, other qualified professionals and corporate bodies interested in the promotion and advancement of nutrition and dietetics to apply for membership. Application forms are available from the Honorary Secretary, Singapore Nutrition and Dietetics Association, Tanglin P.O. Box 180, Singapore 912406 or e-mail: hixson@po.pacific.net.sg

## Membership

**FULL MEMBERS**

A Full Member shall be any person holding a degree, diploma or any other recognised professional qualification in dietetics or nutrition. Dietitians must have completed a minimum of six months internship in clinical dietetic practice.

To expedite the application process, applicants for full members are required to submit the following: copy of conferred degree or diploma; course syllabus and contents; transcripts; verification of membership in other professional nutrition/dietetics associations; and any other supporting documents or information, such as a brief summary of work experience.

**AFFILIATE MEMBERS**

An Affiliate Member shall be any person holding a recognised scientific qualification in medicine, health or food science and who, in the opinion of the Committee, occupies a position allied to the profession of dietetics and nutrition. Persons eligible for full membership do not qualify for affiliate membership.

Affiliate members shall not use their affiliation with the Association for self promotion as nutritionists or dietitians or any other term that infers they are nutritionists or dietitians.

**CORPORATE MEMBERS**

A Corporate Member shall be any suitable corporate body interested in the work of the Association and who, in the opinion of the Committee, is proactive in the promotion of scientifically sound nutrition and dietetics. Each corporate member may nominate a maximum of three employee-representatives to the Association.

Corporate members shall not use their affiliation with the Association for commercial gain or product endorsement, without the prior approval of the Main Committee.

**STUDENT MEMBERS**

Student members include full-time students studying nutrition and/or dietetics at tertiary level. Student membership shall expire at the receipt of the graduation certificate and does not automatically progress to full / affiliate membership. Separate application for respective membership must be made. Persons eligible for full / affiliate membership do not qualify for student membership.

Student members shall not use their relationship with the Association to call themselves nutritionists or dietitians or any other term that infers they are nutritionists or dietitians, nor shall they practise as nutritionists or dietitians.

***Affiliate, Corporate and Student members are not entitled to vote.***

## Membership Fees (Membership year: June – May)

- Full members shall be required to pay an annual membership fee of S$80. Full members joining part of the way into the year may pay a pro-rated subscription, this being calculated from the beginning of the month after membership is confirmed.
- Affiliate members shall pay an annual membership fee of S$60. Those joining December – May are to pay S$30.
- Corporate members shall pay an annual membership fee of S$500. Those joining December – May are to pay S$250.
- Student members shall pay an annual membership fee of S$20. Those joining December – May are to pay S$10.

Payment is only required upon the confirmation of your membership status.

**JOURNAL SUBSCRIPTION FORM**
**(The Journal and Newsletters are distributed free to all members)**

To: The Editor, The Singapore Journal of Nutrition and Dietetics, Singapore Nutrition and Dietetics Association, Tanglin P.O. Box 180, Singapore 912406.

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