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Preface

In an effort to strengthen clinical nutrition research and activities in the country, the Institute for Medical Research convened the 1st National Symposium on Clinical Nutrition from 28-30 March 1994. The Symposium provided a forum for discussing clinical nutrition activities in the country, including research, preventive, curative and training activities. This meeting also facilitated the sharing of experiences and improve linkages between clinicians, nutritionists, researchers, dietitians, pharmacists and nurses. Two round table discussion sessions were also held to deliberate on ways to strengthen the nutrition support team, and training and research in clinical nutrition in the country.

The Symposium was co-organised by the Nutrition Society of Malaysia, and with the support of the World Health Organization. The Organising Committee comprised members from 9 organizations/ departments. The IMR is grateful for the spirit of cooperation exhibited by all members throughout the many months of preparations for the Symposium. Staff members of the Division of Human Nutrition of the IMR played key roles in the organization of this Symposium.

A total of 47 papers were presented by 38 speakers in the 3-day meeting. Thirty-one of these papers were presented by 28 local workers and researchers in clinical nutrition from 11 departments and organizations. In addition, 9 foreign speakers from Australia, Canada, India, Japan, and the United States of America were invited to share their experiences with local participants. Dr Ian Darnton-Hill, WHO Regional Advisor in Nutrition delivered the keynote address.

Some 200 participants were registered for the Symposium. This gathering of the main key persons involved in clinical nutrition research and activities in the country, and the presence of several prominent foreign experts provided a forum for useful interactions and exchange of experiences. This Symposium signifies the commencement of an important chapter in nutrition research and activities in Malaysia.

It was felt important to document the papers presented in the Symposium. The wide variety of papers presented should serve as a useful reference to workers in this field. Reponse from authors to publish their full papers has been very good, enabling a total of 37 full papers to be published in this volume.

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1995

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Experience in establishing TPN service in Malaysian hospitals

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ABSTRACT

Total parenteral nutrition (TPN) service in Malaysian Hospitals was first established at Kuantan General Hospital in 1986. A year later, 3 other hospitals started TPN services, namely Penang Hospital, Kuala Lumpur Hospital and Universiti Sains Malaysia Hospital. I participated in the establishment of the TPN service in Penang Hospital and Universiti Sains Malaysia Hospital. Prior to the implementation of the TPN service, a series of 8 hr. lectures were given to the medical and nursing staff and 12 hr. lectures to the pharmacy personnel. The content of the lectures focussed on the roles and responsibilities of each profession. Several meetings between doctors, nurses and pharmacists were carried out before and after the initiation of the service to discuss the policy, procedures and problems related to the TPN service. Standard TPN request forms for adult and pediatric patients were designed based on the standard TPN request form used in the University of Minnessota Hospital, USA. These request forms were later modified to suit local needs. After a few years of service, a retrospective study was done to evaluate the cost-effectiveness of the TPN service in these two hospitals. The data obtained showed that the average cost for pediatric TPN was RM92 per day, and adult TPN was RM142 per day (1). The data on the effect of TPN in pediatrics with necrotising enterocolitis (NEC) showed that the mortality rate among the NEC cases were reduced from 80% to less than 25% (2). To strengthen the service, we are now providing on-the-job training in the form of lectures to all personnel involved in the TPN service. We are also sending our staff to attend conferences or workshops related to TPN to update their knowledge and skill in TPN service. At present our TPN service have been recognised as a site of training for the South East Asian countries and G 15 countries.

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1 Joseph A, Hussain SH, Bahari MB, Heah SG, Kaur P. Total parenteral nutrition: a retrospective study on the usage and cost-benefit. Silver Jublee Malaysian-Singapore Congress of Medicine, 2-6 October, 1991.

2 Bahari MB, Shamsuddin AF, Review of the TPN in necrotising enterocolitis, 24th Singapore-Malaysian Congress of Medicine, 1990.

Proc 1st Natl Symp Clin Nutr 144-1649, 1994

Role of the pharmacist in nutritional support: experience in a teaching hospital

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ABSTRACT

Parenteral nutrition service was started in HUSM in 1987. The latest data available (1993) show that the mean TPN preparation rate was 2.38 per day (634 preparations for 266 TPN days, ranging from 1 to 7 preparations per day). Only one preparation (0.16%) encountered complications. The average duration of TPN for each patient was 8.8 days (ranging from 1 day to 32 days; n=62 patients). Fifteen (24.2%) of the patients were adults.

Patients needing nutritional support are managed by the various health professionals, namely, the paediatricians, surgeons, medical officers, pharmacist and dietician. The pharmacist concerned is the clinical pharmacist.

The pharmacist's role in nutritional support has advanced from compounding of the nutrition solutions to monitoring, interventions and decision making pertaining to nutritional therapy.

In nutritional support, the pharmacist is involved in:

a. Pre-initiation review of patients.
b. Calculation and determination of requirements (including filling up request forms for adult cases).
c. Compounding of the solutions.
d. Monitoring (including interventions)
e. Post-administration review
f. Pharmaceutical care.

The active role of the pharmacist in nutritional therapy is being acknowledged and referred to with the aim of avoiding, reducing and overcoming any misadventure that can be attributed to the administration of parenteral nutrition, hence acquiring maximum benefits from this therapy.

INTRODUCTION

The parenteral nutrition service of the Hospital Universiti Sains Malaysia (HUSM) was first started in 1987 by the Aseptic Dispensing Unit of the Pharmacy Department, catering initially for the paediatric patients. Ever since then it has expanded its services to also include the adult cases (especially the surgical patients).

The objective of this presentation is to enlighten the participants and fellow professionals pertaining to the expanded role of the TPN pharmacist of HUSM in nutritional support.

PHARMACIST'S ROLE IN NUTRITIONAL SUPPORT

Although it has been more than a decade since the introduction of parenteral nutrition in Malaysia, the contribution of pharmacists in nutritional support is still generally underutilised. The pharmaceutical preparation of the nutrient mixture or compounding seemed to be the only major contribution of the pharmacists in this specialised area of supportive therapy, although their clinical role has also been emphasised (1). According to Rombeau and Hamaoui (2), TPN compounding is only one aspect of the pharmacist's responsibilities in nutritional support.

The pharmacist's role in nutritional support in HUSM, over the years, has advanced from merely compounding of the parenteral nutrition solutions to monitoring, interventions (provisions of suggestions) and even decision making on the approach to therapy.

In this teaching hospital, patients needing nutritional support are managed by the various health professionals, who will work together (although not as an official team) for an integrated management approach. These professionals are usually the surgeons, paediatricians, medical officers, the TPN pharmacist and dietician; with the TPN pharmacist, at times, assumming the pivotal role. In HUSM, the TPN pharmacist concerned is the clinical pharmacist.

In nutritional support, six important functions or contributions of the HUSM's TPN pharmacist have been identified. They are:

1. pre-initiation review of patients,
2. calculation and determination of requirements,
3. compounding of the TPN solutions (now a major role of the pharmacy assistants under the pharmacist's supervision),
4. monitoring (including provision of suggestions and interventions),
5. post-administration review, and
6. provision of pharmaceutical care.

It is hoped that from this presentation, the pharmacists' role in nutritional support will be better utilised so as to provide a higher level of health care to the patients.

Pre-Initiation Review

In HUSM all requests will be screened by the TPN pharmacist prior to initiation. Especially for the adult surgical patients, new cases for TPN will be referred to the TPN pharmacist. This process is known as pre-initiation review (of the patient). It entails the pharmacist to review the patient (and not to diagnose) for the planning of the TPN regimen, based on the patient's diagnosis, history, plan of therapy and current clinical and biochemical status.

The basis of this review, besides planning of the regimen, is to determine whether TPN is warranted in a particular patient or otherwise. The decision whether to accept or reject the request will then be made. If the need arises, the patient will usually be asked to refer to another professional (such as a gastroenterologist or a dietician) before venturing into TPN. Usually in any given case, feeding through the alimentary route which is usually is very much preferred, whenever feasible, as it is less invasive and less expensive.

The pharmacist's involvement in assessing the nutrition status of a malnourished patient has been shown to contribute to a more appropriate initiation of TPN (3).

The pre-initiation review will also help to determine the amount of the various constituents of the nutrition solution to be administered based on the patient's nutritional status and also the various supportive therapies the patient has been receiving (especially the medications and also the fluid therapy).

Calculation and Determination of Requirements

Based on the patient's nutritional and clinical condition and on his/her latest biochemical profile, the nutritional requirements for a particular patient will then be determined and calculated. The patient's nutritional status is determined anthropometrically (usually by the dietician), clinically and also through laboratory or biochemical analysis. In this hospital clinical evaluation and laboratory results are the primary means of assessing the patient's nutritional status.

The patient's nutritional requirement for the TPN regimen will then be determined, based on the various guidelines available from the hospital's TPN potatoes, textbooks and literature.

The pharmacist will then fill up the requirement of the parenteral nutrition regimen on the request form, especially for the adult cases; this is usually agreed upon and then signed by the consultant, surgeon or medical officer in charge of the patient.

The requirement will be computed into the TPN calculation programme which will then furnish the pharmacist with the amount of the respective constituents to be added to the parenteral nutrition solution in a matter of minutes. Individualisation of the nutritional regimen for each patient is thus possible with the availability of this computer programme.

Compounding of the Parenteral Nutrition Solution

As the TPN pharmacist is more clinically involved in nutritional support in this hospital, the task of compounding of the parenteral nutrition solution has been passed down to the house-pharmacist or the pharmacy assistant, under the supervision of the pharmacist. The compounding is done in the laminar flow hood in the unit's clean room. Strict aseptic technique is emphasised. The staff working in this unit will usually be sent for training in aseptic dispensing before being given the task of performing the preparation of the parenteral nutrition solution. Samples of the solution will then be sent for sterility testing and also for analysis of contents.

The involvement of the pharmacy personnel (i.e. the pharmacists and also the pharmacy assistants) in compounding of TPN solutions will help minimise wastage and also ensure that incompatibility and other physico-chemical instabilities of the nutrition solution do not occur.

Monitoring (including provision of duggestions and interventions)

The TPN pharmacist will usually do his own rounds to monitor the patients put on TPN. This involves the usual monitoring parameters emphasised when a patient is being fed intravenously. The pharmacist will discuss the particular case with the medical officers in charge and also write TPN review notes in the patient's folder. The TPN pharmacist's comments have been accepted as part of the patient progress notes in HUSM. Discussions will usually revolve around patient's response or progress on TPN, patient's clinical status, changes in the TPN regimen, current biochemical indices and nutritional plans for the patient.

In this hospital the TPN pharmacist suggests the various tests to be performed that can help to evaluate the patient's progress pertaining to this mode of nutrition. For example the correct moment to take the next LFT, nitrogen balance and so on.

With respect to monitoring, the physician's clinical judgement based on the patient's signs and symptoms is the order of the day. Laboratory results are just guidelines and the pharmacist's role in this area is to enlighten the doctor on the biochemical patterns or trends, and profile of the patient. Nutritional plans for the patient will be determined based on the latest clinical profile and laboratory findings.

Post Administration Review

Post-administration review involves the monitoring of the patient after discontinuation of the parenteral nutrition. TPN is usually discontinued in the following situations;

a. the patient is put on oral feeding,

b. technical complications such as failure to get vein access,

c. biochemical complications such as severe electrolyte imbalance (eg hyponatraemia

with level less than 120 mmol/L),

d. clinical complications such as cardiac arrest, severe respiratory depression and other clinical instabilities.

In the post-administration review, the pharmacist will try to determine the reasons for discontinuation. If it is due to complications which can be attributed to the administration of TPN, the pharmacist will then find ways to overcome these complications and also take the necessary steps to avoid further TPN related misadventures. The effects of the last TPN administration prior to discontinuation on the patient's clinical and biochemical profiles could also be determined through this review.

If the patient is to be put on oral or enteral feedings, then the post-administration review will help the pharmacist to calculate TPN regimen to facilitate the weaning process. This is important so as not to allow any discrepancies pertaining to the energy, nutrient and fluid supplementation and also to avoid complications such as rebound hypoglycaemia, and electrolyte imbalance.

The post-administration review will also help the TPN pharmacist to suggest appropriate steps to be taken in term of nutritional support plan for the patient to the medical officers in charge.

Provision of Pharmaceutical Care

Hepler and Strand (4) have defined pharmaceutical care as the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient's quality of life. It involves the process through which a pharmacist cooperates with a patient and other professionals in designing, implementing, and monitoring a therapeutic plan that will produce specific therapeutic outcomes for the patients.

This in turn involves three major functions;

1. identifying potential and actual drug-related problems,
2. resolving actual drug-related problems, and
3. preventing potential drug-related problems.

In relation to nutritional support, it must always be remembered that a patient will normally be put on various medications that will have influence on his/her clinical state and also on the parenteral nutrition solution and regimen which the patient is receiving. For example the administration of diuretics will have an influence on the sodium load.

A parenteral nutrition solution itself contains the various nutrients (i.e the nutrient substrates, electrolytes, trace elements and vitamins) in their rather pure forms. Thus the impact of these elements are generally immediately seen. It is therefore the pharmacist's responsibility to furnish the other professionals with the facts concerning dosing, rate of administration and the compatibility profile of the constituents to be added in the parenteral nutrition solution and

it's pharmacological impact on the patient. It is also the pharmacist's responsibility to anticipate problems pertaining to concurrent drug and parenteral nutrition administrations and try to avoid and overcome them.

CONCLUSIONS

It is a known fact that pharmacists are trained in drug metabolism, pharmacokinetics, drug interactions, fluid and electrolyte monitorings, acid-base balance and aspects of pathophysiology and pharmacotherapy. With their expertise in various aspects of IV therapy, pharmacists can contribute significantly in assessing and monitoring of TPN patients.

. The science of clinical nutrition has progressed significantly in the past decade, and nutrition (especially TPN) has been accepted as an important mode of supportive therapy in the hospitalised patients. Ramanujam (5) has emphasised that a good state of nutrition is not only mandatory for optimal resistance to infection and trauma but also for optimal efficacy of medical and surgical treatment.

These new developments have led to the expanded role of the pharmacists in providing nutritional support. Monitoring laboratory profile and clinically assessing TPN patients are important elements in the provision of a high level of care and the minimisation of complications. This level of care provided by pharmacists will result in safer, cost-effective and more efficient TPN therapy.

The active role of the TPN pharmacist in nutritional support in HUSM, and his involvement in the therapeutic management of patients receiving parenteral nutrition have been acknowledged and referred to with the aim of avoiding, reducing and overcoming any misadventure that can be attributed to the administration of TPN; hence acquiring maximum benefits from the administration of the nutritional therapy.

REFERENCES

1. Othman H. Pharmacist's role in parenteral nutrition. In: *Proceedings of a Symposium on Parenteral Nutrition Therapy*, eds Tan NWB, 1987; pp 69-71.

2. Hamaoui E & Rombeau JL. The nutrition support team. In: *Parenteral Nutrition*, eds Rombeau JL & Caldwell MD, Vol. 2. Philadelphia PA: Saunders, 1986; 241.

3. Matsunaga S & Wolk R. Role of clinical pharmacy specialist in metabolically managing nutrition patients. *Nutrition* 1992; 8:149-154.

4. Hepler CD & Strand LM. Opportunities and responsibilities in pharmaceutical care. *Am J Hosp Pharm* 1990; 47:533-543.

5. Ramanujam TM. Clinical nutrition - Basic concepts. In: Clinical Nutrition Seminar. *Proceedings of the College of Surgeons of Malaysia Annual Scientific Meeting*, 1993; pp 40.

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Clinical nutrition in patients with burns

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ABSTRACT

Following a burn, the patient's metabolic rate is greatly increased, the extent of the increased being proportional to the extent and severity of the burn. Like all injuries, this hypermetabolism can be minimised by reducing pain, emotional stress, reducing heat loss and by providing supplemental nutrition. In burn patients, this is compounded by the loss of the heat conserving skin and frequent dressing changes. To overcome this catabolic state, adequate nutrition must be provided to reduce the negative nitrogen balance and weight loss. The enteral route is preferred in the majority of cases, because of its ease of use, the reduced cost and the avoidance of catheter related septic complications of parenteral nutrition in these already immuno-comprimised patients. Enteral nutrition has the added advantage of preventing translocation of gut bacteria in these patients.

The daily intake of calories and protein can be calculated from various formulae. At the University Hospital, we use the modified Sutherland formula for adults and Solomon's formula for children.

Adults

Caloric requirement:	30 kcal/kg body wt + 40 kcal per % BSA
Protein requirement:	1.5 - 2.0 g/kg body wt or 1 g/kg + 3 g per % burn (for burns > 30%)

Children

(Solomon 1985) Normal requirement (WHO/FAO) + burn requirement calculated as follows:
Energy 30 kcal/1% TBSA & protein 1.5 g/1% TBSA and adjusted to 0-9 kg 50% of above, 10-13 kg 67% of above, 14-18 kg and if > 40% TBSA 67% of above.

Requirements should be reviewed every week as wounds heal.

Enteral nutrition can be delivered by using fine bore feeding tubes and a continous mechanical pump to overcome the problem of bolus feeding. Enteral feeding should be started as soon as the patients is stable following the resuscitative period. The amount can be gradually increased over a number of days. The importance of feeding via the enteral route in these patients cannot be over emphasised. The role of the resident dietitian is invaluable.

Proc 1st Natl Symp Clin Nutr 151-154, 1994

Nutritional care intervention in post paralytic ileus – a case report

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Post paralytic ileus can present as a challenge during the nutritional care intervention of ill patients. This is a case report of the dietary management of a patient with motor neuron disease involving paralytic ileus. Motor neuron disease is an uncommon neurological problem and its cause is unknown. There is degeneration and loss of motor neurons leading to muscle weakness and wasting. The muscles which control swallowing can also be affected.

This patient is an apparently healthy 30 year old man with no family history of motor neuron disease, diabetes mellitus and coronary heart disease. On 18.2.93, he presented himself as an outpatient at the Neurology Clinic with complaints of numbness and weakness of his limbs on one side of his body. Medication was prescribed before he was sent home. However one week later on 25.2.93, he was admitted to GICU with respiratory distress and was put on a ventilator.

Total parenteral nutrition (TPN) was started early when this patient was found to have paralytic ileus. The TPN provided 950 kcal and 25 gm of protein.

This was given as:
500 ml Aminosol 5%
500 ml Intralipid 10%
1000 ml dextrose saline +
5 gm KCl (peripheral line)
(3.5 gm Na).

The amount of Na and K included in the TPN reflect the average consumed in a normal diet. On 28.2.93, the patient's condition suddenly deteriorated and he became semi conscious. During this period, he also had a trachea infection which required antibiotics.

Enteral feeding was commenced on 3.3.93 by the doctors before the patient was referred to the dietitian. It was deemed that the paralytic ileus had resolved. A proprietory product named here as PEM was used. It contain complete whole protein together with other essential nutrients and is a complete enteral feed on its own. The feeding was given in 90 ml at 3 hourly intervals at full strength i.e. 1 kcal/ml.

Subsequently the patient developed about 4 episodes of diarrhoea. After this the Dietetics Department was called in to assist with the nutritional management of this patient.

The dietitian immediately reduced the concentration and the volume of feeding as shown in Table 1 but was unsuccessful in controlling the diarrhoea. It was then decided that the method of feeding be changed from bolus to slow infusion using an enteral pump.

The diarrhoea persisted even though the feeding had been reduced to only 1/4 strength and given at a very slow rate of 20 ml/hr. This prompted the dietitian to think that may be the paralytic ileus had not fully resolved. So, the product of the feeding was changed instead. A semi elemental product containing readily absorbable free amino acid and medium chain triglyceride (MCT) was used. It is named as PGM in Table 2. The concentration and rate of delivering for PGM was maintained as for the previous mixture of PHM (complete protein formulation). The diarrhoea stopped when this new dietary regimen was introduced. The nutritional contribution from the PGM feeding was not significant at the initial stage but the main objective of the feeding then was to maintain a functioning gut while the parenteral nutrition provided the nutrient intake.

Table 1. Dietary intake (with diarrhoea episodes)

3/3	PHM	F/S 1 Kcal/ml	90 ml 3 hrly (Bolus)
4/3	PHM	0.8 Kcal/ml	50 ml 3 hrly (Bolus)
5/3	PHM	0.4 Kcal/ml	50 ml 3 hrly (Bolus)
6/3	PHM	0.25 Kcal/ml	20 ml hrly (Pump)
7/3	Feeding withheld due to tracheostomy		
8/3	PHM	0.25 Kcal/ml	20 ml hrly (Pump)
9/3	PGM*	0.3 Kcal/ml	20 ml hrly (Pump)

*PGM – semi element product containing some free amino acids and MCT and corn syrup solids.

Table 2. Composition of PGM (semi elemental)

PGM Ingredients:
Hydrolysed casein (60% free amino acids),
Fat: 60% MCT, 20% corn oil, 20% safflower oil;
CHO: 61% corn syrup solids, 20% corn starch, 19% dextrose

23g PGM give:
105.1 kcal
2.9 g protein
4.2 g fat
14.2 g CHO
98.4 mg Ca
49.2 mg Na
115 mg K
1.8 mg Fe

As the patient's condition improved, the nutritional intake progressed accordingly. The rate of feeding was kept constant while the concentration of the feed was increased gradually. Later the rate of the feed was increased while the concentration was kept constant as shown in Table 3. When the patient's condition indicated that the nutritional intake could be stepped up more rapidly to achieve a better nutritional balance the parenteral nutrition was decreased. To allow the patient to accommodate for an increasing volume of enteral feed, the TPN was decreased to 500 ml (100 kcal) from the previous volume of 2000 ml. Throughout the dietary management, multivitamin and iron was supplemented. The 5 gm KCL was also decreased to 2 gm on 17.3.93, when the enteral feed contributed to a significant amount of potassium from the PGM. In a period of 2 weeks from 12/3 - 24/3 (Table 3, Table 4) the patient's intake was increased from 1055 kcal to 2225 kcal and the protein intake from 31 gm to 61 gm, without any adverse feeding problem, even though this patient did develop septicaema on 17.3.93, for which antibiotics was prescribed.

Around 25.3.93 the patient was able to swallow, so oral feeding was introduced. Initially only 2 - 3 tablespoons of fruit cordial was given to encourage oral intake. The diet progressed to dilute rice porridge before minced meat and vegetables could be added. Before this patient was weaned off the enteral pump and reverted back to bolus feeding, the semi-elemental product was discontinued. The previous whole protein formulation (PHM) was used instead of the PGM. As a precautionary measure

Table 3. Nutritional intake

Date	9/3	12/3	14/3	15/3	16/3	17/3	19/3
Kcal/ml	0.40	0.40	0.60	0.70	/	0.75	0.80
ml/hr	20	40	/	/	80	100	120
Kcal (enteral)	105	206	342	408	1088	1097	1440
Kcal (parenteral)	850	850	850	850	160	160	100
Total kcal	955	1055	1192	1258	1248	1257	1540
Total protein (g)	28	31	35	37	23	31	41

Table 4. Nutritional intake

Date	24/3	28/3	4/4	7/4	9/4	23/4
Kcal/ml	1.0	1.0	1.0	1.0	1.0	–
ml/hr	160	160	120	120 (bolus)	200 (blus)	–
Kcal (tube)	2125	2400	1800(PHM)	960 (PHM)	1600 (PHM)	–
Kcal (IV)	100	100	100	100	100	–
Kcal (oral)	–	60	235	460	500	800 (oral) 1000 (PHM)
Total Kcal	2225	2560	2135	1520	2200	1800
Total protein (g)	61	68	77	55	79	69

these 2 feeding procedures were carried out for 2 - 3 days consecutively (Table 4). In early April 1993, this patient developed sodium imbalance but this was easily corrected with addition of 1/4 - 1/2 teaspoon table salt 3 times per day. Throughout the whole of his dietary regimen, the fluid intake was maintained above 2 litres per day to ensure adequate hydration. This is to prevent renal calcium calculi forming in a patient with prolonged bed rest and immobility (see Table 4).

On 23.4.93, the patient was well enough to be transfered to the Neurology Ward although he still required a respirator. He is still with us today in the same ward and is managing very well on an ordinary diet, although the texture of his food has to be modified a bit. He can chew fairly well but it is an effort for him to do so especially when he is still dependent on his respirator. PHM is supplied daily to him as a supplement. The motor neuron disease has left him with immobility of his limbs, so he has to be fed by others at every meal time. In spite of these limitations, the patient is very cooperative about his dietary regimen.

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Vein blockage and rebound hypoglycaemia due to dextrose from TPN, should these misadventures still occur? - a case report

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CASE

OC (56 years old, male, 60 kg) was admitted for headache and sleep problems. Diagnosis later showed multiple cranial nerve palsy and TB meningitis. During hospital stay, patient developed GIT bleeding, was clinically malnourished and dehydrated. TPN was initiated when oral feeding failed.

BUSE prior to TPN: sodium 151 mmol/L, potassium 3.0 mmol/L, urea 3.0 mmol/L. TPN was started at 2100 kcal/day (35 kcal/kg/day), proteins 75 gm/day, dextrose 450 gm/day (18%), sodium 100 mmol/day, potassium 70 mmol/day; the rest of the requirements as for maintenance (no fats). Fluid requirement was 2500 ml/day. Central route was then advised.

Unfortunately TPN was administered peripherally and vein blockage occurred after completion of first bag, and TPN was stopped. Nothing was administered then until the TPN pharmacist intervened (> 12 hours after the incident). Diascan/finger-prick at six-hourly interval (after TPN was stopped) showed blood sugar at 6.7 mmol/L, 3.1 mmol/L and going down to 'low'. Level rose to 8.4 mmol/L after administration of IV dextrose 5%. Rebound hypoglycaemia was thus avoided.

DISCUSSION

Dextrose misadventures (e.g. thrombosis and rebound hypoglycaemia) from TPN, sadly, still occur today. Nystrom(1), in his study of the occurrence of bacteremia in surgical patients with intravenous devices, has reported the incidence of peripheral vein thrombophlebitis in 7 - 28% of cases. The incidence of thrombophlebitis should be avoided as it can increase the risk of developing sepsis 18-fold(2).

Proper management of patients on TPN should therefore be emphasised because the contents of the TPN solutions are good growth media for both bacteria and fungi. Good IV line and catheter care by the nursing staff should also be emphasised. Taylor(3) has listed the following as the major factors known to contribute to these complications:

a. duration of catheterisation
b. thrombogenic properties of catheter materials

c. the preparation and maintenance of asepsis at infusion site
d. chemical composition
e. pH and osmolality of infusates.

In the above case, thrombophlebitis, and the subsequent vein blockage occurred because the TPN solution was not administered centrally as advised. The dextrose content of the solution was 18%. Peripheral dextrose administration should not exceed a concentration greater than 12%. In the case of TPN to be administered centrally, central line placement should be confirmed first. Sometimes it is even necessary to have an X-ray prior to the TPN administration to avoid catheter-related complications (such as pneumothorax or hydrothorax).

TPN solutions with high dextrose concentration should not be withdrawn abruptly. In this case the sudden withdrawal of the TPN administration led to a sudden drop in blood sugar levels as was detected through the diascan readings. Prompt action by the TPN pharmacist by ordering the administration of a 5% dextrose solution avoided the incidence of rebound hypoglycaemia.

Complications such as these can and should be avoided. The proper management of patients on TPN should be emphasised. It is imperative for the pharmacists in the nutrition support service to play a more active role in the monitoring and management of TPN patients, in order to furnish the fellow professionals with information regarding TPN and to avoid future TPN misadventures.

REFERENCES

1. Nystrom B *et al.* Bacteremia in surgical patients with intravenous devices: a European multi-centre incidence study. *J Hosp Infection* 1983; 4:338-349.

2. Maki D. Attachable silver-impregnated cuff for the prevention of infection with peripheral intravenous catheters: a randomised multicentre trial. *Am J Med* 1988; 85:307-314.

3. Taylor S. Complications of TPN. In *Nutritional support: a team approach*, eds Taylor S & Goodinson-McLaren S, Wolfe Publishing Limited, London, 1992; pp 329.

Proc 1st Natl Symp Clin Nutr 157-161, 1994

Long term nutritional support in short bowel syndrome

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ABSTRACT

Two cases of adult short-bowel-syndrome secondary to superior mesenteric vein thrombosis were seen in U.H. K.L. during the past 5 years. The first patient, a 25-year-old lady was referred from a district hospital to U.H.K.L. in October 1989, two weeks after she underwent massive small bowel resection for superior mesenteric vein thrombosis. As her residual small bowel was only 50 cm, she required long term parenteral nutrition. Central venous access was achieved with a conventional central line via the subclavian vein initially. This was converted to a Port-A-Cath for long term use. We experienced 3 episodes of central line sepsis which required the removal of the port. The patient developed several episodes of dermatitis diagnosed to be related to zinc deficiency. This was corrected by increasing the zinc content in the TPN fluid. The frequency of parenteral nutrition was gradually reduced from daily to every other day and then finally twice weekly, orally supplemented with Vital, an elemental diet. She has maintained her body weight during this period. Her serum albumin and total protein has been normal. The second patient, a 22 year old Malay man, similarly had massive small bowel resection for superior mesenteric vein thrombosis, leaving behind 50cm of distal ileum. After one month of total parenteral nutrition, he was started on enteral feeding with Pregestimil and Sustain. His bowel adapted well and subsequently he was only on normal diet.

INTRODUCTION

Short bowel syndrome involves malabsorption and malnutrition following extensive resection of the small intestine. Causes of short bowel syndrome include mesenteric infarction, radiation enteritis, Crohn's disease and intraperitoneal malignancy, requiring resection of the involved small bowel. Severity of the short bowel syndrome depends on many factors. These are: extent of resection, site of resection, intact ileo-caecal valve, involvement of stomach, duodenum, pancreas and colon, etc. In the presence of intact ileo-caecal valve, short bowel syndrome will occur if the remnant small intestine after resection is less than 80cm. However, if the

ileo-caecal valve is resected with the small bowel, short bowel syndrome will occur even with a remnant small bowel length of up to 150cm long. Proximal small bowel resection is better tolerated than distal small bowel resection because distal ileum has greater potential for absorption and adaptation.

Metabolic and nutritional management of short bowel syndrome can be divided into 3 distinct therapeutic periods. (1) Immediate Post-operative Period during the first 2 months. (2) Bowel Adaptation Period from 2 months to 2 years. (3) Long Term Management after 2 years.

1. Immediate post-operative period

During the first period, the main problems are massive fluid and electrolyte loss from the gastro-intestinal tract. Therefore, management during this period involves vigorous fluid and electrolyte replacement to prevent life-threatening hypovolaemia, dehydration,hypotension and electrolyte imbalance. Total parenteral nutrition is started on the second or third post-operative day, once the patient's cardio-vascular and pulmonary status has stabilized. This will help maintain the nutritional status of the patient until his bowel adapts maximally. Oral feeding is introduced early to promote bowel adaptation and mucosal atrophy.

2. Bowel Adaptation Period

During the second period, oral feeding is offered as tolerated, in increasing volume and concentration. At the same time, parenteral nutrition is gradually reduced reciprocally. Usually, within 2 years, 90-95% bowel adaptation potential would have been realized. Little further improvement in absorption and adaptation can be anticipated.

3. Long Term Management

After 2 years, nutritional stability has occured. By this time, if oral feeding is still inadequate to maintain nutrition, life-long parenteral nutrition would be required.

CASE REPORTS

Two cases of adult short bowel syndrome secondary to superior mesenteric vein thrombosis were seen in UHKL during the past 5 years. In both cases, massive small bowel resection was done, leaving behind about 50 cm of distal ileum. Duodenum, ileocaecal valve and colon were intact. The outcome of the two patients after maximal bowel adaptation was at different ends of the spectrum. One can be maintained on normal diet only while the other required permenant parenteral nutrition.

Patient 1

LYS was a 20 year old lady who was referred to University Hospital Kuala Lumpur in October 1989, two weeks after she underwent massive small bowel resection for superior mesenteric vein thrombosis, leaving behind 50 cm of distal ileum.

Immediate Post-operative Period

When we first saw her, she was already started on parenteral nutrition via a conventional

subclavian central venous line and oral liquid diet. She was grossly underweight, with a body weight of only 35 kg for a height of 162 cm. She was having severe diarrhoea with the oral feeding.

Initially, she was given daily continous parenteral nutrition using the single infusion bag prepared by our pharmacist. Oral feeding, which was already started, was continued to prevent intestinal mucosal atrophy and to promote bowel adaptation. This was gradually increased. Initially she was given nutitionally complete liquid formula diet (Isocal, Progestimil).

Bowel Adaptation Period

Central venous access was later converted to subcutaneous port with silicone central venous catether inserted into the internal jugular vein. The port was placed in the subcutaneous space in the infraclavicular area.

Oral feeding was gradually increased. A low fat diet was later introduced, as tolerated. Since her intestional absorption was still insufficient, she was given an elemental diet, VITAL. VITAL, is a nutritionally complete, partially hydrolysed elemental diet that is low in residue. It contains peptides from partially hydrolysed protein, added free amino acids, glucose, oligo- and polysaccharides and a low level of fat.

With bowel adaptation and improvement in her intestinal absorption, The TPN ration was gradually reduced from daily to every other day, then three times weekly, and then twice a week.

Long Term Management

After maximal bowel adaptation, her absorption power was still inadequate. Everytime we cut down her TPN to once a week, her body weight dropped.

For the past 2 years, she has been on twice weekly cyclical parenteral nutrition, supplemented by elemental diet and low fat diet. Her body weight, serum protein and albumin have been well-maintained.

Table 1. Nutritional Requirement and Intake

Nutrients	Daily Requirement	TPN (/bag)	VITAL (/packet)	Daily Intake
Energy (Kcal)	1700	2000	300	870
Protein (g)	35	68	12.5	35
Calcium (mg)	450	560	200	360
Fe (mg)	28	28	3.6	12
Vit A (μg)	750	750	300	515
Vit D (μg)	2.5	3	2	2.8
Thiamine (mg)	0.7	2	0.6	1.2
Riboflavine (mg)	1	1.8	0.7	1.2
Folic Acid (μg)	200	600	160	330
Vit B12 (μg)	2	2	2.4	3
Vit C (mg)	30	30	60	68

Table 1 shows her daily nutritional requirement and her intake from the twice weekly TPN and 1-2 packets of Vital daily. Her nutritional requirement is met with the TPN, Vital and some modified oral diet.

Table 2 shows the cost of TPN for this patient, which comes to RM1500 per month. This is equivalent to that of maintaining a chronic renal failure patient on peritoneal dialysis or haemolysis.

Table 2. Cost of TPN

TPN infusion bag	$120/bag
Soluvit	$ 14/10ml vial
Addamel	$ 14/10ml vial
Vitlipid	$ 14/10ml vial
Heparin solution	$1.50/10ml vial
Needle (90 degree bend)	$ 3/each
Total cost of TPN per month	$1500

Except for the twice weekly overnight stay in the hospital for the cyclical parenteral nutrition, she is leading a fairly normal life. Presently, she is working as a shop assistant and a part-time computer programmer.

Patient 2

WBS was 22 years old when he had superior mesenteric vein thrombosis, requiring massive small bowel resection from proximal jejunum to ileum, leaving a remnant of 45 cm of distal ileum.

Immediate post-operative Period

TPN was commenced immediately after operation, with a single TPN infusion bag via a subclavian central venous line.

Oral feeding was commenced 2 weeks after the operation.

TPN was suspended 6 weeks after the operation.

He was discharged 8 weeks post-op with liquid formula and modified diet.

Bowel Adaptation Period

Eight months after the operation, his intestine appeared to have fully adapted. He was taking a normal diet. His body weight has gradually returned to his pre-op level, ie, 58kg. He has gone back to ITM to continue his study. He is able to go jogging 2km/day and plays squash once a week.

Long Term Management

His nutritional status is well-maintained with normal a diet, without any other supplements. Presently, he is doing his final year of degree course in the UK.

DISCUSSION

The advent of total parenteral nutrition has revolutionalised the management and outcome of short bowel syndrome which used to be a fatal condition. Parenteral nutrition keeps the patient alive by maintaining his nutritional status while bowel adaptation takes place.

However, TPN is not without problems. Our first patient developed three episodes of catheter sepsis which required

removal and replacement of the subcutaneous port. This complication is not only life-threatening but also costly. Each port costs about RM800.

This patient also had a few episodes of dermatitis, diagnosed to be due to zinc deficiency. The zinc content in her TPN was increased and the dermatitis responded well and subsided.

Both the two cases reported had the same underlying aetiology for their short bowel syndrome, similarly underwent massive small bowel resection and had almost equal length of remnant small bowel consisting of distal ileum. However, their outcome was at different ends of the spectrum after maximal bowel adaptation. There are a few possible explanations for these discrepancies. Firstly, capacity of bowel adaptation and absorption, and the nutritional requirements for different individuals are very variable. Secondly, there were probably errors in the measurement of the remnant small bowel length. Accurate intra-operative measurement of bowel length has always been a difficult problem. The standard measurement is by measuring the antimesenteric border of the intestine. Furthermore, bowel length varies greatly with the state of contraction and relaxation. Inflamed oedematous bowel tends to shorten after recovery. The first patient underwent only one operation and her remnant distal ileum was probably still inflamed when the measurement was done. The second patient had two further 'second-look' operations after the first one. By the time the final measurement of bowel length was done, oedema and inflammation of the remnant bowel would have subsided. Therefore, the actual remnant small bowel length of the first patient is probably shorter than that of the second patient.

Lastly, from our experience with the first patient, we can conclude that long term parenteral nutrition is both feasible and affordable in this country.

REFERENCES

1. Dudrick SJ, Latifi R & Fosnocht DE. Management of short-bowel syndrome. *Surgical Clinics of North America* 1991; 3:625-641.

2. Dudrick SJ *et al.* 100 patient-years of ambulatory total parenteral nutrition. *Annals of Surgery* 1984; 199(6):770-81.

3. Kurkchubasche AG, Smith SD & Rowe MI. Catheter sepsis in short-bowel syndrome. 1992; *Arch Surg* 127:21-25.

4. Gouttebel *et al.* Total parenteral nutrition needs in different types of short bowel syndrome. *Digestive Diseases and Sciences*; 1986 31(7):718-723.

5. Reilly JJ & Gerhardy AL. Modern surgical nutrition. *Current Problems in Surgery* 1985; 22(10):1-81.

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Enteral nutrition - a closed delivery system in intensive care

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Critically ill patients are frequently hypermetabolic and nutritional support is an essential therapeutic measure. Enteral feeding is preferred to parenteral feeding.

However, there are problems with enteral feeding. Nausea and vomiting are related to odour, rapid infusion rate, high fat content, lactose intolerance, high osmolarity and delayed gastric emptying. Diarrhoea may result from bacterial infection, drug therapy or may be related to the feed, for example because of contamination, lactose intolerance and hyperosmolarity. Aspiration is a common fatal complication (the rates quoted in various studies are 1% to 44%). Metabolic problems arise from inadequate replacement of essential nutrients, fluids or electrolytes. Other dangers include naso-pharyngeal erosion, sinusitis, otitis media, oesophagitis, malposition of tube and oesophageal reflux.

To overcome some of these risks associated with enteral feeding there are modifications to the basic delivery system. One such modification has been to use a closed system to minimize potential contamination of enteral nutrient solution. Bacterial contamination of enteral nutrient solution has been reported to occur in 30%-90% of open enteral feeding systems. As a result there is an increased potential for iatrogenic enteric illness due to bacterial overgrowth in patients receiving enteral nutrition, especially diarrhoea (1,2) and its associated increased morbidity related to fluid and electrolyte loss. Contaminated enteral feeding has been implicated as the cause of *Pseudomonas* and *Enterobacter* species septicaemia (3,4) and has been shown to induce persistent colonization and sepsis in mice (5).

The availability of a closed feeding system should minimize the possibility of microbial contamination of milk feeds associated with the open system of enteral feeding, by eliminating the need for transfer of product from the original container to a feeding reservoir.

The main objective of the study was to evaluate the bacteriological contamination of a closed tetrapack administration enteral delivery system, called the Entera-Flo Spike System (Fresenius AG Pharma, New Brunswick, NJ) in intensive care.

Ten ventilated patients in the Intensive Care Unit, Department of Anaesthesiology, University

University Hospital, entered the study and they fulfilled the following criteria:

1. >18 years old
2. requiring tube feeding for nutritional support
3. no hepatic or renal failure.

They were on H2 receptor antagonist for prophylaxis against stress ulcers. They received an average of 1800 ml Isocal Ready-To-Use Aseptic (Mead Johnson) daily, administered continuously by gravity drip for a minimum of three consecutive days. Full strength formula was administered directly from the tetrapack using the Entera-Flow Spike System connected to a naso-gastric tube. The spike system consisted of a spike and tubing set. The spike was inserted aseptically into the Isocal package to allow delivery from the package. The spike system contained a filter valve to allow air to enter the package to equalize pressure inside and outside the package as the Isocal flowed down the spike system. Near the distal end of the tubing, 30cm from its connection to the nasogastric tube, is an injection port which served as a site for flushing or administration of medication together with the flushes. It also served as a sampling port.

Isocal samples were collected at 0 hour, on Day 1, from the tetrapack itself (Sample 1); when it flowed down from the tetrapack into the tubing, at 0 hour on Day 1, from the first tubing (Sample 2); at the end of 24 hours from the first tubing (Sample 3); at the end of 24 hours from the new second tubing, immediately after the change to new tubing and new tetrapack (Sample 4); at the end of 48 hours from the second tubing before switching to a third tubing and a new tetrapack (Sample 5).

Twenty mls of Isocal were collected aseptically using a sterile syringe, the needle carefully recapped without any hand contact and then sent to the Microbiology Laboratory immediately for qualitative and quantitative tests. Aseptic precautions were stressed: careful handwashing by the personnel was practised before and after collection of samples. Disinfection of sampling site was made with a swab containing 70% alcohol.

No bacteria was cultured from samples taken from the tetrapack and fresh tubing set on Day one (Samples 1, 2). Thus the enteral nutrition was sterile at the time it was spiked with the administration set. However, significant bacterial growth occured within 24 hours in the first tubing in 8 patients (Sample 3), namely, *Klebsiella, Enterbacter, Acinetobacter, Pseudomonas, Bacillus, Streptococcus faecalis* and *Staphylococcus epidermidis*. At the end of 24 hours, with a change of tetrapack and administration set, one patient had *Pseudomonas* species cultured from his enteral feed with a viable count $4x10^3$ organisms/ml (Sample 4). One patient had no growth in all samples. For the five days under study no patient had diarrhoea or vomiting.

In a clinical setting in ICU contamination occured after 24 hours. This was an open system, in practice, because of the necessity of having a port of entry for flushing and medication which

could be the port of entry for bacteria. The system was therefore functionally not a closed system. No signs of infection directly related to feeds like diarrhoea, vomiting and fever were seen during administration. However, the period of observation might have been short and the patients were still on courses of antibiotics for the infection that precipitated their admission into ICU.

Contamination could have been from endogenous or exogenous sources. Bacteria could have come from patients, medical/nursing staff or hospital environment. 73% of the isolates were Gm(-) bacteria and such bacteria are associated with colonization of the gut, respiratory tract and skin but also frequently found in hospital food, water and moist sites like ventilators. Streptococcus is a human commensal and Bacillus and Staphylococcus are common contaminants in air, dust and dry environments. We could not identify the source of contamination in this group of patients.

CONCLUSION

Enteral feeding in critically ill patients has to be carried out as aseptically as possible, irrespective of the mode of delivery. An early return to oral feeding is encouraged although parenteral feeding may still be considered when enteral feeding has failed.

REFERENCES

1. Bastow MD. Complications of enteral nutrition. *Gut* 1986; 27(S1):51-55.

2. Cataldi-Betcher EL, Seltzer MH, Slocum BA & Jones KW. Complications occuring during enteral nutrition support: a prospective study. *J Parent Ent Nutr* 1983; 7:546-552.

3. Casewell M, Cooper J & Webster M. Enteral feeds contamination with enterobacter cloacae as a cause of septicaemia. *Br Med J* 1981; 282:973.

4. deVries E, Mulder N, Houwen B *et al.* Enteral nutrition by nasogastric tube in adult patients treated with intensive chemotherapy for acute leukemia. *Am J Clin Nutr* 1982; 35:1490-1496.

5. Van Enk R & Furtado D. Bacterial contamination of enteral nutrient solutions: intestinal colonization and sepsis in mice after ingestion. *J Parent Ent Nutr* 1986; 10:303-7.

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SUMMARY OF ROUND TABLE DISCUSSION SESSIONS AND RECOMMENDATIONS

GROUP 1: PROMOTING RESEARCH & TRAINING IN CLINICAL NUTRITION

1. Broad definition of clinical nutrition

Clinical nutrition (CN) was provisionally defined as the application of food and nutrition science to the prevention and management of nutrition-related diseases. This would include, among others, clinical nutritional epidemiology, experimentation with animal models for human application and clinical nutritional diagnosis.

Basic premises: The consensus was that CN should not be developed as a separate discipline in Malaysia at this time for the following reasons:

i. lack of critical mass of people working in CN;

ii. most of the activities on CN are carried out as an adjunct to people's normal duties and responsibilities; and

iii. lack of career path in CN.

2. Staff requirement for clinical nutrition

Categories of staff who have a potential interest in CN include:

* State nutrition officers
* Dietitians
* Medical practitioners
* Nurses
* Pharmacists
* Researchers (incl. biochemists)
* Nutrition/health educators
* Laboratory staff
* Academic staff

In discussing personnel requirements it was pointed out that among the above staff, there is currently a lack of dieticians and well-trained laboratory technical support staff.

3. Training opportunities and needs

3.1 There is currently inadequate training in the medical undergraduate

course due to:-

i. the low priority of nutrition in medical model of curative medicine;

ii. lack of trained staff;

iii. lack of appropriate role models including the lack of bedside teaching on CN; and

iv. exclusion of CN in final examinations.

It was therefore recommended that high priority should be given to increasing the amount of clinical nutrition in the training of medical undergraduates, including more clinical bedside training and examination in the final assessment.

3.2 Although current dietetic training is considered adequate the internship period should be increased.

It was therefore recommended that the assistance and committment of all dieticians in the country be obtained in order to provide the required supervision and training for dietetic trainees, given the increase in workload that this entails.

3.3 An inadequate amount of teaching in clinical nutrition was also identified in the course for pharmacy training.

It was therefore recommended that this also be increased.

3.4 Postgraduate training

3.4.1 Clinical nutrition should be represented to a greater extent in the curriculum of post-graduate courses.

3.4.2 MSc and PhD for medical and non-medical graduates should be recognised for career advancement. This will sustain active interest in clinical nutrition as a career path.

3.4.3 The input of foreign experts is needed to carry out training in clinical nutrition at post-graduate level.

3.5 Training of supporting technical personnel

Training of supporting technical personnel should be intensified to enable the use of new equipment and to facilitate repair of equipment related to nutrition laboratory analysis.

4. Research areas and needs

Existing CN research is currently being carried out in IMR, universities and hospitals. Some areas in CN where research is needed were

identified as:-

i. Nutritional requirements for Malaysian population;
ii. Development of dietary guidelines for Malaysians;
iii. Improvement of existing Malaysian Food Composition database;
iv. Studies in body composition of Malaysians;
v. Fats and oils in human nutrition; and
vi. Nutritional status and nutrition interventions in hospitalised patients.

Priority areas in nutrition research under the Intensification of Research Priority Areas (IRPA) mechanism were identified in a broad way in 1988 at a conference held in University of Malaya. It is now recommended to review these priority areas in the light of the current nutrition situation and needs.

It was pointed out that a specific context for discussing priority areas in nutrition research will be the development of the national plan of action for nutrition being undertaken as a follow-up to the FAO/WHO International Conference of Nutrition.

5. Promotion of collaboration in research and training in clinical nutrition

It was agreed that existing resources could best be utilized by collaboration in research and training.

To facilitate this collaboration it was recommended that:

5.1 a network of people and institutions involved in CN be established.

This can be achieved by the compilation of a directory on nutrition, including CN and the following aspects:-

a. personnel involved;
b. research activities; and
c. laboratory/technical capabilities of institutions.

It was recommended that the directory be developed by IMR and that it be updated on a regular basis.

5.2 Organise meetings or roundtable discussion sessions at which the interested parties can examine what needs to be done to expand and promote activities in various areas of clinical nutrition, and what action is required to achieve these objectives.

5.3 Promote the exchange of staff and students among local and foreign institutions for the purpose of gaining experience in certain fields or to conduct short research projects as part of diplomas/degrees. Short courses in clinical nutrition should be organized on a regional basis.

5.4 Take turns to organise talks on topics/activities of common interest to be arranged at each institution.

5.5 The need for access to current literature was emphasised.

5.6 Short courses on clinical nutrition should be organised on a regional basis. This could be done under the auspices of the Asia-Pacific Society of Clinical Nutrition and of the International Union of Nutritional Sciences (IUNS). The first of these courses could be held within 1-2 years.

5.7 A Regional Conference on Clinical Nutrition should be organised, in about two years time. The IMR could be the organiser, in collaboration with institutions of other countries in the region.

6. Assessment of laboratory/technical facilities

With the advancement in the understanding of molecular mechanisms, biochemical indicators of nutritional status and the role of micronutrients in health and disease, there is a need for new technology and equipment.

These recommendations were adopted in a plenary session of the Symposium

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GROUP 2:
THE NEED FOR A NUTRITIONAL SUPPORT TEAM: STRENGTHENING THE RELATIONSHIP BETWEEN CLINICIANS, DIETITIANS, PHARMACISTS & NURSES

It was recognised that proper nutritional support decreases morbidity and mortalility, decreases hospitalization, decreases convalescence and improves the patient's quality of life.

In order to provide this service, a formal Nutrition Support Service (NSS) needs to be established. The team approach strengthens the relationship between clinicians, dietitians, nursing staff, pharmacists and other paramedical personnel and to promote collaboration, cooperation, coordination.

In other words, the team approach :

* maximizes the benefits,
* minimizes the complications, and
* is cost effective

1. In most of the hospitals, no organised nutrition support is currently available. It was agreed that there is a need to start nutrition support with the existing personnel.

   1.1 In the district hospitals, the service can be started with the clinician, nurse, pharmacist and/or dietitian depending on the availability.

   With the help of these existing staff it should be possible to provide adequate enteral/parenteral nutrition to the patients except for those who are critically ill. Transferring all the patients to GH/UH, just for nutritional support will overload the already crowded facilities at these centres.

   1.2 In general hospitals and teaching hospitals, this team can have a slightly larger representation, consisting of other personnel interested in nutrition.

2. Even though there is an acute shortage of dietitians and pharmacists at district hospital level, it is still possible to provide the Nutritional Support Service. However, filling up these posts will improve the service and provide better quality of Nutrition Support.

3. There was a consensus that training should be provided to interested physicians, dietitians, pharmacists/pharmacy assistants and nurses either at locally established centres or overseas. It was recommended that a one-year on the job training course leading to a post-graduate diploma such as the Certified Nutrition Support Dietitian (CNSD) may be started by existing established educational centres.

   Self assessment examinations on clinical nutrition should be offered by the Nutrition Society of Malaysia to clinicians, dietitians, pharmacists and nurses, every 2 or 3 years, as part of a continuing education programme.

4. There was a consensus that medical and para medical staff should receive more training in clinical nutrition.

   The importance of nutritional support should be taught to medical, nursing, pharmacy and dietetics students and both at the undergraduate and the post-graduate levels.

5. Due recognition and incentives should be given to qualified personnel.

6. Dietitians should be more involved in clinical nutrition and patient management. A change in attitude is required, especially among clinicians, who should not consider dietitians as caterers.

7. Budgetary requirements

   Existing facilities can be used or upgraded to start the nutritional service. Each hospital can work out the cost of maintenance according to the needs and requirements in providing nutritional support.

8. Every hospital under the umbrella of a Nutrition Support Service should establish guidelines on enteral and parenteral nutrition. This will reduce wastage, complications and infection thereby proving to be most cost-effective.

These recommendations were adopted in a plenary session of the Symposium.

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Preventing iron deficiency anaemia in preterm and fullterm infants

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ABSTRACT

Iron deficiency had been identified as the most prevalent nutritional problem in the world, affecting two thirds of children in most developing nations. One third of these children have the more severe form of the disorder, anaemia. Recently it has been demonstrated that moderate iron deficiency anaemia (haemoglobin <100 g/L) depresses mental and motor functioning in affected infants. Although there is controversy regarding the effectiveness of treatment with iron to reverse these effects, there is universal consensus that iron deficiency anaemia is associated with developmental cognitive and motor deficits, and that its prevention is essential for every infant.

Infants born prematurely are at risk for late iron deficiency anaemia because of low stores at birth, very rapid increase in blood volume during the first year of life and limited iron intake from the diet. Strategies for the prevention of iron deficiency anaemia in premature infants will be discussed.

Fullterm infants are also at risk of iron deficiency anaemia, especially in the second six months of life. In the exclusively breast fed infant, iron intake (and absorption) will not meet the iron needs of the infant and neonatal iron stores will be mobilized and utilized. These stores will be exhausted by 9 months of age at which time an additional source of iron is needed. In a non-exclusively breast fed infant, neonatal iron stores will become depleted after 6 months of age. At around this age, the foods typically eaten by the infant include cow's milk, cow's milk-based formulas, cereals, fruits and vegetables and meats. Cow's milk is a poor source of iron. In the past there has been controversy regarding the availability of iron from iron-fortified infant cereal products. Data will be presented from a recently completed study which shows that the iron from cereal is available and utilized by infants in the second six months of life.

INTRODUCTION

Iron deficiency has been identified as "the most prevalent nutritional problem in the world", affecting "two thirds of children ..... in most developing nations" (1). One third of these children have the more severe form of the disorder, anaemia. The consequences of iron deficiency anaemia are not benign. In addition to the effect of anaemia on oxygen carrying capacity directly, the non-haematologic consequences of iron deficiency anaemia include poor weight gain, anorexia, irritability and decreased physical performance (2). Recently it has been demonstrated both in developing countries and in Canada that moderate iron deficiency anaemia (haemoglobin <100 g/L) depresses mental and motor functioning in affected infants (3,4). Although there is controversy regarding the effectiveness of treatment with iron to reverse these effects, there is universal consensus that iron deficiency anaemia is associated with developmental, cognitive and motor deficits, and that its prevention is essential for every infant.

In this article on the prevention of iron deficiency, I would like to focus on five issues. These are: how much iron is an infant born with - is the preterm infant more at risk; the iron content of foods used by infants in the first year of life; factors affecting iron absorption; health effects of inadequate iron intake; and, strategies for the prevention of iron deficiency anaemia.

How much iron is an infant born with - is the preterm infant more at risk?

Normal infants born at full term have about 75 mg of iron per kilogram of body weight (5). Thus the typical 3.5 kg infant is born with a total body store of 265 mg of iron. Most of the iron (>50 %) is found in haemoglobin. Infants during the first year of life will on average triple their birth weight and their blood volume. Thus about 0.5 mg of iron is needed each day during that first year of life simply to meet the iron needs for haemoglobin synthesis. In addition, it has been estimated that obligatory iron losses, which include intestinal, skin and urine losses during this time period average 0.2 mg per day. Thus the amount of iron required to support haemoglobin synthesis is around 0.7 mg/day during the first year of life (1). Over a year, therefore, more iron is needed than is available from stores at birth. Obviously the additional iron must come from the infant's diet.

At birth, the iron stores of the preterm infant are significantly lower than is the case of the fullterm (6). Stores of iron, like other minerals, are primarily deposited during the last trimester of pregnancy. Thus an infant born prematurely, weighing 1 kilogram, would have body stores of about 64 mg of iron (compared to 265 mg in the fullterm infant). Survivors of preterm birth have been specifically identified as being at

high risk of developing two types of anaemia, 'early' and 'late' anaemia of prematurity. This increased risk may be explained by their low iron stores at birth, rapid growth in the first months of life and frequent blood letting during the early weeks of life. 'Early' anaemia is due to the many blood samples that are taken to aid in their acute management. Later in their hospital course, preterm infants develop a 'late' anaemia of prematurity that is characterised by a progressive fall in haemoglobin concentration, relatively low absolute reticulocyte counts, and bone marrow erythroid hypoplasia. Inadequate erythropoietin production is thought to be the primary pathophysiologic abnormality responsible for this 'late' anaemia.

Although endogenous stores of iron in the preterm infant are clearly inadequate to supply the iron needs for rapid growth, because most preterm infants receive blood transfusions in the early neonatal period, it is very difficult to establish a universal quantitative iron requirement for this population. Nevertheless, it has been recently recommended that all preterm infants maintain an iron intake of 2.0 to 2.5 mg/kg of iron per day to prevent late anaemia of prematurity (7).

Iron content of foods used by infants in the first year of life

The average iron content of human milk is 0.35 mg/L. Based on an average milk intake of 750 mL/day during the first months of life, the iron intake would be 0.26 mg/day. Assuming that 50% of the iron in human milk is absorbed, the amount of absorbed iron would be 0.13 mg/day. This is considerably less that the estimated 0.7 mg/day iron requirement for the fullterm infant (1). Even if all the iron in human milk were absorbed (an unlikely scenario), the infant would have to ingest 2 litres of milk per day to meet the estimated iron needs. Infants are unable to ingest such large volumes of milk, thus, all infants must use endogenous stores to meet their iron needs. Eventually as the stores are depleted, unless an additional supply of iron is provided, the infant's ability to synthesize haemoglobin will be compromised.

Cow's milk based formulas contain varying quantities of iron depending on whether they are fortified or not. Unfortified formula contains 1.0 - 1.5 mg/L of iron. Iron-fortified cow's milk-based formulas and soy-based formulas contain 12 - 13 mg/L of iron. Absorption of iron from cow's milk formulas is significantly lower than from human milk (5-10% vs 50%).

Infant cereals that have been fortified with iron are an important source of dietary iron. They usually contain between 30 to 50 mg of electrolytic elemental iron per 100 g of cereal. Recently Dr. Sam Fomon from the University of Iowa questioned the notion that iron fortified infant cereals provide infants with a good dietary source of iron (8). He argued that the form of iron used to fortify infant cereals is so poorly bioavailable as to be an inconsequential source of iron to the infant. The estimated bioavailability of the iron in cereal is around 4%. This estimate is based on studies in infants where small particle size iron was added

to a mixture of wheat, barley and maize. No study on the absorption rate of electrolytic iron-fortified infant cereals has been conducted. Regardless, the recommendations set out by the American Academy of Pediatrics and the Canadian Pediatric Society with respect to the use of iron fortified infant cereals are based on the knowledge of this bioavailability. Two servings of infant cereal (7 - 14 g/day) containing 45 mg of iron per 100 g of cereal provides 3.15 - 6.3 mg of iron. This amount of iron from cereal is considered to be an adequate source of supplemental iron for most infants.

Factors enhancing and impeding iron absorption

Iron absorption depends on the iron status of the subject and the solubility of iron in the intestine. There are two broad categories of iron in food. Heme iron, the iron present in haemoglobin and myoglobin, and iron salts (non-heme iron). Since infant diets contain little meat in the first 6 months, the vast preponderance of iron is in the non-heme form. The absorption of non-heme iron depends on how soluble it becomes in the intestine. Intestinal solubility is determined primarily by the composition of foods that are eaten in a meal. Food may contain substances which either enhance or impede iron absorption. For example, the assimilation of non-heme iron is increased by the presence of ascorbic acid. On the other hand, absorption is decreased by the formation of insoluble compounds such as phosphates, tannates and oxalates. Bran in cereals, polyphenols in many vegetables and tannins in tea all substantially inhibit iron absorption.

In the late 1950's, the use of radioisotopes for the first time allowed researchers to determine iron absorption with accuracy. Schultz and Smith showed, by using both extrinsic (adding the isotope in vitro to milk) and intrinsic (giving the isotope to the cow to have it incorporated into the milk) labelling, that about 10% of the iron in cow's milk was absorbed (9). The same authors also pointed out that the percentage of iron absorption decreases with the amount of iron provided. Therefore, only a small fraction (4%) of iron is absorbed from iron-fortified formula (12 mg/L). The bioavailability of iron from human milk (49%) has also been determined using the extrinsic tag method.

Iron deficiency and iron deficiency anaemia

(i) Stages of deficiency

Unfortunately, there are very limited Canadian data on the prevalence of iron deficiency and iron deficiency anaemia. Iron deficiency, however, is the most common nutritional deficiency in the world today. It is estimated to affect between 10 - 20% of the world population. Infants and young children, and menstruating and pregnant women are the primary groups at risk for developing this nutritional deficiency.

Iron deficiency develops slowly over time as iron stores become depleted, however, one may depict the development of iron deficiency

anaemia in three stages. The initial stage of deficiency results from an inadequate dietary supply of iron, or occasionally from increased iron needs due to infant or adolescent growth spurts. During this stage, iron stores are released to ensure the synthesis of haemoglobin and other compounds that contain iron. Biochemically, one would see depressed serum ferritin concentrations, but no change in haemoglobin or any of the indices of erythropoeisis. As the iron stores become depleted under the stress of an insufficient exogenous iron supply, the next stage of iron deficiency occurs. Erythroid precursors are not provided with sufficient iron to mature properly, however, mature red blood cells remain unaffected. In this stage one would detect low ferritin levels, microcytosis and a normal haemoglobin concentration. In the final stage, overt anaemia occurs as the normal mature red blood cells are replaced by the microcytic cells that developed as a result of insufficient iron during formation.

(ii)Health implications

There are a number of significant health effects associated with both iron deficiency and iron deficiency anaemia. These include decreased capacity for work, an impaired immune response and impaired tissue function. Infants between the ages of 6 and 36 months, because of their rapid growth, are at particular risk. Iron deficiency during infancy may lead to a retarded growth rate. Infancy is also a period of critical development of sensoryperceptual and behavioural skills, and muscle co-ordination. Deficits in attention span, cognitive development and learning ability in iron deficient infants, preschool and school-age children have been reported (4). These cognitive and behavioural effects associated with iron deficiency anaemia in infancy may, in fact, be irreversible in some cases.

Five recent studies have examined behaviour and development of infants with iron deficiency anaemia (10-14). All carefully defined iron status; all included comparison groups without anaemia; all showed that infants with anaemia scored lower on tests of mental development administered before treatment, than infants without anaemia (an average of 6-14 points on the Bayley Scale of Infant Development); and, four of the studies found that anemic infants' scores on tests of motor development were lower as well (by an average of 9 - 11 points). One to two weeks of iron treatment compared to placebo had no effect on developmental scores. After a 2-3 month course of iron therapy similar to that used in clinical practice, most infants with iron deficiency anaemia did not have improvement in test scores, although they had a good hematologic response to iron therapy. In the latest 5 year follow-up study of the infants originally described, all had excellent hematologic status and growth at age 5 years, however, those who had moderately severe iron deficiency as infants (hemoglobin <100g/L) had lower scores of mental and motor functioning at school entry than the rest of the children (15).

Questions remain unanswered about the degree to which iron

deficiency affects development and behaviour and the degree to which the effect is permanent. However, there is no question that children with iron deficiency anaemia in infancy are at risk for long-lasting developmental disadvantage as compared with those with better iron status.

Strategies for the prevention of iron deficiency anaemia

New recommendations for the prevention of iron deficiency and iron deficiency anaemia have recently been put forward by the Nutrition Committee of the Canadian Pediatric Society (16). These include: exclusive breastfeeding during the first 6 months of life; delayed introduction of unmodified cow's milk until at least 9 months of age; the introduction of iron containing foods and enhancers of iron absorption (ascorbic acid) into the infant's diet by six months of age; and the use of iron fortified formula.

Unlike the situation in the United States where iron fortified formulas have been used for the past fifteen years, the use of unfortified formulas are the norm in Canada. The decrease in the prevalence of iron deficiency anaemia since 1969 in the United States has been attributed to the increased (and longer) use of iron-fortified formulas, the increase in breast feeding and the use of iron fortified cereals (17). It should be noted, however, that formula is provided free of charge in the USA to groups of infants at high risk of iron deficiency through the WIC program (Women and Infant Children Program). In Canada, there is no WIC program, thus infants at risk, who are likely receiving cow's milk, may not benefit from iron fortified formula. Unfortunately, there is no good data on the prevalence of iron deficiency anaemia in Canada (although it probably is not too high). Nevertheless it has been well documented that the use of iron fortified formula is safe and contrary to popular belief, most infants on iron-fortified formulas do not develop significant gastrointestinal problems (18,19). Therefore, despite the lack of documentation of widespread iron deficiency in Canadian infants not in high risk categories (eg. preterm, low socioeconomic status, etc), the committee decided to 'play it safe' by recommending that *all* formula fed infants receive iron fortified formula.

Decisions regarding nutrient fortification are not at all straightforward. Currently, most babies receiving non-fortified formula will likely *not* develop iron deficiency anaemia. Some, however, will. By recommending that iron-fortified formula be used, the incidence of iron deficiency may decrease, although not necessarily, since those at highest risk (lower socio-economic groups and new immigrants) are likely to continue to use regular cow's milk. However, since fortification is essentially without risk it was in my opinion, the right decision. It would probably be preferable to identify those at risk of iron deficiency anaemia through screening - although there is no guarantee that the screening would be successful.

Once the decision was made to recommend iron-fortified formula,

the only remaining question was how much iron to include in the formula. In the United States, formula is fortified to a level of 12-13 mg/L. In Europe the range of iron fortification is 6 - 8 mg/L. There is good documentation in the European literature that the 6 - 8 mg range is adequate to prevent the depletion of iron stores. Certainly the combination of fortified infant cereals, some fruits and meats and the lower level of formula fortification should be more than adequate to prevent iron deficiency and iron deficiency anaemia in the second six months of life.

REFERENCES

1. Scrimshaw NS. Iron Deficiency. *Sci Amer* 1991; 46-52.

2. Dallman P, Siimes M & Stekel A. Iron deficiency in infancy and childhood. *Am J Clin Nutr* 1980; 33:86-118.

3. Lozoff B. Has iron deficiency been shown to cause altered behavior in infants. In *Brain, Behaviour, and Iron in the Infant Diet*, ed Dobbing J, 1990; London: Springer-Verlag; pp 107-131

4. Oski F, Honig A, Helu B & Howanitz P. Effect of iron therapy on behavior performance in nonanemic and iron deficient infants. *Pediatr* 1983; 71:877-880.

5. Stekel A (1984). Iron requirements in infancy and childhood. In *Iron nutrition in infancy and childhood*, ed Stekel A, 1984; New York: Raven Press, pp 1-10.

6. Shannon K. Anaemia of prematurity: Progress and prospects. *Am J Pediatr Haematol Oncol* 1990; 12:14-20.

7. Committee on Nutrition of the Preterm Infant: European Society of Paediatric Gastroenterology and Nutrition. Iron. Oxford, England: Blackwell Scientific Publications, 1987; pp. 133-142.

8. Fomon S. Bioavailability of supplemental iron in commercially prepared dry infant cereals. *J Pediatr* 1987; 110:660-661.

9. Schulz J & Smith N. A quantitative study of the absorption of food iron in infants and children. *Am Med Assoc J of Dis of Child* 1958; 95:109-119.

10. Lozoff B, Brittenham GM, Viteri FE, Wolf AW & Urrutia JJ. The effects of short-term oral iron herapy on developmental deficits in iron-deficient anemic infants. *J Pediatr* 1982; 100:351-357.

11. Walter T, Kovalskys J & Stekel A. Effect of mild iron deficiency on infant mental development scores. *J Pediatr* 1983; 102:519-522.

12. Grindulis H, Scott PH, Belton NR & Wharton BA. Combined deficiency of iron and vitamin D in Asian toddlers. *Arch Dis Child* 1986; 61:843-848.

13. Lozoff B, Brittenham GM, Wolf AW *et al.* Iron deficiency anaemia and iron therapy effects on infant developmental test performance. *Pediatr* 1987; 79:981-995. [Erratum, Pediatrics 1988; 81:683]

14. Walter T, De Andraca I & Chadud P. Iron deficiency anaemia: adverse effects on infant psychomotor development. *Pediatr* 1989; 84:7-17.

15. Lozoff B, Jimenez E & Wolf AW. Long-term developmental outcome of infants with iron deficiency. *N Eng J Med* 1991; 325:687-694.

16. Nutrition Committee, Canadian Pediatric Society. Meeting the iron needs of infants and young children: an update. *Can Med Assoc J* 1991; 144:1451-1454.

17. Yip R. The changing characteristics of childhood nutritional status in the United States. In *Dietary iron: birth to two years*, ed Filer LJ, 1989; New York: Raven Press, pp 37-56.

18. Nelson S, Ziegler E, Copeland A, Edwards B & Fomon S. Lack of adverse reactions to iron-fortified formula. *Pediatr* 1988; 81:360.

19. Oski F. Iron-fortified formulas and gastrointestinal symptoms in infants: a controlled study. *Pediatr* 1980; 66:168.

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Iron nutrition, anaemia and intelligence

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ABSTRACT

Iron is an essential micronutrient which has many biochemical functions. Iron deficiency anaemia occurs only when the body's iron stores are severely depleted, but before that other signs of iron deficiency can be found. These include decreased work ability and impaired mental functioning. These changes can be severe enough to have a long-term effect on lifestyle but they are reversible when the iron deficiency is corrected. This iron deficiency is due mainly to poor dietary intake associated with poverty and may contribute to poor school achievement and so perpetuate the poverty. Iron medication may be a cost-effective method of improving school achievement in deprived communities.

INTRODUCTION

Iron deficiency is common among children and pregnant women, particularly in developing countries. In some countries more than 50% of children and pregnant women are anaemic, that is have a haemoglobin level below 110 grammes/L. Iron is an essential nutrient which can be stored in the body. So long as iron is available in the iron stores,and there are no other causes of anaemia, then the person will have a normal haemoglobin. Only when the stores are depleted will the serum iron and the haemoglobin levels drop significantly. There are therefore two stages in iron deficiency (a) the preclinical stages when there is still some iron in stores. At this time biochemical tests are needed to detect the deficiency (b) clinical iron deficiency anaemia when iron stores are exhausted.

The effect of anaemia on work output is well known (1) and is due mainly to the lack of oxygen in working muscles. This effect is removed when the anaemia is corrected. However, iron is needed in many biochemical pathways, particularly those involving energy metabolism. A deficiency of iron, even without anaemia, affects energy metabolism, including brain function, so even iron deficiency without anaemia is associated with delayed mental development and reduced work output.

IRON DEFICIENCY AND WORK OUTPUT

Athletes who are anaemic do not have maximal performance, but those with iron deficiency, as shown by low serum ferritin levels, may also be handicapped. It has been recommended (2) that athletes should have haemoglobin and ferritin levels measured regularly and iron given if either is low.

IRON DEFICIENCY AND MENTAL DEVELOPMENT

There have been many studies showing that children with iron deficiency performed less well at IQ tests than those with good iron stores. A study conducted in Selangor, Malaysia (3) showed that primary school children with iron deficiency had poorer grades in classwork than children with good iron stores. All the children were treated, some with iron and some with a placebo. The children who had good iron stores before treatment did not improve their school grades, but the children who had previously been iron deficient and were treated with iron improved to the same level as the non-anaemic children. The children treated with the placebo did not improve (see Table 1).

Other studies, particularly in Indonesia have shown similar results (4). The evidence is very strong that iron deficiency, even without anaemia, slows mental development and scholastic achievement. This delay is reversed when iron stores are replete.

CAUSES OF IRON DEFICIENCY

Red blood cells take up iron when they are formed and return the iron to stores when they are destroyed after 120 days. This iron is therefore well conserved and recycled. Growing children need iron to maintain the haemoglobin levels while their blood volume is increasing with growth; women need extra iron to make up for losses during menstruation and pregnancy. However, if the diet is good, the necessary iron is available and absorbed.

The absorption of iron depends on many factors, but the most important is the form of the iron in the food (5). There is 15% - 20% absorption of iron bound to the protein haem, which is found

Table 1. The mean values of serum ferritin and scorers in Bahasa Malaysia and Mathematics in children in Selangor (from Kandiah et al. 1993)

Group	Treatment	Serum ferritin		Scholastic scores			
				Bahasa Malaysia		Mathematics	
		Before	After	Before	After	Before	After
Iron deficient	Placebo	9.5	9.8	67.9	66.8	70.0	72.1
	iron	9.7	55.5	66.7	75.5	69.8	79.1
Not anaemic	Placebo	39.8	40.4	72.7	74.3	80.2	78.5
	Iron	38.5	88.7	73.0	72.4	81.7	84.3

Table 2. The effects of Vitamin C and tea on absorption of iron from medication and foods (data from Disler et. al., 1975)

Source of dietary iron	Percentage absorbed when iron followed by	
	Water	Tea
Ferrous sulphate	21.7%	6.2%
Ferrous sulphate + Vit C	30.9%	11.2%
Bread	10.4%	3.3%
Uncooked haemoglobin	14.7%	6.0%
Cooked haemoglobin	13.5%	14.3%

mainly in meat. By contrast, only about 1% - 10 of the iron in cereals and vegetables is absorbed. However, various combinations of food can promote and inhibit the absorption of iron. If cereal foods are eaten at the same time as haem-iron, then the absorption of the iron from the cereal rises. Similarly, if the cereals are eaten at the same time as a food or drink containing vitamin C, then the absorption of iron from the cereal rises. However, if tea is drunk at the same time as a cereal or vegetable is eaten, then the tea, and to a less extent coffee also, will inhibit the absorption of iron (6,7). The changes found by Disler and co-workers (8) illustrate this and are shown in Table 1.

PREVENTION AND MANAGEMENT OF IRON DEFICIENCY

Iron deficiency and iron deficiency anaemia are usually associated with poverty. Poor people cannot afford meat and similar sources of haem-iron. Even vegetables and cereals containing good levels of iron are not widely eaten, so the iron intake in the food is low. The iron in these non-haem foods is not well absorbed and this may be further compromised by drinking tea with meals.

Children from these families have low iron stores, so their mental development is slowed and their school performance poor; they therefore drop out of education and become the next generation of poor people. They will still be iron deficient and perhaps anaemic as adults, so their ability to physical work is reduced. They are locked in the poverty trap.

The best way of breaking this cycle of iron deficiency->poverty->iron deficiency is to improve economic conditions and hence improve diet. In a country where economic conditions are generally improving, this may be possible, but it will be slow. A simple and quicker way to break the cycle is to give iron medication.

If a community survey finds a number of anaemic adults and children, then it is likely that there are many more adults and children who are iron deficient but not yet anaemic. To get scientific proof of this we should test the serum ferritin levels on all

the people, but this is expensive and time consuming, so we assume that a moderate prevalence of iron deficiency anaemia means a high prevalence of iron deficiency without anaemia. The Institute for Medical Research and the World Health Organisation are conducting a major trial and preliminary results, and also preliminary results from others (9), suggest that that iron tablets given once a week can correct iron deficiency and anaemia. This method is cheap and simple and will help break the vicious cycle of iron deficiency and poverty, so that other long-term measures can be taken.

IMPLICATIONS OF IRON DEFICIENCY AND ITS MANEGEMENT

There is now strong evidence that iron deficiency, even without anaemia, can slow mental development and scholastic achievement in children and also decrease work capacity in adults. The management of iron deficiency should therefore be one of the national priorities. Giving one tablet of ferrous sulphate to school children each week is simple, safe and cheap and is likely to produce more improvement in academic achievement than more complex and expensive educational strategies. Cooperation between the Ministries of Health and Education could produce considerable benefits at little cost.

REFERENCES

1. Scrimshaw NS. Iron Deficiency. *Scientific American* 1991; 264:24-30.

2. Risser WL & Risser JM. Iron deficiency in adolescents and young adults. *Physician Sports Med* 1990; 18:87-101.

3. Kandiah M, Kuladevan R & Mohd Rusli Z. Iron supplementation, mental ability and scholastic performance among primary rural school children. *Proc Nutr Soc Malaysia* 1993; 8:9-15.

4. Idjradinata P & Pollitt E. Reversal of developmental delays among iron-deficient anaemic infants treated with iron. *Lancet* 1993; 341:1-4.

5. Shils ME & Young VR (editors). Modern Nutrition in Health and Disease. Lea & Febiger, Philadelphia.

6. Rossander L, Hallberg L & Bjorn-Rasmussen E. Absorption of iron from breakfast meals. *Amer J Clin Nutr* 1979; 32:2484-2489.

7. Morck TA, Lynch SR & Cook JD. Inhibition of food iron absorption by coffee. *Amer J Clin Nutr* 1983; 37: 416-420.

8. Disler PB, Lynch SR, Charlton RW, Torrance JD, Bothwell TH, Walker RB & Fatima M. The effect of tea on iron absorption. *Gut* 1975; 16:193-200.

9. Gross R, Schultink W & Juliawati. Treatment of anaemia with weekly iron supplementation. *Lancet* 1994; 344:821.

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Clinical and laboratory diagnosis of micronutrient deficiency syndromes

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ABSTRACT

The advances in artifical feeding during the past 20 years have resulted in some unique mineral and vitamin deficiency syndromes: P, Cl, Mg, Zn, Cu, Cr, Mo, Se, biotin, folic acid, vitamins A, D, E and K. In addition, deficiencies of essential fatty acids and certain amino acids have been described. These iatrogeNic syndromes have significantly advanced our understanding of the metabolic function of these nutrients. These syndromes were due to several factors:

1. Lack of availability of a parenteral product.
2. Nutrient sequestration in the delivery sets.
3. Abnormal metabolism of nutrients infused into the systemic, rather than the portal venous system.
4. Excessive losses of endogenous nutrients as a result of interrupted entero-hepatic cycles.
5. Harmful nutrient-nutrient interactions.
6. A greater need for "conditionally" essential nutrients because of unusual metabolic demands or immaturity of key metabolic system.

Clinical examples will be given of these different types of metabolic defects.

INTRODUCTION

Advances in artificial feeding during the past 20 years have resulted in some unique mineral and vitamin deficiency syndromes: [P, Cl, Mg, Zn, Cu, Cr, Mo, Se, biotin, folic acid, vitamins A, D, E, and K]. In addition, deficiencies of essential fatty acids and certain amino acids have been described. These iatrogeNic syndromes have significantly advanced our understanding of the metabolic function of these nutrients.

This paper will describe several mechanisms by which parenteral nutrition has caused a nutrient deficiency and for each mechanism one or two specific clinical examples will be given. In addition, the metabolic function and laboratory tests needed to confirm a specific nutrient deficiency are summarized in Table 1.

LACK OF AVAILABILITY OF A PARENTERAL PRODUCT

Until the late 1970's there was no commercial intravenous fat solution available. A preparation of soy oil solubilized with egg lecithin and glycerol was available for investigational purposes and this could be obtained for compassionate clinical use if a patient developed manifestations of essential fatty acid deficiency (EFAD). Biochemical evidence of EFAD, a triene/tetraene ratio >0.7 occurred within a few weeks of starting fat-free, round-the-clock, total parenteral nutrition (TPN). The clinical syndrome is a flaky, excoriated skin rash, particularly in moist folds, that appears somewhat like seborrheic dermatitis. This rash can develop after only a few weeks of TPN in growing infants, but usually requires several months of fat-free TPN in adults. Since adults have generous reserves of EFA in their fat stores, this syndrome does not develop in adults who are cycled on TPN, because their stores are mobilized during the non-fed phase. EFAD produces an abnormality of all cell membranes including intracellular structures as manifest by mega mitochondria. Altered membrane fluidity resulting in impaired coupling of energy via oxidative-phosphorylation and increased heat and evaporative losses through the skin, together seem to account for poor patient growth despite a generous supply of calories. EFAD may also increase red cell fragility and impair surfactant production by alveolar cells in the lung.

The diagnosis of EFAD is made by analysis of the fatty acid content of serum or red cell membrane lipids (GLC or HPLC) demonstrating the presence of an abnormal fatty acid, trieico-satrienoic acid (20:3), and depletion of the normal fatty acid, arachidonic acid (20:4).

The water soluble vitamin biotin was not a component of commercially available intravenous multivitamin products until the late 1970's. As a result, in the past, biotin deficiency could develop in patients on long term TPN. This was especially true for patients with underlying biotinidase deficiency, which makes them more dependant on parenteral biotin. Biotin, like essential fatty acids, is crucial to the synthesis of normal lipid membranes. Biotin deficiency presented as swelling of the face, thinning of the hair and inflammation and exudation of mucocutaneous junctions, particularly around the eyelids and lips. Laboratory testing shows increased hemolysis and the serum biotin level is low on microbiologic testing.

The early intravenous multivitamin products provided only 2 mg per dose of alpha tocopherol. Although vitamin E

Table 1. Daily Enteral (EN) and Parenteral (PN) Requirements and Clinical and Laboratory Assessment of Essential Fatty Acids, Minerals and Vitamins

Nutrient	Daily requirements adult range EN	PN	Clinical assessment: Metabolic function	Clinical assessment: Deficiency	Laboratory assessment: Test	Laboratory assessment: Normal	Laboratory assessment: Deficient
Essential fatty acids % Kcal	1-2	2-4	Components of all lipid membranes. Presursor of prosta-glandins	Scaly dermatitis	GLC[a] of plasma or red-cell membrane	Triene/tetraene ratio < 0.4	Triene/tetraene ratio > 0.7
Iron, mg	10	1-2	Body content 4g, heme compounds, cyto-chrome enzymes, iron stores	Microcytic anemia, immuno-competence thyroid hormone activation ↓ ↓ catecholamine activity	Atomic absorption or colorimetric	Serum iron > 10.0 umol/l (60 ug/dl): TIBC) 45 umol/l (250 ug/dl): plasma ferritin > 30 mg/dl	Serum iron < 9 umol/l (50 ug/dl), TIBC > 55 umol/l (300 ug/dl): plasma ferritin <12 mg/dl
Zinc, mg	15	3-12	Body content 2g, cofactor for many enzymes including carbonic anhydrase, alcohol dehydro-genase, carboxy-peptidase	Growth retardation and hypogonadism impaired would healing and immuno-competence	Atomic absorption	10.0-20.0 umol/l (70-120 ug/dl)	< 8.0 umol/l (50 ug/dl) if albumin normal
Copper, mg	2-3	0.3-0.5	Body content 100mg, cofactor for lysyl oxidase (collagen synthesis), cytochrome oxidase, tyrosinase	Anemia and neutro-penia, scorbutic-like osteopenia in children	Atomic absorption	14.0-20.0 umol/l (90-130 ug/dl)	< 8.0 umol/l (50 ug/dl) if albumin normal

Table 1 (cont'd)

Nutrient	Daily requirements adult range EN	PN	Clinical assessment: Metabolic function	Clinical assessment: Deficiency	Laboratory assessment: Test	Laboratory assessment: Normal	Laboratory assessment: Deficient
Iodine, mg	0.15	0.15	Body content 30mg, component of thyroid hormones	Cretinism/myxedema	Thyroxine (T4, T3, TSH)	300-900 nmol/l (4-11 ug/dl)	<300 nmol/l (4 ug/dl) if binding protein normal
Manganese, mg	2-5	2-5	Body content 20mg, cofactor for lipid, cholesterol, muco-polysaccharide metabolism	Abnormal clotting not corrected by vitamin K	Atomic absorption of whole blood	100-200 nmol/l (6-10 ng/ml)	<100 nmol/l (1 ng/ml)
Chromium, mg	0.05-0.2	0.015	Body content 6 mg, part of insulin receptor mechanism	Glucose intolerance	Atomic absorption of plasma	40.0-80.0 nmol/l (2-4 ng/ml)	<20 nmol/l (1 ng/ml)
Molybdenum, mg	0.15-0.3	0.01-0.5	Body content 5 mg, cofactor for xanthine oxidase	Confusional state secondary to increased methionine	Colorimetric of plasma	5.0-20.0 nmol/l (0.5-2 ng/ml)	<5.0 nmol/l (0.5 ng/ml)
Selenium, mg	0.05-0.2	0.05-0.1	Cofactor for glutathione peroxidase (GP)	Muscle weakness, macrocytosis without anemia	Fluorometric of whole blood or GP activity of red cell	0.3 nmol/l (0.02 ng/ml)	<0.2 nmol/l (0.01 ng/dl)
Cobalt	As cobalamin		Body content 80ug, metallo-cofactor for cobalamin (B_{12})	Unknown in man	Atomic Absorption	33-100 nmol/l (2-5 ng/ml)	<34 nmol/l (2ng/ml)

Table 1 (cont'd)

Nutrient	Daily requirements adult range EN	PN	Clinical assessment Metabolic function	Deficiency	Laboratory assessment Test	Normal	Deficient
Ascorbic acid, mg	60	100	Microsomal electron transport, tyrosine, tryptophan and dopamine synthesis, steroid synthesis, hydroxylation of collagen proline and lysine residues: folic acid metabolism.	Scurvy, perifollicular hemorrhages, bleeding gums, osteopenia, and subperiosteal hemorrhages: defective wound healing	Colorimetric analysis of: a. serum b. leukocytes	a. 28.0-60.0 umol/l (0.5-1.0 mg/dl) b. 852-1703 umol/l (15-20 mg/dl)	a. < 6.0 umol/l (0.1 mg/dl) b. < 397 umol/l (7 mg/dl)
Thiamine, mg	1.4	3.0	Cofactor (TPP*) for transketolase, pyruvate and ketoglutarate decarboxylase, oxidation of branched-chain ketoacids	High output cardiac failure, polyneuritis	Red cell a. transketolase b. TPP stimulation effect	a. 8-15 IU b. < 10% TPP effect	a. < 8 IU b. > 20% TPP effect
Riboflavin, mg	1.6	3.6	Converted to electron acceptors and donators, flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD)	Cheilosis, glossitis, seborrheic dermititis	Red cell glutathione reductase activity	< 1.2 EGR[b] activation coefficient	> 1.2 EGR[b] activation coefficient
Niacin, mg	18	40	Converted to electron acceptors and donators, nicotinamide dinucleotides (NAD, NADP)	Pellagra: pigmented dermatitis, ulceration of mucous membranes, CNS depression	Microbiologic determination of whole blood, fluorometric analysis of urine metabolites	Niacin: 30.0-75.0 umol/l (4-9 ug/ml) 2-pyridone/N methyl ratio > 2.0	< 25.0 umol/l (3 ug/ml) < 2.0

Table 1 (Cont'd)

Nutrient	Daily requirements adult range EN	PN	Clinical assessment: Metabolic function	Clinical assessment: Deficiency	Laboratory assessment: Test	Laboratory assessment: Normal	Laboratory assessment: Deficient
Biotin, ug	60	60	Cofactor for carboxylation enzymes where CO_2 is added such as pyruvate oxaloacetate, acetyl-CoA malonyl-CoA	Alopecia, seborrhaic dermatitis, neuritis	Microbiologic assay of serum	800-2000 pmol/l (200-500 pg/ml)	< 800 pmol/l (200 pg/ml)
Panthothenic acid, mg	5	15	Converted to coenzyme A	Irritability, burning parasthesias	Microbiologic assay of serum	700-2000 nmol/l (150-400 ng/ml)	< 700 nmol/l (150 ng/ml)
Pyridoxine, mg	2	4	Cofactor (PLP [#]) for many enxymes including transaminases, phosphorylases, amino oxidases	Glossitis, polyneuritis seizures microcytic hypochromic anemia	Red cell GOT	EGOT[c] index < 1.5	EGOT[c] index < 1.5
Folic acid, ug	400	400	Cofactor for purine and pyrimidine synthesis and metabolism of serine, histidine, homocysteine, and ethanolamine	Megaloblastic defect of red blood cells and mucous membranes	Microbiologic assay a. serum b. red cell	a. 7.0-20.0 nmol/l (3-9 ng/ml) b. 400-1400 nmol/l (150-600 ng/ml)	a. < 7.0 nmol/l (3 ng/ml) b. < 300 nmol/l (100 ng/ml)
Cobalamin, ug	3	5	Methyl B_{12} involved in methyl donor reactions, 5'-deoxyadenosyl B_{12} involved in carboxylation reactions	Megaloblastic defect of red blood cells and mucous membranes, central and peripheral neuropathy	Isotopic dilution or microbiologic assay	150-700 pmol/l (200-900 pg/ml)	< 100 pmol/l (150 pg/ml)

Table 1 (Cont'd)

Nutrient	Daily requirements adult range EN	PN	Clinical assessment: Metabolic function	Clinical assessment: Deficiency	Laboratory assessment: Test	Laboratory assessment: Normal	Laboratory assessment: Deficient
Vitamin A, RE	1000	1300	Light sensitive pigment in retinal epithelial maintenance (retinoic acid)	Night blindness and xerophthalmia testicular atrophy, keratosis of skin	Colorimetric, fluorometric or HPLC[d] assay of serum	0.7-2.0 umol/l (20-60 ug/dl)	< 0.7 nmol/l (20 ug/dl)
Vitamin D, ug	10	5	Calcium, phosphorus and possibly magnesium absorption from intestine, calcium deposition and mobilization from bone.	Osteomalacia (rickets in growing children), muscle weakness	Radioimmunoassay of serum 25-(OH)D	20-200 nmol/l (10-80 ng/ml)	< 10 nmol/l (5 ng/ml)
Vitamin E, mg	8	10	Prevents peroxidation of polyunsaturated lipids	Hemolytic anemia of newborn, dystrophic changes of retina and posterior column nuclei	Colorimetric or HPLC assay of serum. In vitro red blood cell peroxide hemolysis	0.02-0.03 nmol/l (0.8-1.2 mg/dl) < 10% hemolysis	< 0.01 nmol/l (0.5 mg/dl) > 20% hemolysis
Vitamin K, ug	100	200	Involved in synthesis of clotting factors II, VII, IX and X	Bleeding tendency presenting as epistaxis ecchymosis: gastrointestinal, urinary or CHS hemorrhage	No direct assay routinely available	Prothrombin time < 1 second prolonged over control	PT > 2 sec prolonged

[a] GLC = gas-liquid chromatography
[b] EGR = erythrocyte glutathione reductase
[c] EGOT = erythrocyte glutamic oxaloacetate transaminase
[d] HPLC = high pressure liquid chromatography
* = thiamine pyrophosphate
\# = pyridoxial phosphate

was a component of intravenous fat solutions, this form of vitamin E was chiefly the less physiologically active gamma tocopherol. For many patients starting long term TPN, this treatment was preceeded by several years of fat malabsorption and therefore these patients were already vitamin E depleted. Vitamin E, like EFA and biotin, is involved with the maintenance of normal lipid membranes by preventing peroxidative damage. Clinically vitamin E deficiency is associated with severe hemolytic anemia in newborns but in older subjects only a reduced RBC life span is seen. There is impairment of normal myelinization affecting the posterior columns and cerebellar pathways, producing ataxia in adults and delayed ambulation in children. The photo receptors of the eye are also damaged and the retina develops degenerative pigment changes, similar in appearance to idiopathic retinitis pigmentosa. A component of the walking difficulty and visual disturbance may reflect muscle weakness. Laboratory confirmation of vitamin E deficiency is not simple. Tocopherol is transported in the serum in association with all classes of lipoproteins, but chiefly with LDL in the fasting state. Altered cholesterol levels affect serum vitamin E levels, thus starving patients can have a low cholesterol and low vitamin E level but not be deficient, and cholestatic patients can have a high cholesterol and high vitamin E level but still be vitamin deficient. For this reason vitamin E levels are usually measured as a vitamin E/total lipid or vitamin E/total cholesterol ratio. Deficiency of vitamin E is one cause of increased in vitro RBC/peroxide hemolysis. There are sophisticated electro physiologic tests for demonstrating the retinal and nerve axonopathy changes.

NUTRIENT SEQUESTRATION IN THE DELIVERY SETS

Sorption of vitamin A onto the plastic or glass of the delivery sets can induce a clinical syndrome of vitamin A deficiency manifest by night blindness. Vitamin A is also converted by light to non-physiologic epoxides. For these reasons it is important to give generous amounts of intravenous vitamin A (3000 iu) each day and to add the vitamin mix just before the infusion starts. Laboratory confirmation of vitamin A deficiency involves measurement of the vitamin level in the serum by a colorimetric test or HPLC. Better still, vitamin A is assessed functionally by dark adaption testing or electroretinographic testing under scotopic conditions. Like vitamin E, vitamin A when first absorbed circulates as the ester, in the lipoprotein fraction. In the liver vitamin A is redistributed to tissues as the alcohol form retinol, attached to retinol binding protein and prealbumin. In pathological syndromes of severe hyperlipidemia, if the patient takes a vitamin supplement, excess retinyl remains in the lipoprotein fraction and a toxic amount of free vitamin A can dissociate, leading to acute vitamin A toxicity.

ABNORMAL METABOLISM OF NUTRIENTS INFUSED INTO THE SYSTEMIC RATHER THAN PORTAL SYSTEM

Many vitamins are converted to their active form in the liver and excess of the nutrient is stored in the liver: this is true for thiamine, riboflavin, niacin, pyridoxine, B12 and vitamins A, D, E and K.

Although in parenteral nutrition these vitamins are delivered directly into the blood stream, implying perhaps, that daily parenteral requirements might be lower than daily oral requirements, this assumption turns out to be untrue for most vitamins, since systemic infusion means immediate unphysiologic loss due to excretion via the kidneys. Thus the daily parenteral requirement of most vitamins is modestly higher than the oral requirement.

This is equally true for certain renally excreted trace elements, such as chromium. Chromium in an organic form, is part of the insulin receptor mechanism. Chromium deficiency induces a diabetic state and weight loss due both to calorie loss in the urine and increased hepatic gluconeogenesis, which is an energy consuming process. Chromium deficiency and the attendant diabetes may not be recognized because the hyperglycaemia is occurring at night during the cycled glucose infusion. Laboratory confirmation is also difficult because only a few research laboratories can accurately measure whole blood chromium. The early case reports usually made the diagnosis by a trial of chromium supplementation.

EXCESSIVE LOSSES OF ENDOGENOUS NUTRIENTS AS A RESULT OF INTERRUPTED ENTERO-HEPATIC CYCLES

Along with fluid and digestive enzymes many minerals and vitamins are secreted into the gastrointestinal tract in response to food ingestion, and then reabsorbed together with the products of digestion, before gut contents are excreted as stool. This is true for the major monovalent and divalent cations and anions (Na, K, Ca, Mg, Zn, Cu, Cl, HCO3), for vitamin B12, folic acid, and perhaps in part for the fat soluble vitamins. If the patient loses most of his or her small bowel, these endogenous nutrients will still be secreted but the reabsorption process may be deficient, leading to depletion of endogenous stores.

A high bowel fistula also loses excessive amounts of copper. Copper deficiency presents as a microcytic hypochromic anemia, with leucopenia and osteopenia. The leucopenia is not understood; the anemia is thought to reflect impaired absorption and mobilization of iron. The bone defect is thought to be secondary to defective collagen formation. Copper is the cofactor for lysyl oxidase which, with proline, forms the cross linkages in the formation of normal collagen in cartilage. The radiological abnormalities are very similar to scorbutic metabolic bone disease.

Zinc losses are also excessive if small bowel secretions are not reabsorbed. Zinc deficiency impairs the normal functioning of a wide range of zinc dependant enzymes including many enzymes

involved in protein synthesis. Zinc deficiency can present as growth failure and delayed sexual maturation. More acutely zinc deficiency induces a skin lesion similar to that seen in EFAD, perhaps because there is a common metabolic link. Both are involved in prostaglandin synthesis. Zinc status is quite difficult to quantitate. Any serum specimen must be drawn up in special acid washed vials without contact and contamination from rubber stoppers. There is current interest in measuring hepatic metallothionine II activity as a functional measure of zinc status. This is a zinc requiring enzyme that circulates in the bloodstream.

HARMFUL NUTRIENT-NUTRIENT INTERACTIONS

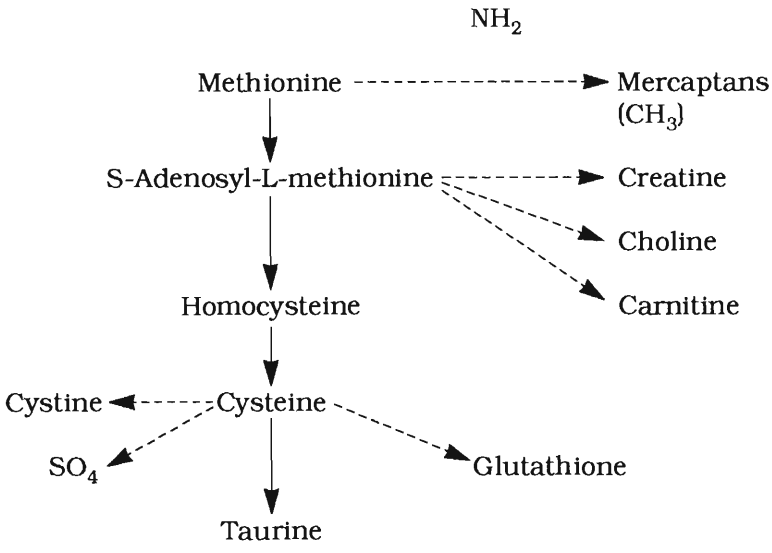
In the early days of TPN, a number of patients died in acute megaloblastic crisis. At the time this was thought to be due to the toxic effects of the alcohol used at that time as an energy substrate. Subsequent studies have shown that this acute megaloblastosis was caused by a metabolic block in the intermediary metabolism of folate. This block was apparently caused by high amounts of the amino acids methionine and glycine in TPN formulas. This syndrome is prevented by providing generous amounts of folic acid in TPN solutions (400 ug/day). The diagnosis of folate deficiency relies on a microbiological assay of serum and RBC folate.

A GREATER NEDD FOR "CONDITIONALLY ESSENTIAL" NUTRIENTS BECAUSE OF UNUSUAL METABOLIC DEMANDS OR IMMATURITY OF KEY METABOLIC SYSTEMS

Although parenteral nutrition was thought to provide all essential nutrients, recent data has shown that this may not be true particularly in respect to certain amino acids and peptides.

Because of the relative insolubility of cysteine and taurine, only methionine, the sulphur containing parent compound, is included in standard intravenous amino acid solutions. Furthermore the methionine content is quite modest because excess is known to be neurotoxic. Recent studies have shown that methionine infused systemically gets disproportionately trans-aminated rather than trans-sulphurated. Transulphuration is the predominant pathway for methionine metabolism in the liver and this transulfuration pathway results in the formation of several key downstream products as shown in Table 2. These products are important antioxidants (glutathione, taurine), are needed for normal oxidation of fat and gluconeogenisis (carnitine) and provide building blocks for the formation of normal cell membranes (choline). There are studies showing depletion of many of these downstream sulphur containing compounds in long term PN patients. This may have important implications for the problems of cholestasis and immune competence in long term PN patients.

Table 2. Summary of metabolic pathways of sulphur-containing amino acids.



■ Methionine transsulfuration pathways in the liver.

The fact that these difficult patient problems, described above, have expanded our knowledge about the functions of these specific nutrients is one more example unfortunately of "sweet are the uses of adversity".

SUGGESTED READING

1. Abumrad NN, Schneider AJ, Steel D & Rogers LS. Amino acid intolerance during prolonged total parenteral nutrition reversed by molybdate therapy. *Am J Clin Nutr* 1981; 34:2551-2559.

2. American Medical Association. Department of Food and Nutrition Guidelines for Essential Trace Element Preparations for Parental Use: A statement by an Expert panel. *JAMA* 1979; 241:2051-2054.

3. American Medical Association. Department of Food and Nutrition Guidelines for Multivitamin Preparations for Parenteral Use: A statement by an Expert Panel. Chicago, American Medical Association, 1975.

4. Cohen HJ, Brown MR & Hamilton D. Glutathione peroxidase and selenium deficiency in patients receiving home parenteral nutrition: Time course for development of deficiency and repletion of enzyme activity in plasma and red blood cells. *Am J Clin Nutr* 1989; 49:132-139.

5. Faintuch J, Faintuch JJ, Toledo M, Nazario M, Nazario G, Machado MC & Rabia AA. Hyperamylasemia associated with zinc overdose during parenteral nutrition. *JPEN* 1978; 2:640-645.

6. Fleming CR, Lie JT, McCall JF, O'Brien JF, Baillie EE & Thistle JL. Selenium deficiency and fatal cardiomyopathy in a patient on home parenteral nutrition. *Gastroenterology* 1982; 83: 689-693.

7. Fleming CR. Trace element metabolism in adult patients requiring total parenteral nutrition. *Am J Clin Nutr* 1989; 49:573-579.

8. Fwjita M, Itakura T & Takagi Y. Copper deficiency during total parenteral nutrition: clinical analysis of 3 cases. *JPEN* 1989; 13:421-425.

9. Hartline JV & Zachman RD. Vitamin A delivery in total parenteral nutrition solutions. *Pediatrics* 1976; 58:448-451.

10. Heller RM, Kirchner SG, O'Neil JA, Hough AJ, Howard L, Kramer SS & Green HL. Skeletal changes of copper deficiency in infants receiving prolonged parenteral nutrition. *J Pediatr* 1978; 92:947-949.

11. Howard L, Bigaouette J, Chu R, Krenzer BE, Smith D & Tenny C. Water soluble vitamin requirements in home parenteral nutrition patients. *Am J Clin Nutr* 1983; 37:421-428.

12. Howard L, Chu R, Feman S, Mintz H, Ovesen L & Wolf B. Vitamin A deficiency from long-term parenteral nutrition. *Ann Int Med* 1980; 93:576-577.

13. Howard L, Ovesen L, Satya Murti S & Chu R. Reversible neurological symptoms caused by vitamin E deficiency in a patient with short bowel syndrome. *Am J Clin Nutr* 1982; 36:1243-1249.

14. Jeejeebhoy KN, Chu RC, Marliss EB, Greenberg GR & Bruce-Robertson A. Chromium deficiency, glucose intolerance and neuropathy reversed by chromium supplementation in a patient receiving long term parenteral nutrition. *Am J Clin Nutr* 1977; 30:531-538.

15. Klein GL, Horst RL, Norman AW, Amenter ME, Slatopolsky E & Coburn JW. Reduced serum levels of 1,25 dihydroxyvitamin D during long-term total parenteral nturition. *Ann Int Med* 1981; 94:638-643.

16. Klein GL, Targoff CM, Ament ME, Sherrard DJ, Bluestone R & Young JH. Bone disease associated with total parenteral nutrition. *Lancet* 1980; ii:1041-1044.

17. Mehta R & Reilly JJ. Manganese levels in a jaundiced long-term TPN patient: Potentiation of haloperidol toxicity? Case report and literature review. *JPEN* 1990; 14:428-430.

18. Mock DM, DeLorimer AA & Liebman WM. Biotin deficiency: An unusual complication of parenteral alimentation. *N Engl J Med* 1980; 304:820-823.

19. Saty-Murti S, Howard L, Krohel G & Wolf B. The spectrum of neurologic disorder from vitamin E deficiency. *Neurology* 1986; 36:917-921.

20. Shah MC & Schwarz KB. Hazards of small amounts of heparin in a patient with subclinical vitamin K deficiency. *JPEN* 1987; 13:324-325.

21. Shike M, Harrison JR, Sturtridge WC, Tam CS, Bobechko PE, Jones G, Murray TM & Jeejeebhoy KN. Metabolic bone disease in patients receiving long-term parenteral nutrition *Ann Intern Med* 1980; 92:343-350.

22. Shike M, Roulet M, Kurian R, Whitwell J, Stewart S & Jeejeebhoy KN. Copper metabolism and requirements in total parenteral nutrition. *Gastroenterology* 1981; 81:290-297.

23. Shils ME, Baker H & Frank O. Blood vitamin levels of long-term adult home total parenteral nutrition patients: The efficacy of the AMA-FDA parenteral multivitamin formulation. *JPEN* 1985; 9:179-188.

24. Vinton NE, Laidlaw SA, Ament ME & Kopple JB. Taurine concentration in plasma and blood cells of patients undergoing long term parenteral nutrition. *Am J Clin Nutr* 1986; 44:398-403.

25. Watson RD, Cannon RA, Kurland GS, Cox KL & Frates RC. Selenium responsive myositis during prolonged home total parenteral nutrition in cystic fibrosis. *JPEN* 1985; 9:58-60.

26. Wolman SL, Anderson GH, Marliss EB & Jeejeebhoy KN. Zinc in total parenteral nutrition - requirements and metabolic effects. *Gastroenterology* 1979; 76:458-467.

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Spectrum of severe protein energy malnutrition in hospital-based patients as seen in the paediatric wards (past and present)

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ABSTRACT

Several cases of severe protein energy malnutrition were being seen in the hospital-based patients in the paediatric wards even up to 1980. Both cases of marasmus and marasmic kwashiorkor were seen with fewer cases of kwashiorkor. Study of the clinical features showed that severe pallor due to iron deficiency anaemia and skin changes with abnormal pigmentation and follicular hyperkeratosis dominated the picture. Biochemical values showed that the serum albumin tended to be low in the cases of kwashiorkor and marasmic kwashiorkor, a normal value was often found in the case of marasmus. The serum vitamin A and carotene levels were often found to be low, even though there were no significant clinical changes of vitamin A deficiency. These children were always admitted for associated illness mainly of the gastro-intestinal tract. Trichuris trichiura infection caused a lot of complications like rectal prolapse and bleeding, resulting in severe anaemia and malnutrition. During the recovery period complications due to hypokalaemia, hypothermia and secondary infections were seen. There were a few deaths. Cases were mainly admitted from pockets of urban slum areas.

In the present period fewer cases are seen due to the effective intervention programmes started by government departments. However, severe cases are seen occasionally among the immigrant population and from urban slums. Underlying pathology should be looked for like coeliac disease, which is rare but still can occur in the local population. As a consequence of the advances in management in the field of oncology, severe nutritional problems are being seen among patients with tumours, as a result of the drug regimes and basic malignant pathology.

The spectrum of protein energy malnutrition has changed considerably. The clinician has to study the cases with a high index of suspicion to understand the basic pathology and to give the correct management.

HOSPITAL-BASED PEM IN THE PAST

Severe protein-energy malnutrition (PEM) among hospital-based patients in the paediatric wards was a major problem even upto 1980. Cicely William who coined the word "Kwashiorkor" in 1935 was probably the first person to record its presence in Malaysia. She identified 2 cases of Kwashiorkor in Kuala Trengganu just before the Japanese invasion (1). Thomson in particular reported its widespread prevalence in Perak between 1951-1958.

The first documentation from Malaysian hospitals was the description of the clinical features, anthropometry, nutritional biochemistry, associated illness and parasitism of 25 severe PEM cases admitted to the Paeadiatric Unit of the General Hospital Kuala Lumpur during 1975, together with short notes on their management by George et al. (2). The Wellcome Party Classification (3) gave the following diagnosis for severe PEM. Marasmus 13, Marasmic Kwashiorkor 7, and Kwashiorkor 5. The racial distribution was 20 Indian, 4 Malay 1 Chinese 18 subjects were below 5 years, with the youngest age being 6 months. The remaining 7 children were above 5 years (the oldest 7 years). The sex ratio was 16 females to 9 males.

Laboratory assessment of the nutritional biochemistry showed that 80% of the subjects were protein deficient on the basis of low values for serum albumin and urinary hydroxyproline index. However, as expected, those with oedema (Marasmic Kwashiorkor and Kwashiorkor) had lower serum albumin values than those who had no oedema.

Although all subjects were anaemic by haemoglobin levels and many had clinical pallor, the majority had acceptable serum iron levels and transferrin saturation was only reduced in 33% of cases, particularly in the cases with Marasmic Kwashiorkor. Biochemical vitamin A deficiency was observed in 63% of subjects, but none of them had eye lesions related to the deficiency. There was a heavy load of parasitic and protozoal infestation in these children.

Several problems had to be faced during the management of these patients. During the initial period there was apathy, lethargy and a lack of interest in food, but this improved as the biochemical indices improved with parenteral nutrition. Chronic diarrhoea was a problem in 8 cases. Cardiac failure was a problem in two cases of Kwashiorkor associated with severe anaemia. One case was successfully managed with small blood transfusion, parenteral iron therapy. The other child however died as a result of circulatory over loading during blood transfusion.

Socioeconomic factors like poverty, large families, poor

housing, ignorance of balanced diet and parental neglect were the main contributory factors resulting in the severe PEM cases. A further detailed analysis of 70 cases of severe PEM was carried out by George R, Chong Y.H Gan S.C. from the cases admitted into the Paediatric Wards of the General Hospital Kuala Lumpur during the period 1st January 1978 to 1st August 1979 (4).

The racial and sex breakdown of the cases was as follows:

Indian	59	Sex Male	22
Malay	9	Female	48
Orang Asli	2		

The undernutrition seen was classified as follows:

Marasmus	43
Marasmic Kwashiorkor	15
Kwashiorkor	6
Significant Undernutrition	6

In this study also there was a predominance of Indian children and female children. Marasmus and Marasmic Kwashiorkor were found in 58 cases. These children came to the hospital as disadvantaged urban poor, from the "squatters" around the city of Kuala Lumpur. The Wellcome Classification for severe PEM was found to be most useful in the hospital diagnosis of PEM especially when these cases did not present with all the extensive clinical features usually attributed to this nutritional disorder.

The age distribution showed some interesting findings:

0 - 6 months	5
6m - 3 years	28
3 yrs - 5 yrs	24
> 5 yrs	13
Total	70

It is significant to note that there were 5 children below the age of 5 months. Four cases were babies of Indian rubber estate workers who were being looked after by child minders, as the mothers had no maternity leave and had to go for tapping rubber. These babies were not breast fed and were being fed on diluted infant milk formula. One was a Malay orphan girl being cared for in the Welfare Home.

These children were found to be affected by Marasmus or Marasmic Kwashiorkor, with extensive skin lesions, and with severe abnormalities in the serum biochemistry, mainly in the vitamin A level, serum iron and serum folate levels. Severe abnormalities were also seen in the other cases. Severe iron deficiency, very low levels of serum albumin and very low levels of serum vitamin A were the significant findings. There was one death from among the 70 cases. This was a case of severe Marasmus, which was complicated by an attack of measles with further suppression of the immune system resulting in severe bronchopneumonia, meningitis, amoebic colitis and hypokalaemia.

THE PRESENT SITUATION (FROM 1980 ONWARDS)

Very few cases of severe PEM due to poor nutrition are being seen. However such cases can be seen:

1. Among the immigrant population
2. In urban slum dwellers living in squatter areas
3. In undiagnosed coeliac disease
4. In oncology cases - after successful treatment regimes (e.g after chemotherapy, bone

marrow transplantation etc.)

5. In post surgical cases

A case report of a 7.5 year old girl is given as an example of a case of coeliac disease in Malaysian children (5). She was referred with a history of diarrhoea for the last 2.5 years. She passed frothy brownish stools 3-7 times a day. She complained of abdominal pain and flatulence. She was very weak and had very poor appetite. Her father was Tamil and mother, Sikh. Her diet included rice, chappathi, roti canai and bread. Upon physical examination, severe growth failure, severe pallor, ankle oedema and brown, thin, dry hair were found. In addition, there was clubbing of fingers, smooth tongue with angular stomatitis and poor muscle bulk with waddling gait. There was a grade 2 ejection systolic murmur upon auscultation of the heart and an enlarged liver (5 cm) with ascitis, at palpation.

Laboratory findings are summarised below:

Investigations	Findings
Haemoglobin	39 g/L
Haematocrit	14%
Eosinophils	30%
Peripheral blood film	hypochromic, microcytic anaemia, poikilocytosis, macrocytes
Serum albumin	21 g/L
Stool occult blood	positive
Stool Trichuris ova	++
Stool Ascaris ova	++
Bone age	3 years
Serum ferritin	3.6 ug/L (N 5 - 277)
Jejunal biopsy	suggestive of coeliac disease

As her mother was of sikh origin, coeliac disease was suspected.

Management procedures included placing the girl on a gluten free diet. Mebendazole, packed cells and vitamin supplements were given. She made a dramatic recovery. Gluten challenge was made, and the diarrhoea recurred. The girl was then able to select a diet which did not cause diarrhoea and abdominal distention. Coeliac disease in children of Asian immigrants has been described in the Lancet as way back as 1973.

17 cases were described by Nelson and McNeish from children of Punjabi and Pakistani origin from Birmingham. Coeliac disease in North Indian children was described by Walia and Sidhu in 100 children aged 3-14 years from New Delhi in the British Medical Journal in 1966.

Severe protein-energy malnutriton - the cardiovascular aspect

This was seen in a 4 year old Indian girl from an urban slum area. She was brought in a moribund condition, drowsy and pale. She was Tachypnoeic and had bilateral ankle oedema. The diagnosis was severe Marasmic Kwashiorkor. She had severe growth failure, with weight way below the 3rd percentile.

Cardiomegaly and tachypnoea with basal crepitations were found. The liver was 4 cm below the costal margin. The haemoglobin level was 16 g/L and the haematocrit was 0.05. Vitamin A concentration was 14 ug/L (N 20-75), carotene was 10 ug/L (N 40-175) and serum albumin was 10 g/L.

The diagnosis included Streptococcus viridans septicaemia, congestive cardiac failure, severe anaemia, hypoglycaemia, hypothermia, hypokalaemia, hypomagnesemia, metabolic acidosis, hypoalbuminaemia and heavy worm infestation.

On day 17 of illness she suddenly became very ill, with tachycardia, raised JVP, cardiomegaly and 2D echogram - evidence of mitral and tricuspid regurgitation. In spite of improvement with digitalisation, correction of anaemia, trace elements and vitamin therapy, she died of severe cardiac failure. Stresses on the heart due to anaemia, sepsis, negative inotropic factors, severe PEM, thiamine deficiency were considered responsible.

CONCLUSION

Severe PEM can still be found in the paediatric wards. The causes may be different, and careful investigation and management is needed.

REFERENCES

1. Williams CD. Kwashiorkor. *Lancet* 1949; 2:719.

2. George R, Foo LC, Chong YH & Abraham SCE. Severe protein-energy malnutrition in Kuala Lumpur. *J Trop Pediatr* 1981; 27(5):259-262.

3. Wellcome Trust Party. Classification of infantile malnutrition. *Lancet* 1970; 2:302.

4. George R, Chong YH & Gan SC. Unpublished data, 1978.

5. Lum LCS. Coeliac disease in a Malaysian child. Unpublished data, 1992.

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What do we mean by the weight-for-height? Implications for nutritional assessment

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ABSTRACT

Milder degrees of malnutrition or growth failure are easily missed clinically but since they manifest themselves as varying degrees of growth retardation, they can be recognized by the use of anthropometry. The indices that the WHO recommends as most promising and practical for nutritional surveillance are (1) percent weight for age(wfa), percent weight for height(wfh) and percent weight for height combined with percent height for age(hfa). It has been concluded by the WHO that wfa just duplicates, but does not add to, information that can be obtained from wfh and hfa (23) and it is stated that wfa does not distinguish between malnutrition of long or short duration (2) and is made up of two components - wfh which indicates malnutrition of short duration and hfa which indicates malnutrition of long duration. The interpretations of these indices have therefore been laid down by the WHO along these lines.

This paper clearly shows that the relationship between wfh and hfa is interactive and thus the wfh is a function of the slope of the linear relationship between wfa and hfa. It is subsequently demonstrated that wfh is just a rough approximation of wfa when age information is missing and has no inherent ability to distinguish the malnourished distinct from the wfa. In other words the greater the deviation of a child's height from the norm, the greater the error in the wfh as an indicator of body weight deficit. The short child with early bodyweight deficits is thus missed by the wfh as it overestimates the wfa. Depending on the median height of children in a community, the cutoff point for wfh as an indicator of bodyweight deficit will vary. It is demonstrated that the cutoff point for the conventional wfh needs to be shifted from the WHO cutoff of 80% to 90% in the community studied by the author. Re-interpretation of the indices for nutritional assessment is thus needed with the wfa being the indicator of acute malnutrition, the hfa being the indicator of chronic

malnutrition and the wfh being a rough approximation of wfa when age information is missing. The interpretation of the wfh is uncertain if the median age of children in the community is not known.

INTRODUCTION

Although among the globally significant nutritional deficiencies, iron, vitamin A and iodine deficiencies rank high (3,4), protein-calorie malnutrition (PCM) represents the major public health problem. 126 million children under 5 years old suffered from protein-energy malnutrition during the 1963-73 decade and 145 million between the 1973-83 decade (5). Protein-calorie malnutrition, also referred to as protein-energy malnutrition, has long been recognized as a common problem - especially of children in the developing countries, whose inadequate nutritional intake is deficient for socio-economic reasons. The term PCM covers a whole range of deficiency states from mild to severe, and has been defined as "a range of pathological conditions arising from coincident lack, in varying proportions, of protein and calories, occurring most frequently in infants and young children, and commonly associated with infections"(6). PCM, affecting principally small children, is a major public health problem in many developing countries in the tropics and subtropics. The severe clinical forms of the disease, like kwashiorkor and marasmus, are easy to recognize and can of course be detected clinically, but milder degrees of malnutrition or growth failure are easily missed. Mild and moderate forms of the disease manifest themselves as varying degrees of growth retardation, which could be recognized by the use of anthropometry or biochemical tests. Of the anthropometric nutritional indices, those based on weight and height are the most widely utilized.

A number of nutritional indices for classifying nutritional status based on weight and height have been described. Weight for age is the basis for the Wellcome Working Party classification which is very widely used (7). Waterlow has emphasized that the relationship between a child's weight and the international standard weight for his age provides an incomplete description of his nutritional status when he is assessed at a single point in time and he introduced a classification system based on the concepts of height for age and weight for height (8,9). Today, relatively simple anthropometry is widely used for the assessment of PCM in children and the three indices mentioned above, namely weight for age (wfa), height for age (hfa) and weight for height (wfh) have been used widely in assessing the nutritional status of large populations with varying degrees of success. All identify the smallest or least well nourished individuals within a population and are helpful epidemiologically in identifying subpopulations who are nutritionally "at risk". The subsequent mortality rate of the "at risk" group identified by these indicators is much higher than that of groups identified as normal (10,11).

In a review of anthropometry in nutritional surveillance, based on the results of the WHO collaborative study on nutritional anthropometry, the indices that emerged as most promising and practical were (12):

(1) Percent weight for age.

(2) Percent weight for height.

(3) Percent weight for height combined with percent height for age.

Wfa and hfa are simply age-standardized weight and height respectively (distance standards). The simplest way of standardizing weight and height for age are by comparisons with the median weight for age or median height for age respectively. These are extensively applied in the field of anthropometric nutritional assessment (usually expressed as a percentage) and are:

$$wfa = \frac{\textit{child's weight}}{\textit{expected weight for child's age}}$$

$$hfa = \frac{\textit{child's height}}{\textit{expected height for child's age}}$$

A wfh standard on the other hand, if it is to be independent of age, is in essence a multiple (non-linear) regression of weight on height and age. This is mathematically equivalent to the univariate regression of age-standardized weight on age-standardized height which is decisively different from the wfh used in the field of nutritional assessment where it has conventionally been taken to mean

$$\frac{\textit{child's weight}}{\textit{expected weight for child's height}}$$

wherein no mention is made of age. The problem of age-dependence therefore remains in the published wfh standards and has been pointed out by several workers (13,14). The National Center for Health Statistics recognized this problem but justified the definition of wfh standards without reference to age on the grounds that the charts would be useful in areas of the world in which accurate birth dates were not recorded (15). Waterlow et al (16) too recommended the use of this definition, with the expected weight for height typically being the median weight for the height in question. Poskitt and Cole (17) used a similar index except that they defined their expected weight as the median weight at the age where the child's height is median. This is approximately equivalent to the former definition since a perusal of the normative standards will confirm that the median weight for a childs height parallels the median weight at the age where the childs height is median.

Currently, wfh measurements occupy an important position in nutritional assessment. Several observations leading on to this may be noted. To begin with, the growth potential of an individual is genetically determined and each individual will follow a predetermined growth curve if conditions are favorable, this being referred to as channelization of growth. Any temporary deflection from this growth path will be followed by readjustment once conditions are favorable. This is termed catch-up growth and restore the individual to his or her growth channel (18). Astonishingly rapid rates of catch-up

growth have been observed in children recovering from severe malnutrition, achieving rates of weight gain that are at least 20 times faster than the rates of weight gain of normal children of the same chronological age. Such rates of weight gain are only observed when wasting is present, that is when there is a greater deficit in weight than length, as determined via a wfh deficit. Thus during the rehabilitation of severely malnourished children who have both a low wfh and hfa, weight gain is rapid until the children attain a weight that is appropriate for their length followed by a sudden slowing in weight gain once wasting is corrected (19). However although the average rate of weight gain is considerably slower in children who are only stunted, it is three times faster than would be expected for chronological age (20). It has therefore been argued that in cases of severe chronic malnutrition, where a child is stunted, the rate of weight gain is limited by the rate of linear growth, so that in conditions of dietary adequacy wfh is rapidly restored to normal. This is partly the reason why the conventional wfh is commonly used as a nutritional indicator distinct from the wfa. It has been maintained that wfh is an indicator of the present nutritional status of a child and if it is within the normal range the child is presently normally fed (21). A low wfa in this state is therefore taken to mean a past history of malnutrition while a high wfa is taken to mean a tall child. Furthermore it has been shown using correlation analysis that the conventional wfh and hfa are completely independent measurements (22). At the same time, multiple regression equations of wfa on wfh and hfa show very high measures of determination and it has been concluded that most of the variations from the median wfa is due entirely to variations from the median in wfh or hfa (23). The conclusion that has been drawn therefore is that wfa just duplicates, but does not add to, information that can be obtained from wfh and hfa (23). In other words wfa, which does not distinguish between malnutrition of long or short duration (24), is made up of two components - wfh which indicates malnutrition of short duration and hfa which indicates malnutrition of long duration.

Of recent, workers have become increasingly puzzled by the low prevalence of wasting in child populations with appalling social and environmental conditions, staggering levels of morbidity and mortality, and high prevalences of stunting (25). This dilemma stems from the inflexible acceptance of the WHO definitions of "wfh as the present state of nutrition and hfa as an indicator of past nutrition". The subsequent portions of this paper explain why this definition cannot be regarded valid any more.

MATERIALS AND METHODS

Children under the age of 5 years who came to the nutritional or well baby clinics of the Ahmadu Bello University Teaching Hospital (including the Sabon-Gari Comprehensive Health Centre, which is an annex of the aforementioned hospital) were eligible to be enrolled in the study. Only those children who initially came to register at the clinics

within a few days of their birth were enrolled in the study. This criterion for the selection of the study group ensured that ages were known accurately. The study children were collected in two groups on the basis of weight-for-age: those above and below 80% of the WHO median. 27 children in the former group and 25 in the latter group were enrolled in the study within the time span allocated for the collection of data. Each child weight was measured without clothes to the nearest 0.1Kg and recumbent length on a measuring board to the nearest 0.5cm using a tailors tape. All measurements were performed as described by Jelliffe (26). Ages were calculated in years using the decimalization scheme of Tanner et al (27). In this study the normal standards utilized were the WHO standards. A case has been made for the use of internal or local standards to be developed from the growth performance of well to do and presumably well fed children living in the same area (28), based on the assumption that genetic or ethnic differences in growth potential are a significant determining factor in the growth of children in different populations. However, a review of available evidence has shown that ethnic differences play a minor role in the actual growth performance of populations if compared with the overwhelming influence of nutrition and disease (29). Analysis and computation of indicator values was carried out using the computer programs produced by the Division of Surveillance and Epidemiologic Studies and the Division of Nutrition, Centers for Disease Control, Atlanta, Georgia (30).

Relationship between WFH, WFA and HFA

Regression of wfa on both hfa and wfh (all indices expressed as percentages) reveals a high coefficient of multiple determination (R^2= 0.96). Multiple regression equations of wfa on wfh and hfa in other studies too have shown very high measures of determination. The regression equation in this study is

$$wfa = 0.912*wfh + 1.744*hfa - 166.45 \qquad eq\ 3\ (r^2=0.96)$$

There is no doubt about the fact that when hfa is median, wfa equals wfh. First, the ratio of wfa to wfh (wfa range 0.77-1.29) in children with around median height {hfa = 0.98±0.03(SD); n=6} from the collected data is 0.98±0.03(SD). Second, a look at the normal standards will immediately reveal that the median weight for any height is equivalent to the median weight for the age where that height is median. In other words, the extent of the hfa deviation from the median determines the slope of the relationship between wfa and wfh. Nevertheless, this is not considered in the fit of the multiple regression of wfa on wfh and hfa characterized above. This is simply because thus far it has been assumed that the effect of wfh and hfa are additive. Hfa, as described above however, is involved interactively with wfh. In other words, a wfh-by-hfa interaction effect exists since the impact of wfh depends on the value of hfa. An interaction variable was therefore created by multiplying the two independent variables together. The basic linear regression using just this single

variable for interaction (without hfa or wfh individually) was

wfa = 0.012*wfh*hfa - 23
eq 4 (r^2 = 0.94; r = 0.97 & 95% conf limits 0.94 – 0.98)

This single variable for interaction explains essentially as much of wfa as the two independent variables used separately. This is because the amount of difference one variable makes on wfa depends on the value of the other. Practically speaking, this means that it really does not make much sense to talk about the separate (or main) effects of wfh and hfa on wfa, since wfh and hfa do not operate independently of one another with respect to their effects on wfa.

Application of this interactive relationship to the data of Cheek et al (31) shows complete agreement with the above findings (regression equation is wfa = 0.011*wfh*hfa - 20.7; r^2=0.97). Furthermore 13 out of 14 clinically malnourished boys with previous edema who had low active tissue mass (ICW values calculated using deuterium and corrected bromide space measurements) were not considered wasted (low wfh) by WHO criteria. Also, all clinically malnourished boys under initial nutritional rehabilitation, again with low active tissue mass, were not considered wasted by WHO criteria. The wfh as defined by the WHO is therefore a poor index of nutritional status. It may be of interest to note that (using ICW as the standard) a 80% cutoff for the wfa resulted in a sensitivity and specificity of 83% & 76% respectively. A 80% cutoff for the wfh resulted in a sensitivity and specificity of 72% & 59% respectively.

A clear picture can now be delineated for the relationship between wfa, hfa and wfh. Since merely the single variable for interaction explains just about all of the variability in wfa, the conventional wfh is clearly related to the slope of the relationship between wfa and hfa. The wfh can thus be used to approximate the wfa once the degree of stunting in a community is known. The greater the degree of stunting in a community, the more the wfa is overestimated and the higher the cutoff point needs to be for good discrimination between the well & malnourished. Wfa is therefore the indicator of acute malnutrition (or wasting) and not the wfh. The wfh is simply a mathematical approximation of the wfa where age information is missing and therefore the statement by the WHO that the wfa represents the sum of the information given by the other two indicators (32) is not correct, since the effects of these two on wfa are interactive - not additive.

The age-specific WFH

As children are split up into increasingly narrow age-groups it has actually been demonstrated that at the extremes of the height ranges, the median weights of a narrow age-group diverge from those of a wider age-group with the same range of heights (33). The median weight of the short, narrow age-group is considerably greater than the median weight of children of the same height, but wider age-range (33). This is because the increase in average height with age

means that the short children in the wider age group will be predominantly young children of average hfa, whereas in the narrow age-group they are children with a low hfa. If weight is predominantly dictated by age, then the child in the narrow age group, when compared with a typical (younger) child of the same height in the wide age group, should be relatively heavier, and the tall child, when compared with a typical (older) child of the same height, should be, to a lesser extent, lighter. Newens and Goldstein (33) demonstrated this and emphasized this importance of age in the wfh assessment. Chinn & Morris (14) support their finding and state that it is the children who are short or tall for their age who are at risk of being wrongly assessed. Newens & Goldstein therefore concluded that joint standards of height and weight should be age-specific, because weight does not indicate the same degree of adiposity for children of the same height but different age (33). In summary therefore, age is an important determinant of weight and creating age-specific wfh standards using narrow age groups essentially brings the median weights for height and age together. The narrower the age groups, the less the difference between the median weights for height and for age. Taking age into account therefore reduces the wfh to a wfa estimate!

IMPLICATIONS

It is clear that age is a much more important determinant of weight than height in normal children. This is evident from the fact that the median weights for height of short or tall children are considerably higher or lower respectively when determined in narrow age groups. The median weight for a particular height is simply the average weight of children who would typically have that height, which would be on the average the weight of children of that age where the height is median. Tall children thus have an overestimation of age and are judged thinner while short children have an underestimation of age and are judged fatter. Narrow age-groups solve this problem by making the median weight for height comparable to that for age.

It has been shown that age is important in the wfh assessment, if it is to be nutritionally valid, and at the same time that the age-specific wfh simply parallels wfa information. We may therefore conclude that the wfh is of trivial service where age information is available. Nevertheless, the conventional wfh is determined without reference to age and can be used in the absence of age information, but if used as such an indicator, the cutoff point depends on the average hfa of those assessed. If on the average the malnourished have less than median height, the conventional 80% cutoff point for the wfh will wrongly assess a majority of them as adequate in weight. In this study too it was found that since most children had lower than median height, only a 90% cutoff point for the wfh was sufficiently able to differentiate those with and without bodyweight deficits. Evidently, since children with bodyweight deficits are usually in the lower percentiles of height, the present cutoff of 80% for the wfh is

certainly unacceptable when it is used as an age-independent indicator of malnutrition. A shift to 90% would on the average compensate for the lower percentiles of height usually seen in acute cases of malnutrition. That such shifts are indeed needed is supported by the study of Anderson (34) who suggested such a shift for the wfh cutoff point after comparing anthropometric measures of nutritional status in five developing countries and the study by Trobridge et al where it was concluded that wfh cutoffs for wasting or obesity may require different interpretations for different populations (35). Where marked stunting is present, an even higher cutoff may need to be set, as is the case with the Guatemalan boys studied by Cheek et al (31). Also a re-interpretation of the same combinations of the three indicators becomes necessary and this is shown in Figure 1.

Figure 1. The relation between low, normal and high for the weight-for-height, weight-for-age and height-for-age calculated from the data for 18-month-old boys in the WHO reference population, with cut-offs at 2SD's above and below the median (from ref 21). Groups 7-12 and 5 are those groups considered by the WHO as normally fed. The non-shaded groups are those re-classified as normally fed in this paper.

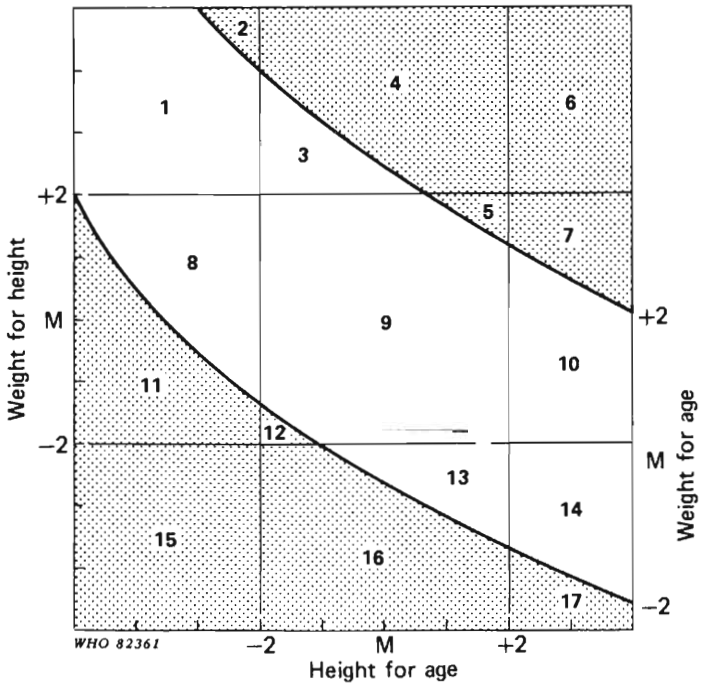

Figure 1. The relation between low, normal and high for the weight-for-height, weight-for-age and height-for-age calculated from the data for 18 month old boys in the WHO reference population with cut-offs at 2SD's above and below the median. (from ref 21) Groups 7-12 & 5 are those groups considered by the WHO as normally fed. The non-shaded groups are those re-classified as normally fed in this paper.

REFERENCES

1. Keller W, Donoso G & DeMaeyer EM. Anthropometry in nutritional surveillance: a review based on results of the WHO collaborative study on nutritional anthropometry. *Nut Abstrac Rev* 1976; 46:591-606.

2. Rao KV, Radhiah G, Raju SVS & Swaminathan MC. Relative importance of various anthropometric measurements and indices for an evaluation of nutritional status. *Ind Ped* 1981; 18:223-231.

3. DeMaeyer EM. Xeropthalmia and blindness of nutritional origin in the third world. In: *Children in the Tropics*. International Childrens Centre, Paris, 1986; No. 165.

4. Thilly CH, Bourdoux P, Contempre B & Swennen B. Strategies for combating endemic goitre. In: *Children in the Tropics*. International Children's Centre, Paris, 1988; No. 175/176.

5. WHO. Nutritional Surveillance. Global trends in protein-energy malnutrition prevalence. *Weekly Epidemiological Record* 1984; 59(25):189-192.

6. WHO and FAO. *Food and nutrition terminology, definition of selected terms and expressions in current use* (compiled with the collaboration of the International Union of Nutritional Sciences). WHO, Geneva, 1973; NUTR. 73.2.

7. Anonymous. Classification of infantile malnutrition. *Lancet* 1970; ii:302.

8. Waterlow JC. Classification and definition of protein-calorie malnutrition. 1972; *Br Med J* 3:566.

9. Waterlow JC. Note on the assessment and classification of protein-energy malnutrition in children. *Lancet* 1973; ii:87.

10. Kielmann AA & McCord C. Weight for age as an index of risk of death in children. *Lancet* 1978; i:1247-1250.

11. Chen LC, Chowdhury AKM & Huffmann SL. Anthropometric assessment of energy protein malnutrition and subsequent risk of mortality among preschool aged children. *Am J Clin Nutr* 1980; 33:1836-1845.

12. Keller W, Donoso G & DeMaeyer EM. Anthropometry in nutritional surveillance: A review based on results of the WHO collaborative study on nutritional anthropometry. *Nut Abstrac Rev* 1976; 46:591-606.

13. Van Wieringen JC. *Secular changes of growth*. Netherlands Institute for Preventive Medicine, Leiden, 1972.

14. Chinn S & Morris RW. Standards of weight-for-height for English children from age 5.0 to 11.0 years. *Ann Hum Biol* 1980; 7:457-471.

15. National Center for Health Statistics, NCHS growth charts. Monthly Vital Statistics Report, 1976; 25, supplement 3.

16. Waterlow JC, Buzina R, Keller

W, Lane JM, Nichaman MZ & Tanner JM. Presentation and use of height and weight data for comparing the nutritional status of growing children under the age of 10 years. *Bull World Hlth Org* 1977; 55:489-498.

17. Poskitt ME & Cole TJ. Do fat babies stay fat? *Br Med J* 1977; 1:7-9.

18. Tanner JM. Catch-up growth in man. *Br Med Bull* 1981; 37:233-238.

19. Ashworth A (1975). In: Chavez A, Bourges H & Basta S eds, *Proceedings of the Ninth International Congress of Nutrition, Mexico, 1972.* Volume 2, Karger, Basel, 1975; pp 280-285.

20. Ashworth A & Milward DJ. Catch-up growth in children. *Nutrition Reviews* 1986; 44:157-163.

21. World Health Organization. *Measuring change in nutritional status: Guidelines for assessing the nutritional impact of supplementary feeding programmes for vulnerable groups.* WHO, Geneva, 1983.

22. Keller W. Choice of indicators of nutritional status. In: B Schurch ed, *Evaluation of nutrition education in third world communities.* Nestle Foundation Publication Series, Hans Huber Publishers, Bern, 1983.

23. Keller W, Fillmore M. Prevalence of protein energy malnutrition. *World Health Statistics Quarterly* 1983; 36:129-167.

24. Rao KV, Radhiah G, Raju SVS & Swaminathan MC. Relative importance of various anthropometric measurements and indices for an evaluation of nutritional status. *Ind Ped* 1981; 18:223-231.

25. Victora CG. The association between wasting and stunting: An international perspective. *J Nutr* 1992; 122:1105-1110.

26. Jelliffe DB. The assessment of nutritional status of the community. *World Health Organization. Monograph Ser* No 53, 1966.

27. Tanner JM, Whitehouse RH & Takaishi M. Standards from birth to maturity for height, weight, height velocity and weight velocity: British children 1965. *Arch Dis Child* 1966; 41:613.

28. Waterlow JC. Classification and definition of protein calorie malnutrition. In: Beaton GH and Bengoa JM eds, *Nutrition in preventive medicine,* World Health Organization Monograph series, 1975.

29. Habicht JP *et al.* Height and weight standards for pre-school children. How relevant are ethnic differences in growth potential? *Lancet* 1974; i:611-615.

30. Dean AG, Dean JA, Burton AH & Dicker RC. Epi Info, Version 5: A word-processing, database and statistics program for epidemiology on micro-computers. Centers for Disease Control, Atlanta, Georgia, USA,

1990.

31. Cheek DB, Habicht JP, Berall J & Holt AB. Protein-calorie malnutrition and the significance of cell mass relative to body length. *Am J Clin Nutr* 1977; 30:851-860.

32. WHO Working Group. Use and interpretation of anthropometric indicators of nutritional status. *Bull WHO* 1986; 64:929-941.

33. Newens EM & Goldstein H. Height, weight and the assessment of obesity in children. *Br J Prev Soc Med* 1972; 26:33-39.

34. Anderson MA. Comparison of anthropometric measures of nutritional status in preschool children in five developing countries. *Am J Clin Nutr* 1975; 32:2339-2345

35. Trobridge FL, Marks JS, Lopez de Romana G, Madrid, Boutton TW & Klein PD. Body composition of Peruvian children with short stature and high weight for height. II Implications for the interpretation for weight-for-height as an indicator of nutritional status. *Am J Clin Nutr* 1987; 46:411-418.

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Microcytosis, iron deficiency and thalassaemia in children aged 6-24 months

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ABSTRACT

This study was undertaken to screen for anaemia in the Child Health Clinic at University Hospital, Kuala Lumpur. Over a three months period, we offered anaemia screening to 160 apparently healthy children, of which 153 (96%) accepted the screening tests. Complete results were available for 150 of them. A total of 24/150 (16%) were found to be anaemic with Hb < 11 g/dl, of which 12 (8%) were associated with microcytosis with MCV < 74 fl. Another 12 (8%) were associated with normocytosis. 15/150 (10%) were found to have microcytosis without anaemia. These children were recalled and given a trial of iron supplement for 4-6 weeks when their responses were monitored and Hb electrophoresis performed. It was found that 14 of them had thalassaemic or Hb E traits, 11 of them were iron deficient and another 2 probably had infections. Our data showed that there was a significant difference in MCV between children with Thalassaemia or Hb E traits (mean MCV 66.1 ± 5.7fl) and children with iron deficiency (mean 75.2 ± 7.8fl). This suggests that care should be exercised before giving prolonged iron supplement to a mildly anaemic child as both the thalassaemia traits and iron deficiency are common in Malaysia.

INTRODUCTION

Anaemia is a common problem in childhood, especially in children aged 6-24 months old. De Maeyer(1) estimated that 12% of children aged 0-4 years in developed countries and 51%in developing countries were anaemic. Studies done in the West have shown that iron deficiency is a common cause of anaemia in this period of rapid growth (2-9). Other causes include infection and hereditary disorders such as haemoglobinopathies. There is increasing evidence that iron deficiency is associated with poorer psychomotor development and behavioural changes of young children (10-17). Thus,it has been suggested that infants and toddlers should be screened for iron deficiency (18-21).

Most screening for anaemia was carried out in Western countries where it was found that children of Asian origin were at higher risk of being iron deficient (2-9). Similar local data is lacking and any screening for anaemia would not only include iron deficiency anaemia but also other causes of anaemia like haemoglobinopathies and infection which are common in this country.

This study was carried out to investigate the prevalence and causes of anaemia in children aged 6-24 months attending Polyclinic L at the University Hospital, Kuala Lumpur. This Clinic is a child health clinic offering health promotion services to normal children who are delivered at the Maternity Unit, University Hospital, Kuala Lumpur.

AIMS

The main objectives of this study were:

1. To assess the acceptance of screening for anaemia in children aged 6-24 months attending the Child Health Clinic, i.e. Polyclinic 'L' at the University Hospital, Kuala Lumpur.

2. To determine the prevalence as well as causes of anaemia and microcytosis in these children.

3. To compare the differences in red cell indices, serum ferritin and serum iron amongst children with iron deficiency and those with thalassaemia / Hb E traits.

SUBJECTS AND METHODS

Place and Duration of Study

The study population comprised children attending the Child Health Clinic on Mondays, Wednesdays and Fridays during the 3-month study period, i.e. 11.9.92-27.11.92. They attended the clinic for their routine physical and developmental screening and to complete their immunisation schedule.

Subjects

Children aged 6-24 months were invited randomly to participate in the study. Prior verbal consent was obtained from the parents. Questionnaire was used to interview the parents.

Collection of Blood

Venous blood samples were taken by the drop method using a size 23 gauge needle punctured through the dorsal venous plexus of either hand. 0.5 ml of blood was collected in micro-EDTA bottle for a full blood count and another 2 mls was taken in plain bottle for serum iron and ferritin. All blood samples were taken by a single investigator.

Analysis of blood samples

The full blood count was performed by the Coulter counter Model S Plus 4. The results generated include haemoglobin (Hb), packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), red cell distribution width (RDW), total white cell count and platelet count.

Assay for serum ferritin was carried out using the IMX system. The IMX ferritin assay is based on Micro particle Enzyme Immunoassay (MEIA) technology. Excess serum was sent for serum iron assay.

The results of Hb electrophoresis were reported by the haematologist of the Hospital.

Follow-up

All children with Hb < 11 g/dl and MCV < 74 fl were recalled and given dietary advice and syrup ferrous sulphate supplement (3 - 4 mg/kg/day as elemental iron). They were followed up 4-6 weeks later to monitor their response to iron supplements. FBC, serum ferritin, serum iron and Hb electrophoresis were repeated during the follow-up examination. The parents whose child was found to be a carrier of haemoglobinopathy were offered screening for haemoglobinopathy and counselling.

Definitions

Anaemia is defined as a haemoglobin level of less than 11 g/dl (22)

Iron deficiency = an increase of 1 g/dl in Hb after 4-6 weeks of iron supplementation and absence of other obvious causes of anaemia such as infection.

Criteria for Thalassaemia/HbE traits
: Hb A2 > 3.5% : Hb F > 1%
: Abnormal band in A2 position on Hb electrophoresis
: Family history of microcytosis

Microcytosis means MCV < 74 fl.

Statistical methods

The data collected was analysed using the statistical package Epi-info 5. Differences between means were compared using the F-test or the Kruskal Wallis test where appropriate. The response to iron supplements in the anaemic children was tested using Student's t test. The differences in proportion for qualitative data were tested using the chi square test.

RESULTS

153 (96%) of the 160 parents of children seen at the clinic gave consent to the screening tests. Only 7 (4%) refused. The racial breakdown of children studied, i.e. Malays (42%), Chinese (28%), Indians (29%) was similar to the proportion of children who attended this clinic.

A total of 24/150 (16%) were found to be anaemic with Hb < 11 gm%, of which 12 (8%) were associated with microcytosis with MCV < 74 fl. Another 12 (8%) were associated with normocytosis. 15/150 (10%) were found to have microcytosis without anaemia. These 3 groups of children were given a trial of iron supplement for 4-6 weeks when their responses were monitored and Hb electrophoresis performed. It was found that 14 of them had thalassaemic or Hb E traits, 11 of them were iron deficient, 2 probably had infections and there were 7 inconclusive results which probably are a mixture of thalassaemia and iron deficiency.

There was a significant difference in MCV between children with thalassaemia or Hb

E traits (mean MCV 66.1 with SD 5.7 fl) and children with mild iron deficiency (mean MCV 75.2 with SD 7.8 fl). There was also significant difference in mean serum ferritin level between the two groups of children (22.4 ng/ml in thalassaemia Vs 12.0 ng/ml in iron deficiency group) as in Table 1. The response to iron supplementation in these two groups of children also differs significantly (Table 2a & 2b). It shows that children with thalassaemia/Hb E traits did not have any increase in haemoglobin, in fact there was a decrease. The mean increment in Hb level of 1.4 g/dl in iron deficient children was statistically significant, at $p < 0.01$. Although there was an increment of 0.3 g/dl in the mean Hb of normal children after the ferrous sulphate supplement, this was not statistically significant.

Table 1. Laboratory data in iron deficiency, Thal or Hb E traits and normal children (mean values, SD in parenthesis)

	Thal or Hb E trait n = 14	Iron deficiency n = 11	Normal n = 115
Hb, g/dl p<0.00001	11.0 (0.8)	10.5 (1.0)	12.2 (0.7)
PCV p<0.00001	0.33 (0.03)	0.31 (0.03)	0.36 (0.02)
MCV, fl p<0.00001	66.1 (5.7)	75.2 (7.8)	79.7 (3.3)
MCH, pg p<0.0001	21.8 (2.1)	25.2 (2.8)	24.1 (0.6)
RBC *1000/ml p<0.0001	5.1 (0.5)	4.2 (0.3)	4.4 (0.3)
RDW p<0.00001	16.3 (2.6)	13.7 (1.7)	13.0 (1.0)
Platelet *1000/ml p = 0.1	461 (115)	386 (93)	411 (105)
WBC *1000/ml p = 0.3	9.4 (2.0)	10.2 (2.3)	10.7 (2.6)
Fe, nmol/ml p = 0.2	13.4 (5.3)	11.7 (6.9)	16.2 (11)
Ferritin, ng/ml p<0.00001	22.4 (7.4)	12.0 (7.6)	32.5 (19.5)

Table 2a. Response to iron supplements.

Indices	Thal or Hb E trait n = 14	Iron deficiency n = 11	Normal n = 17
Hb, g/dl	mean (SD)	mean (SD)	mean (sd)
pre-supp	11.0 (0.8)	10.5 (0.1)	12.3 (0.9)
post-supp	10.8 (0.7)	11.9 (0.3)	12.6 (0.8)
mean changes	-0.2 (0.5)	+1.4 (0.9)	+0.3 (1.2)
t-value	0.3	5.17	1.31
p-value	p>0.2	p<0.01	p>0.2
	N.S.	S	N.S.
MCV, fl			
pre-supp	66.4 (5.8)	75.1 (7.8)	76.5 (2.4)
post-supp	67.6 (6.7)	78.3 (4.1)	77.3 (2.6)
mean changes	+1.2 (2.4)	+3.2 (4.1)	+0.8 (2.3)
t-value	2.03	2.58	1.43
p-value	p>0.05	p<0.05	p>0.1
	N.S.	S	N.S.

SD = standard deviation
NS = not significant
S = significant

Table 2b. Response to iron supplements

Indices	Thal or Hb E trait n = 14	Iron deficiency n = 11	Normal n = 17
Iron, umol/l	mean (SD)	mean (SD)	mean (SD)
pre-supp	12.0 (4.8)	11.8 (6.9)	15.1 (14.1)
post-supp	15.3 (7.0)	19.5 (13.3)	12.0 (5.6)
mean changes	+3.2 (11.1)	+7.7 (15.5)	–3.1 (13.7)
t-value	1.08	1.65	0.94
p-value	p > 0.2	p > 0.1	p > 0.2
	N.S.	N.S.	N.S.
Ferritin, ng/ml			
pre-supp	22.3 (7.8)	12.0 (7.6)	27.2 (19.4)
post-supp	31.2 (15.0)	20.6 (8.5)	32.9 (16.2)
mean changes	+8.9 (12.7)	+8.6 (6.9)	+5.7 (13.5)
t-value	2.62	4.13	1.73
p-value	p < 0.05	p < 0.01	p > 0.1
	S	S	N.S.

SD = standard deviation
N.S. = not significant
S = significant

The mean increment in MCV after ferrous sulphate supplementation in iron deficient children was 3.2 fl and this is statistically significant at $p < 0.05$ compared to that of thalassaemia trait (1.2 fl), which was not statistically significant.

The mean increment in serum iron after the ferrous sulphate supplements was highest in the iron deficient children (8.3 umol/l) compared to 7.4 umol/l of that of thalassaemia traits. However, the increment was not statistically significant for either group.

The thalassaemia group had the highest increment in serum ferritin, 9.4 ng/ml. This was followed by the iron deficient group (8.6 ng/ml). The increment in both groups of children were statistically significant.

DISCUSSION

Most parents agreed to have a screening test for anaemia done on their children, the 96% acceptance rate being similar to those of E. Marder(7) and John James (96%) (23). The good response obtained might be because this group of parents were health conscious and well motivated to provide the best care for their children.

The results showed that both thalassaemia/Hb E traits and iron deficiency were common in this group of infants studied, i.e. 9.3 % and 7.3% respectively. However amongst the anaemic children, iron deficiency was the commonest (35%), followed by thalassaemia traits (26.9 %).

The high percentage of thalassaemia traits in our population should caution us to be more careful in treating an anaemic child as iron deficient without further investigations. If any child fails to respond to initial trial of iron supplement, they should be investigated for thalassaemia or HbE traits.

The prevalence of thalassaemia traits was quite close to that suggested by H.B. Wong(24) in 4% of beta-thalassaemia trait for Malays and Chinese, and 5% for alpha-thalassaemia trait for Malays and Chinese. The prevalence of HbE trait of 3% in Malays was slightly lower than the 5% reported by H.B. Wong(24). It should be noted that the number of children in this study was relatively small. To validate the above data, larger prevalence studies need to be undertaken.

It is important to differentiate iron deficient children from thalassaemia/Hb E traits. This is because iron deficient children would benefit from iron supplements whereas long-term iron supplements for thalassaemia/Hb E traits might cause more harm than good. Although a short trial of iron supplements will help to differentiate iron deficient children by an increase in Hb, there is always the question of poor compliance in some children who do not respond.

There were 73% of iron deficient children with MCV >74 fl. It is known that mild iron deficiency anaemia might develop before microcytosis becomes apparent (5,25,26). Children with MCV less than 74 fl would have a greater chance of being thalassaemia/Hb E traits, thus haemoglobin

electrophoresis should be performed to avoid prolonged iron therapy. It should be noted that in moderately severe to severe iron deficient subjects, the MCV will also be severely depressed to levels which are found in children with thalassemia traits. The serum ferritin and serum iron will also be low. This enabling one to differentiate iron deficiency from thalassaemia traits. This is consistent with report by Hershko et al that MCV and serum ferritin can differentiate children with iron deficiency from thalassaemia traits(27).

It has been reported in adults that MCV < 80 fl is a good index for selecting patients for Hb electrophoresis (28,29). The results of this study confirm the above, except that in children the cut-off point should be lower, at MCV < 74fl.

The response to iron supplements may also help to differentiate iron deficiency from thalassaemia traits; children with iron deficiency show significant increase in Hb, MCV and ferritin post-supplementation, whereas children with thalassaemia/Hb E traits show a significant increase in serum ferritin level without significant increase in their Hb level. This probably relates to increased iron absorption in children with chronic haemolysis as in thalassaemia/Hb E trait, as suggested by Hershko(32). Thus, any mildly anaemic child who failed to respond to iron supplements should be screened for thalassaemia/Hb E traits which are common in this region. This will prevent unnecessary long-term iron therapy which may lead to the danger of iron overload in these children, as they have a tendency to increased iron absorption.

Causes of Iron Deficiency

Infancy is one of the groups most susceptible to iron deficiency, due to rapid growth and inadequate nutritional intake. Unmodified cow's milk, inadequate weaning with solid food and exclusive breast-feeding for more than 6 months without iron supplement were associated with increased risk of iron deficiency(6,31) Although iron in breast-milk is better absorbed than in infant formula, it is not sufficient as the main source of iron after 6 months of age. Three out of 11 children with iron deficiency in this study were given breast-milk exclusively with inadequate introduction of solid food; in another 5 of them, the diluted milk was probably the cause of iron deficiency. The recommendation for exclusively breast-feeding mothers is that their infants should have an additional source of iron providing at least 1 mg/kg/day after about 5 months of age (32) is quite reasonable. Low birth weight infants were also at risk of iron deficiency. P.R. Dallman(32) recommended the following total amounts of iron to be provided by a supplement or a supplement plus iron-fortified formula, from about one to about 12 months of age, as follows: 2 mg/kg/day for infants with a birth weight between 1.5 and 2.0 kg, 3 mg/kg/day between 1.0-1.5 kg, and 4 mg/kg/day below a birth weight of 1.0 kg.

REFERENCES

1. De Mayer E, Adiels-Tegmon M & Rayston E. The prevalence of anaemia in the world. *Wld Hlth Statis Quat* 1985; 38:302-316.

2. Ehrhardt P. Iron deficiency in young Bradford children from different ethnic groups. *BMJ* 1986; 292:90-93.

3. Grindulis H, Scott PH, Belton NR & Wharton BH. Combined deficiency of iron and vitamin D in Asian toddlers. *Arch Dis Child* 1986; 61:843-848.

4. Aukett MA, Parks YA, Scott PH & Wharton BA. Treatment with iron increases weight gain and psychomotor development. *Arch Dis Child* 1986; 61:849-859.

5. Earley A, Valman HB, Altman DG & Pippard MJ. Microcytosis, iron deficiency and thalassaemia in pre-school children. *Arch Dis Child* 1990; 65:610-614.

6. Mills AF. Surveillance for anaemia: Risk factors in patterns of milk intake. *Arch Dis Child* 1990; 65:428-431.

7. Marder E, Nicoll A, Polnay L & Shulman CE. Discovering anaemia at child health clinics. *Arch Dis Child* 1990; 65:892-894.

8. Wright CM, Reading RF, Halse PC & Watson JG (1989). Iron deficiency in adolescents. *BMJ* 298:1035-1036.

9. James J, Evans J, Male P, Pallister C, Hendrikz JK & Oakhill A. Iron deficiency in inner city pre-school children: Development of a general practice screening programme. *J R Coll Gen Pract* 1988; 38:250-252.

10. Lozoff B, Brittenham GM, Viteri FE, Wolf AW & Urrutia JJ. The effects of short term oral iron therapy on developmental deficits in iron deficient anaemic children. *Paediatr* 1982; 100:351-357.

11. Walter T, Kovalskys J & Stekel A. Effect of mild iron deficiency on infant mental developmental scores. *J Pediatr* 1983; 102:519-22.

12. Lozoff B, Brittenham GM, Wolf AW *et al.* Iron deficiency anaemia and iron therapy: Effects on developmental test performance. *Pediatr* 1987; 79:98-95.

13. Deinard AS, List A, Lindgren B *et al.* Cognitive deficits in iron deficient anaemic children. *J Pediatr* 1986; 108:681-689.

14. Oski FA, Honig AS, Helm B *et al.* Effects of iron therapy on behaviour performance in non-anaemic iron deficient infants. *Pediatr* 1983; 71:877-880.

15. Oski FA & Honig AS. The effects of therapy on the developmental scores of iron deficient infants. *J Pediatr* 1978; 92:21-25.

16. Walter T. Behavioural and cognitive effects of iron deficiency anaemia. *Paediatr & Nutr Review* 1990; 4(3):1-11.

17. Lozoff B, Jimenez E & Wolf AW.

Long-term developmental outcome of infants with iron deficiency. *N Engl J Med* 1991; 325:687-694.

18. Anonymous. Iron deficiency - Time for a community campaign [Editorial]. *Lancet* 1987; i:141-142.

19. Addy DP. Happiness is iron. *Br Med J* 1986; 292:969-970.

20. Illingworth RS. Anaemia and child health surveillance. *Arch Dis Child* 1986; 61:1151-1152.

21. Hall MB (ed). *Health for all children*. Oxford Medical Publications, 1989; pp 34-36.

22. World Health Organisation. Nutritional anaemia. WHO Tech Rep Ser, 1972, No. 503.

23. James J, Lawson P, Mole P & Oakhill A. Preventing iron deficiency in pre-school children by implementing an educational and screening programme in an inner city practice. *Brit Med J* 1989; 299:838-840.

24. Wong HB. Thalassaemia in Singapore: Problems and solutions. *Family Practitioner* 1984; 7(3):75-86.

25. Beather E. The red cell indices in the diagnosis of iron deficiency anaemia. *Ann Intern Med* 1959; 50(2):313-322.

26. Emile R Mohler. Iron deficiency and anaemia of chronic disease: Clues to differentiating these conditions. *Postgrad Med* 1992; 123-128.

27. Hershko C, Konijn AM & Lovia A. Serum ferritin and mean corpuscular volume measurement in the diagnosis of beta-thalassaemia minor and iron deficiency. *Acta Haemat* 1979; 62:236-239.

28 Li A & Cheng MY. Anaemia and thalassaemia in healthy adolescents from southern Chinese families. *J Paediatr Child Health* 1990; 26(6):339-342.

29. Menaka N. Electronic cell counters and microcytic anaemias. Paper presented in VII Congress Asian Pacific Division, International Soc. Haemat., Hong Kong, Nov 1991; pp 17-21.

30 Hershko C. Storage iron regulation. Progress in Hematology, 1977; vol x:105-148.

31. Picciana MF & Deering RH. The influence of feeding regimens on iron status during infancy. *Am J Clin Nutri* 1980; 33:746-853.

32. Dallman PR. Progress in the prevention of iron deficiency in infants. *Acta Paediatr Scand* 1990; 365(Suppl): 28-37.

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Ultrasound in assessing thyroid volume (goitre) - Malaysia's experience

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ABSTRACT

A portable ultrasound was used in assessing thyroid volume among Aborigines and Malays in selected villages in Peninsular Malaysia. Subjects aged 10 years and above were randomly selected from each village for thyroid examination. Thyroid volume ranged between 4.2 ml to 108.3 ml. It was higher among the Aborigines in remote rural areas compared to the Aborigines and Malays in rural or urban areas ($p<0.05$). The correlation between goiter staging and thyroid volume was significant ($r=0.549$, $p<0.05$). In conclusion, portable ultrasound is a useful and practical method to assess thyroid volume (goiter) of populations, especially in areas with endemic goiter.

INTRODUCTION

The most obvious sign of iodine deficiency is goitre, an enlargement of the thyroid gland at the base of the neck. Large goitres are easily visible with the naked eye, more subtle enlargements must be detected by palpation or by using ultrasound equipment. Populations in developing countries are mostly affected with goitre particularly among the settlers in remote areas (1). Endemic goitre is particularly frequent in certain geographical areas and the prevalence exceeds 10% among children aged 6 to 15 years or in adult populations (2). Endemic goitre is a major problem in certain parts of the world, especially in the inland and mountainous areas such as the Himalayas of Asia, the Alps of Europe and the Andes of South America (3). Goitre volume can be measured accurately using ultrasound equipment. A previous study showed that portable ultrasound had been used to determine the stages of goiter by assessing the thyroid volume (4). Therefore in this study, thyroid volume was measured among the Aborigines and the Malays of a few selected villages in Peninsular Malaysia, using the ultrasound technique.

MATERIALS AND METHODS

All subjects were examined by experienced endocrinologists for the presence of goitre. Goitre stage was determined by palpation using the WHO classification. All goitrous subjects were later examined by an experienced radiologist using the portable ultrasound TOSHIBA SONOLAYER. We also examined non-goitrous subjects chosen randomly using the ultrasound technique in order to determine its validity. The head of subjects was supported by a pillow, with their neck lying supine and gel was used as interphase material. Measurements were done by using a 5 MHz transducer, firstly cross-sectionally to determine the thickness and maximum width of the thyroid gland, secondly longitudinally to determine its length.

The thyroid volume can be calculated using a formula:

Volume = width x thickness x length x 0.479*

* = correction factor

Volumes of more than 18 ml for adult females and more than 25 ml for adult males were taken as goiter (4,5).

RESULTS AND DISCUSSION

This study found that the mean thyroid volume was 15.2 ml, with a standard deviation of 9.9 ml. Volume ranged from 4.2 ml to 108.3 ml. We also found that median thyroid volume did not increase with age in males and females. There was a significant difference in the volume of thyroid glands between remote inland locations and urban areas. Remote inland populations had larger volumes compared to urban areas ($p<0.0001$) (Table 1). Betau Post, being the most remote area, showed the largest thyroid volume with the mean value of 24.1 ml. This is followed by FELDA Sungai Koyan (rural area), Hulu Sungai village (rural area), Bukit Lanjan (urban area) and lastly Kg. Kerinci (urban area).

When thyroid volume was classified as goitrous and non-goitrous, there was a relationship between goiter measured by

Table 1. Thyroid volume by locations

	Location	Thyroid volume	
		n	mean
a.	Betau Post, Pahang	46	24.1^{bcde+}
b.	Bukit Lanjan, Kuala Lumpur	51	12.6^{cd}
c.	Hulu Sungai Village, Pahang	55	16.6^{e}
d.	FELDA Sungai Koyan, Pahang	28	18.5^{e}
e.	Kg. Kerinci, Kuala Lumpur	89	10.2

+ there is a significant difference in comparison with the other areas marked p significant at 0.05

ultrasound and goiter determined by palpation (Table 2).

Goitre grading by the WHO classification has a significantly correlated with thyroid volume: the higher the grade, the larger the volume (Table 3). The correlation between goitre staging and thyroid volume was significant ($r=0.549$, $p<0.05$). Subjects with grade 0 goitres had the smallest mean thyroid volume, 12.5 ml while subjects with grade 3, as the highest grade, showed the largest mean thyroid volume, with the value of 64.2. In this study, sensitivity of palpation was 65.5% and specificity was 81.5% (Table 2).

DISCUSSION

Our study showed that portable ultrasound equipment was a useful tool for assessing thyroid volume (goitre) in endemic areas. In term of feasibility, ultrasonography is non-invasive and safe. It is a specialized technique in which individuals have to be trained. A trained worker can perform up to 200 examinations per day. The portable ultrasound equipment is relatively rugged; however, it requires electricity (6). In our experience, a portable generator can be used to supply the electricity for field study.

Table 2. Relationship between goitre measured by ultrasound and goitre determined by palpation

Factor		Goitre (by ultrasound)		chi sq	p*
		present	not present		
Goitre (by palpation)	present	36	39	47.5	0.0001
	not present	19	172		

*p significant at 0.05, sensitivity = 65.5%, specificity = 81.5%

Table 3. Thyroid volume by goitre grade

Indices		Thyroid volume (ml)	
		n	mean
Goitre	a. Grade 0	193	12.5
	b. Grade 1	42	17.3
	c. Grade 2	32	25.6
	d. Grade 3	3	64.2
ANOVA test	F	53.0	
	p*	0.0001	

*p significant at 0.05

Performance-wise, compared to palpation, ultra-sonography provides a more precise measurement of thyroid volume. This becomes especially significant when the prevalence of visible goitres is small, and for monitoring iodine control programmes where it would be expected that thyroid volumes will decrease over time. Children 8 to 10 years of age should preferably be studied, but if an adequate number to ensure statistical precision cannot be obtained, the range may be extended from 6 to 12 years of age (6). This is because the measurement of goitre in schoolchildren is important for public health considerations, as this group effectively reflects the current status of iodine deficiency disorder (IDD) in the general population. The smaller the child, the smaller its thyroid and it is more difficult to examine it, especially in children less than six years of age. Thus, there is a practical reason for not mesuring very young age groups.

In terms of cost, portable ultrasound equipment with a 5 MHz transducer currently costs RM 30,000. This price is expected to decline with the availability of smaller machines.

CONCLUSION

Portable ultrasound is a useful and practical method to assess the thyroid volume (goitre) of populations, especially in areas with endemic goitre.

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REFERENCES

1. Maberly GF. The significance of endemic goitre in Sarawak, Borneo. Bachelor of Science Thesis, University of New South Wales, 1975.

2. Delange F, Bastani S, Benmiloud M *et al.* (1986). Definitions of endemic goitre and cretinism, classification of goitre size and severity of endemias, and survey techniques. In: Dunn JT, Pretell EA, Daza CH & Viteri FE eds, *Towards the eradication of endemic goitre, cretinism, and iodine deficiency*, Pan American Health Organization World Health Organization, Washington DC, 1986; pp. 373-376.

3. Menzies Gow N & Cochrane JPS. The effect of epidural analgesia on postoperative sodium balance. *Br J Surg* 1979; 66:864-867.

4. Hegedus L, Perrild H, Poulsen LR, Andersen JR, Holm B, Schnohr P, Jensen G & Hansen JM. The determination of thyroid volume by ultrasound and its relationship to body weight, age and sex in normal subjects. *J Clin Endocrinol Metab* 1983; 56:260.

5. Gutekunst R, Fierro-Benitez R, Teichert HM & Stanbury JB. The effect of iodinated oil and

salt on thyroid volume determined by ultra-sonography in two villages in Equador. *Proceedings of the Tenth International Thyroid Congress*. The Hague, 1991.

6. National Meeting Towards The Elimination of IDD, 17-20 November, 1993, Genting Highlands. Maternal & Child Health Unit, Health Division, Ministry of Health, Malaysia.

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Dietary management in cardiac rehabilattion: the IJN experience

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ABSTRACT

Institut Jantung Negara Sdn. Bhd. was corporatised on the 1 September 1992. It occupies a brand new seven storey building with 275 beds and suites. IJN is a referral centre and is exclusively dedicated to the treatment of heart diseases. The Dietary Department is an annexe to the main building of 720 sq.m. in area. It operates as a cost centre. The initial staff consists of 14 staff. The operations of dietary services started off early August 1992 serving breakfast and snacks only. Lunch and dinner was provided by Dietary Services of Hospital Kuala Lumpur. By the end of August all meals were provided by the dietary services of IJN.

With the appointment of the dietician in January 1993, new protocols were set up. Diet counselling for both inpatients and outpatients were carried out. For the first time choice menus were introduced to patients of all classes and doctors-on-call. Upgrading staff in finer skills of cooking and strict disciplines were maintained. Setting up of standards in clinical nutrition i.e. guidelines of low cholesterol, low fat and healthy eating was carried out. Modification of standard recipes, different types of cooking methods were established. Cardiac rehabilitation programmes is the present project that the Dietary Department is involved. To upgrade information and training the department is presently in the computerisation system. Upgrading of the Dietary Service in the Institut is truly a challenge.

INTRODUCTION OF INSTITUT JANTUNG NEGARA SDN. BHD. (IJN)

* IJN began its services with 3 wards, ICU and CCU units on 22 June 1992.
* IJN was corporatised on 1 September 1992
* It is a 275 bed referral centre providing first, second and third class ward facilities for adult and paediatric cardiology and cardiothoracic patients

OBJECTIVES OF IJN

* To provide excellent cardiology and cardiothoracic care to inpatients and outpatients in all age groups

* To serve as a national reference centre for cardiovacular diseases

* To give access to public as well as private patients

* To promote awareness through public education on heart diseases and its preventive measures

Outpatient Treatment Services for referral and follow-up cases

i. Cardiology (Non-invasive) services

  * E.C.G.
  * Stress test
  * Echo
  * Pacemaker follow-up

ii. Cardiothoracic

  * Pre and Post operative consultation

iii. Executive screening programme (ESP)

Inpatient Treatment Service

i. Cardiology (invasive)

  * Management of patients with unstable angina, myocardial infarction, heart failure, etc.
  * angiogram
  * angioplasty
  * other

ii. Cardiothoracic services

  * Open heart surgery
    - Bypass surgery
    - Valve Repair/Replacement
  * Close heart surgery
    - Shunts
    - Pacemaker
  * Thoracic surgery
  * 24-Hours Emergency

24-hours emergency treatment service for those who experience chest pain or are suspected of getting 'heart attack'.

* Support Services

  Dietary Services
  Laboratory and Blood Bank
  Pharmacy
  Radiology
  Physiotherapy
  Central Sterile Supply Department
  Medical Records
  Engineering
  Housekeeping

Wards

1 First class ward
2 2nd. class wards
3 3rd. class wards
4 Paediatric ward

Other Units

1 Coronary Care Unit (CCU)
1 Cardiothoracic Intensive Care Unit (ICU)
1 Observation Unit
4 Operation Theatres
3 Cardiovascular Laboratories

DIETARY SERVICES OF IJN

The operations of the dietary services started off in early August 1992 serving breakfast and afternoon snacks for patients.

Lunch and dinner were then provided by the Dietary Department of Hospital Kuala Lumpur. By the end of August 1992 all meals were provided by the dietary department of IJN. The IJN operates as a cost centre. The department is currently in the initial stages of computerisation.

Dietary Services provided at IJN

1. Diet counselling
   Inpatient/Outpatient
   * Individual - Cardiology cases
   * Group - Cardiothoracic cases, usually post operative cases
   * Follow-up cases - patients who need to lose weight and control their blood sugar

2. Nursing aide education
   * In-house education and training on nutrition, tray-services, feeding patients and listening to patients problems regarding food

3. In-house lectures
   * Lectures on Nutrition and Dietetics to all category of nursing divisions and paramedics

4. Talks
   * These are for the general public, associations and clubs related to cardiac diseases and nutrition, and are conducted with the cardiologists

5. Food quality control progamme
   Questionnaire on food service/meals are given to patients in Bahasa Malaysia and English. These data are collected and review and changes are made to improve food service standards.

6. Dietary personnel education
   * In-service education and training on various aspects of sanitation, cooking methods, meal preparation and therapeutic diets

7. Meals and snacks
   * Snacks for functions, Board Meetings and visitors
   * Meals for staff - O.T., I.C.V.L. and Dietary personnel

8. Cooking classes
   * The objective is to teach recipes for cooking healthy meals to all patients and staff in the hospital

Types of therapeutic diets served and modification of recipes

* All meals have low cholesterol content

* Salt use is limited. If soya sauce is used then salt is omitted

* Coconut milk for curriesis replaced with a combination of low fat milk and milk powder. Low fat yoghurt is also used in curry preparation

* Food is generally baked, grilled, steamed and sometimes fried

* Whole eggs are limited to 2-3 per week

* The meat used is lean. All visible fat and skin areremoved from chicken

* Polyunsaturated margarine is used instead of butter

* Oil is kept to a minimum

Types of food services in IJN

Decentralised services

* Food is transported from the kitchen to the wards via heated trolleys
* Food is served from each pantry to the ward supervised by a nurse
* Microwave ovens are provided at each pantry to serve hot food
* The respective wards are responsible for their own cutlery, crockery and trays

Type of menus available in IJN

Weekly cycle menu

First class: Choice menus with western meals and fruit juices for breakfast

Second class: Choice menus without western meals except for weekends

Third class: Choice menus without western meals

Companion meals: Meals available for accompanying relatives

Paeds: Choice menu for 1st. Class

Standard menu for 2nd. and 3rd.Classes

Meals are provided for the patient's parent

DIETARY MANAGEMENT OF PATIENTS IN CARDIAC REHABILITATION

Individual counselling

1. Patients are referred by cardiologists or surgeons via individual diet referral forms
2. Clinical Evaluation e.g. medical history, laboratory results etc are also provided by the doctors concerned
3. A patient's past diet history, like and dislikes, allergies, lifestyle, occupation, etc. is taken into account, in addition to smoking, consumption of alcohol and exercise level
4. Patients are encouraged to be frank, discuss their food problems, occupation, the travelling involved in their work, business luncheons etc. The patient's spouse or family memberssit in for counselling
5. Based on the discussion, changes which can accepted by the patient are recommended
6. Patients who are diabetic or overweight are counselled and encouraged to control their blood sugar and lose weight gradually
7. Follow-ups are recommended and appointments are fixed at the same time they see their respective doctors

Group counselling

1. This is usually recommended for post-bypass patients and their spouses
2. Patients are referred via group diet referral forms
3. Counselling rooms are available in the respective wards

4. Clinical evaluation, medical history and laboratory results are recorded from case notes

5. Dietary education on basic nutrition is given

6. A group discussion is then encouraged. Patients and their spouses ask questions and clarify doubts

7. In all the diet counselling management, positive approach and genuine concern is given

CARDIAC REHABILITATION PROGRAMME

A team of professionals consisting of the cardiologist, dietician, physiotherapist and nurse is involved in the programme.

1. Patients learn how to assess themselves in terms of recovery, etc.

2. Understanding the possible side effect of medications.

3. Determining when it is safe to resume exercise, job, etc.

4. Coping with emotional issues of heart diseases.

5. Making dietary changes to achieve a balanced, varied and moderation food intake.

Definition of cardiac rehabilitation

The World Health Organisation defines cardiac rehabilitation as the sum of activities required to ensure cardiac patients are in the best possible physical, mental, and social conditions, so that they may by their own efforts regain as normal as possible a place in the community and lead an active and productive life.

Phase 1: the Inpatient Programme

Aim:

* stablize patient
* Exercise efforts
  prevents too much of bed rest
  provide medical surveillance
  prepare patient for more vigorous phase before discharge

* Diet modifications

Emphasis on healthy eating habits - low cholesterol, low fat, blood sugar count, weight reduction, change in lifestyle

Phase 2: the Outpatient Programme

Aim (6 weeks after discharge):

* to further advise patients on medication

* to continue to reverse any reduction in fitness caused by hospitilization and bed rest

* to advise patients to follow a structured, medically directed exercise programme

* to discuss with patients on dietary problems

Phase 3: the Long Term Community Programme

Aim:
* to maintain fitness

* to check medication of patients
* continue to monitor diet modifications

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Nutritional problems in geriatric medicine

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ABSTRACT

Mostly the nutritionally-related health problems of later life are seen to be a mix of the ageing process, poorly defined, and of the cumulation of non-communicable disease (obesity, cardiovascular, diabetes, neoplastic disease, degenerative joint disease, osteoporosis and associated fractures, and, possibly dementia).

But what is regarded as aging may in some measure be attributable to reduced physical activity and to associated reduction in food intake. The problem of reduced food intake may also occur for socio-economic reasons, isolation and depression, physical handicap, the development of eating disorders, and the use of multiple medication. The importance of these several factors affecting food intake has become clearer through several community based studies (IUNS Food Habits in Later Life, SENECA (Survey in Europe on Nutrition and the Elderly, a Concerted Action), Adelaide-Mossgiel). Underappreciated is the problem of immunodeficiency in community and institutionalized elderly, its contribution to infectious disease, neoplastic and cardiovascular disease, and its potential partial reversibility. As antibiotic resistance grows, there will be an even greater imperative to improve host defence by nutritional and other means.

With ageing populations the nutritional prevention and management of their health problems requires better definition!

HOW NUTRITION CONTRIBUTES TO HEALTH STATUS IN THE AGED (1-6)

Nutrition may contribute to health status in later life in several ways as shown in Table 1.

Table 1.

In later life, nutrition contributes to health status via

1. Ageing process by poorly defined mechanisms
2. Development of non-communicable diseases
3. Nutrient and non-nutrient food factor deficiency
4. Immunodeficiency and, potentially,
   - Infectious disease
   - Neoplastic disease

There may be nutrient and non-nutrient food factor deficiency or excess in each case. For example, inadequate intake of a number of factors in food, nutrient and non-nutrient, may contribute to the ageing process, to development of certain non-communicable disease, like macrovascular disease and osteopenia, and immunodeficiency. Again, the development of immunodeficiency may contribute to the ageing process. But it is helpful to endeavour to make the separations of mechanisms since it avoids a sense of inevitability and encourages the discovery of what is reversible, even with ageing. Nutritional contributors to health in later life and the way in which they operate, can also be difficult to unravel since nutritional events early in life may account for health phenomena later in life. Again, intracommunity food-health relationships may not be apparent when they are between communities; and commonalities in the conferrence of nutrition on health between communities may not be in evidence when the prima facie food cultural diversity of communities is impressive. An example of the latter is the observation that communities of elderly people very culturally diverse, from Scandinavia to Japan to the Mediterranean, have comparable longevity, and also eat fish on a regular basis, so that a fish intake-longevity relationship may transcend the apparent food cultural diversity (7).

Another deceptive aspect of looking at food-health relationships is that they are often couched in nutrient terms only, when other physico-chemical properties of food and non-nutrient factors in food of biological importance may be equally important in the ageing process, in protection against macrovascular disease or in immunomodulation (8,9).

NUTRITIONALLY RELATED NON-COMMUNICABLE DISEASE IN THE AGED

This dominates the thinking of disease in the aged (Table 2).

Table 2. Nutritionally related non-communicable disease in the aged

1. Obesity
2. Cardiovascular
3. Diabetes
4. Neoplastic
5. Degenerative joint disease
6. Osteoporosis and fractures

(1) Obesity in the aged

The potential health outcomes of being overfat, or in particular, abdominally obese, in later life are serious (Table 3). The problem is that, for survivors to later life, prospective studies show little adverse impact on total mortality (10). Weight change, and especially weight loss are of greater concern (11-16).

Table 3. Obesity in the aged

Health outcomes
1. Diabetes
2. Neoplastic disease
3. Cardiovascular disease
4. Mechanical problems (mobility, self-care)
Mortality
More to do with weight change than degree of obesity (10)

Clinical efforts to perturb weight in the aged should proceed cautiously and by methods which allow for other aspects of health, and promote general health (Table 4).

Table 4. Obesity in the aged management considerations

1. How mobile
2. Insuring adequate nutrient intake
3. Reducing risks by means other than weight reduction
4. Preserving lean mass

Such methods are likely to be those which encourage modest and regular physical activity and the consumption of a nutritious diet.

(2) Diabetes in the aged

The extent to which the advent of diabetes, albeit increasingly prevalent with advancing years, influences life expectancy once aged (say after 70 years) is unclear. Hence the emphasis needs to be on minimising morbidity with relatively risk free therapies (Table 5) (17).

Table 5. Diabetes in the aged

Major Considerations
1. Avoidance of hyper osmotic status
2. Effects on vision
3. Effects on renal function
4. Contribution to macrovascular disease
5. Contribution to neuropathy
Management Risks
1. Adequacy of food intake
2. Side effects of oral hypoglycaemic agents
3. Over-insulinisation with increasing fatness

(3) Cardiovascular disease in the aged

The forms of macrovascular disease which affect the cerebrovasculature and coronary vasculature are of increasing importance with age - and are accompanied by disease in other vascular beds, the periphery, mesenteric and renal. The disease is progressive and focal and, therefore, ought to be amenable to prevention and intervention at any

age (7) (Table 6).

Table 6. Cardiovascular disease in the aged

1. Risk Factor (RF) management by nutrition means preferred to pharmacotherapeutic wherever possible
2. Greater benefit of RF modification in secondary prevention (ie identified high risk individuals)
3. Atherosclerosis, thrombotic events, vascular hyper-reactivity, remain modifiable by nutritional means at all ages
4. Nutritional pathways to morbid and lethal C-V events operate additional to those which are vascular eg. myocardial electrical stability and substrate metabolism

The value of a nutritional approach is that it can take account of several pathways for the expression of macrovascular disease (Table 6) with an emphasis on the broader health needs of elderly people as met by:

- food variety, especially of plant food
- low saturated and trans fatty acid intake
- regular fish intake (say 2-3 meals/week)
- low sodium intake (50-100 mmol/day)
- modest alcohol intake (0-2 standard drinks/day, less in women than men)

(4) Neoplastic disease

The prevention of neoplastic disease by nutritional means must be distinguished from nutritional support of those with cancer (Table 7). The relative potential benefits of food intake in prevention apply to each of breast, colorectal, prostate, ovarian and pancreatic cancer (18).

Table 7. Neoplastic disease in the aged

1. Nutritional prevention
2. Nutritional support

The increase in prevalence of nutritionally-related immunodeficiency with age (19) is likely to contribute to the development of neoplastic disease (see below).

Non-nutrients in food like salicylate may be preventive in gastroenterological cancers (20,21)

(5) Degenerative joint disease in the aged

Much disability amongst the aged is attributable to the arthritides (3,6). Osteoarthritis (in relation to obesity) (Table 8), gouty arthritis (alcohol intake, obesity) and the inflammatory process in rheumatoid arthritis (through increased omega-3 fatty acid intake) may be amenable to nutritional modification.

Table 8. Nutritional considerations in arthritides in the aged

1. Degenerative disease may be contributed to by obesity for weight-bearing joints; and management improved by reduction in joint load (22).
2. Gouty arthritis may reflect hyperuricaemia of obesity and/or alcohol excess.
3. Inflammatory arthritides (eg. Rheumatoid/respond to omega-3 fatty acids).
4. Reduces ability to exercise and therefore energy requirements, with greater emphasis on need for nutrient dense foods.

(6) Osteoporosis and fractures

Both men and women become increasingly osteopenic with age, with women suffering the added impact of oestrogen deficiency at the menopause. Fracture risk increases as a result, especially in the vertebral column, hip and wrist, accounting for much costly morbidity (Table 9).

Table 9. Osteoporosis and fractures

1. Osteoporosis continues to be a risk factor for fracture into advanced age.
2. A number of nutritional factors can influence bone density - nutrients and no n-nutrients in food (eg. calcium, phosphates, boron, copper, ascorbic acid, vitamin D, vitamin K, caffeine, phytoestrogens, alcohol)
3. Simple nutritional measures can reduce risk of fracture in later life eg. fish liver oil by 1 year (23)

Simple nutritional measures may reduce osteopenia and fracture rates. In this respect the non-nutrient components of food, like phytoestrogens, are becoming of greater interest (21,24,25).

Meunier and colleagues have shown that 20 ug of Vitamin D3 from fish liver oil will reduce fracture by 1 year in later life (23). To some extent this may be by effects on muscle strength and risk of fall in the presence of secondary hyperparathyroidism (26).

NUTRITION AND IMMUNE FUNCTION IN THE AGED (19,27)

The immune functions impaired with age may be several (Table 10).

Table 10.

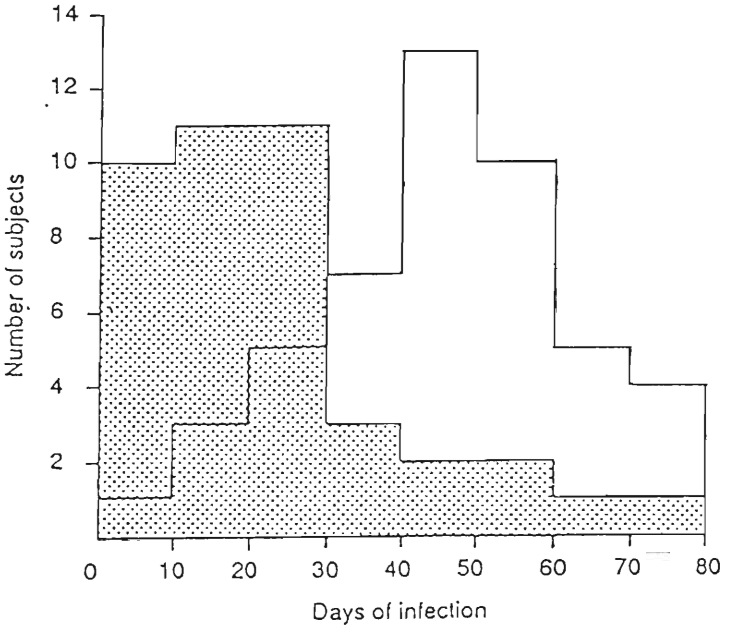
Major variables affected are:

- Innate immunity
  - *Soluble*
    - complement
    - acute phase reactants
  - *Cellular*
    - Phagocytes (neutrophils, macrophages)
    - Natural killer (NK) cell
  - *Physical*
    - mucosal
- Adaptive immunity
  - Cellular mediated immunity
  - T lymphocytes
  - Humoral immunity
  - antibody

Some of these have been shown to partly reversible with nutrient supplementation (19) (Figure 1). Additionally, the risk of infectious

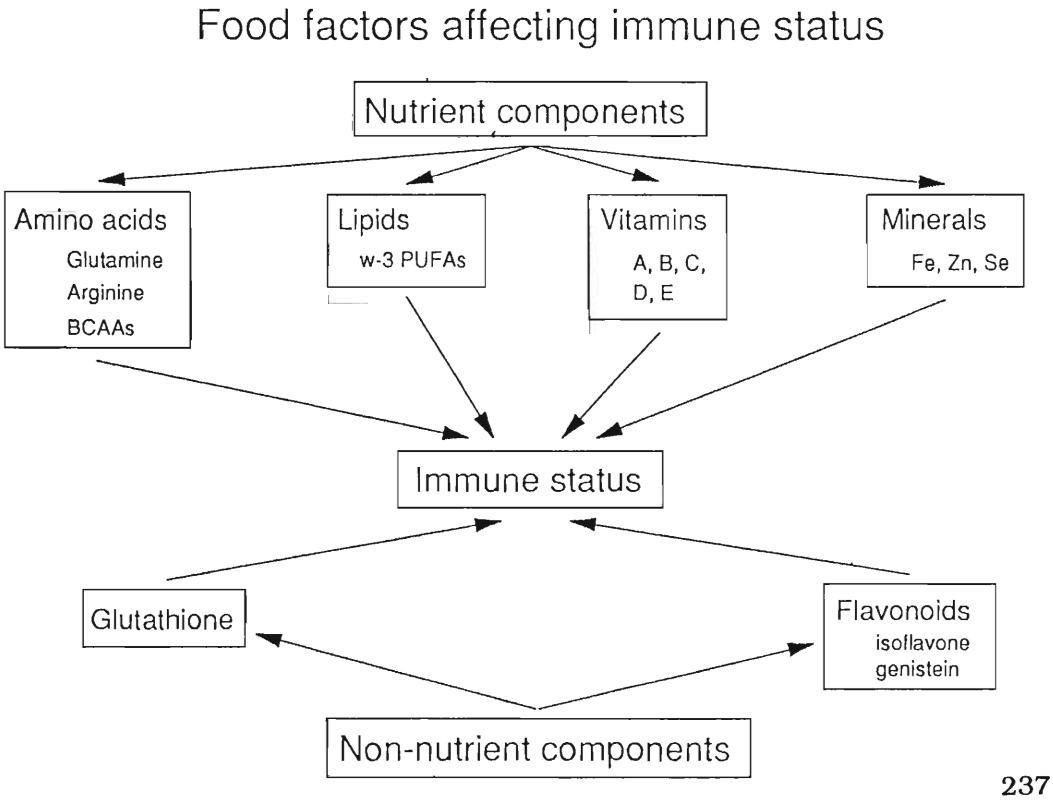
disease can be reduced (28). It is increasingly evident that non-nutrient factors in food like flavonoids (29), carotenoids, may modulate immune responses in useful ways (Figure 2).

Figure 1.



Distribution of infection-related morbidity in placebo (open) and supplemented (shaded) groups.

Figure 2.



As antibiotic resistance grows, there will be an even greater imperative to improve host defence by nutritional and other means.

COMMUNITY BASED STUDIES OF FOOD INTAKE AND HEALTH IN THE AGED

The major sets of cross-cultural community based studies of food intake and health in the aged are the Survey in Europe on Nutrition in the Elderly, a Concerted Action (SENECA), the IUNS "Food Habits in Later Life" project (Table 11), and the Adelaide (Australia) and Mossgiel (New Zealand) studies of Caroline Horwath and colleagues (30-33).

Table 11. Principle findings of the IUNS "Food Habits in Later Life" project

- Social activity, food variety and well-being go together
- Physical activity allows the ingestion of more food with less body fatness
- A diversity of food cultures can be associated with similar levels of health
- Both high BMI (> 30) and low BMI (< 18.5) may be relatively well tolerated by some elderly people (33)

VALUE OF PHYSICAL ACTIVITY IN THE AGED

Of all of the preventive and management strategies for nutritional and general health in the aged, modest, available and regular physical activity (like walking) must be one of the most attractive. There are several values of physical activity in the aged (12):

1. Mood and well-being
2. Higher plane of energy nutrition and food component throughput
3. Control of adiposity
4. Preservation of lean mass
5. Strength
6. Bone density maintenance
7. Decreased non-communicable disease
8. Decreased communicable disease (?)
9. Social and environmental contact

CLINICAL GERIATRIC NUTRITION

The application of nutrition to geriatric medicine requires an appreciation of the relevant clinical and nutritional epidemiology, the underlying sciences and the appropriate diagnostic and management skills, including those of nutrition assessment and counselling. The nutrition problems in this age group are significant and prospects for health improvement considerable.

REFERENCES

1. Horwitz A, MacFadyen DM, Munro H, Scrimshaw NS, Steen B & Williams TF. *Nutrition in the elderly.* Oxford University Press, New York, 1989.

2. Prinsley DM & Sandstead HH. *Nutrition and Aging.* Alan R Liss Inc, New York, 1990.

3. Wahlqvist ML & Flint-Richter DM. Vitamins. In: *Nutrition in*

the elderly, eds Horwitz A, MacFadyen DM, Munro H, Scrimshaw NS, Steen B & Williams TF, Oxford University Press, New York, 1989.

4. Wahlqvist ML. Vitamins, Nutrition and Ageing. In: *Nutrition and Aging*, eds Prinsley DM, Sandstead HH, Alan R. Liss Inc, New York, 1990.

5. Wahlqvist ML & Lukito W. Nutrition in the elderly. In: *Update in Geriatric Medicine Part 1*. Excerpta Medica (Aust) Pty Ltd, 1993.

6. Weissmann G. Aspirin. Scientific American, January 1991, pp 58-64.

7. Wahlqvist ML. Lipids, Cardiovascular Disease and the Elderly. In *Proceedings of the 3rd Annual ASEAN Lipid Forum: Current Issues*, Melbourne 27-28 March 1993. Excerpta Medica (Aust), 1993; pp 41-46.

8. Wahlqvist ML. Non-nutrients in foods, implications for the food industry. *Food Australia* 1992; 44(12):558-560.

9. Wahlqvist ML. Non-nutrients in foods: a changing nutrition-health paradigm. In: *Proceedings of Australasian Clinical Nutrition Society Meeting*, August 1993, Dunedin, New Zealand.

10. Steen B, Landin I & Mellstrom D. Nutrition and health in the eighth decade of life. In: *Proceedings of IUNS 15th Congress of Nutrition*, Smith-Gordon & Co Ltd, London, 1994.

11. Andres R, Muller DC & Sorkin JD. Long-term effects of change in body weight on all cause mortality: a review. In: Methods for Voluntary Weight Loss and Control. National Institutes of Health Technology Asssment Conference. *Annals of Internal Medicine* 1993; 119(7 pt 2):737-743.

12. Blair SN. Evidence for success of exercise in weight loss and control. In: Methods for Voluntary Weight Loss and Control. National Institutes of Health Technology Assesment conference. *Annals of Internal Medicine* 1993; 119(7 pt 2):702-706.

13. Blair SN, Shaten J, Brownell K, Collins G & Lissner L. Body weight change, all-cause mortality, and cause specific mortality in the multiple risk factor intervention trial. In: Methods for Voluntary Weight Loss and Control. National Institutes of Health Technology Assesment Conference. *Annals of Internal Medicine* 119 1993; (7 pt 2):749-757.

14. Danford D & Fletcher SW. Introduction. In: Methods for Voluntary Weight Loss and Control. National Institutes of Health Technology Assesment Conference. *Annals of Internal Medicine* 1993; 119(7 pt 2):642.

15. Higgins M, D'Agostino R, Kannel W & Cobb J. Benefits and adverse effects of weight loss: observations from the Framingham study. In: Methods for Voluntary Weight

Loss and Control. National Institutes of Health Technology Assesment Conference. *Annals of Internal Medicine* 1993; 119(7 pt 2):758-763.

16. Pamuk ER, Williamson DF, Serdula MK, Madans J & Byers TE. Weight loss and subsequent death in a Cohort of US adults. In: Methods for Voluntary Weight Loss and Control. National Institutes of Health Technology Assesment Conference. *Annals of Internal Medicine* 1993; 119(7 pt 2):744-748.

17. Wahlqvist ML & O'Brien R. Nutrition and Diabetes. *Asia Pacific Journal of Clinical Nutrition* 1993; 2(4).

18. Warne RW & Prinsley DM. A manual of geriatric care. Williams and Wilkins & Associates Pty Ltd, NSW, Australia, 1988.

19. Lukito W, Boyce NW & Chandra RK. Nutrition on immunity. In: *Medical Practice of preventive nutrition*, eds Wahlqvist ML & Vobecky JS, Smith-Gordon & Co Ltd, London, 1994.

20. Thun MJ, Namboodiri MM, Calle EE, Flanders WD & Heath CW. Aspirin use and risk of fatal cancer. *Cancer Research* 1993; 53:1322-1327.

21. Wilcox G, Wahlqvist ML, Burger HG & Medley G. Oestrogenic effects of plant-derived foods in postmenopausal women. *British Medical Journal* 1990; 301:905-906.

22. Pi-Sunyer FX. Medical Hazards of Obesity. In: Methods for Voluntary Weight Loss and Control. National Institutes of Health Technology Assesment Conference. *Annals of Internal Medicine* 1993; 119(7 pt 2):655-660.

23. Chapuy MC, Arlot ME, Duboeuf F, Brun J, Crouzet B, Arnaud S, Delmas PD & Meunier PJ. Vitamin D3 and calcium to prevent hip fractures in the elderly women. *N Engl J Med* 1992; 327(23):1637-1642.

24. Love RR, Mazess RB, Barden HS, Epstein S, Newcomb PA, Jordan C, Carbone PP & DeMets DL. Effects of tamoxifen on bone mineral density in postmenopausal women with breast cancer. *The New England Journal of Medicine* 1992; 326:852-856.

25. Love RR, Wiebe DA, Newcomb PA, Cameron L, Leventhal H, Jordan VC, Feyzi J & DeMets DL. Effects of tamoxifen on cardiovascular risk factors in postmenopausal women. *Ann Intern Med* 1991; 115(11)860-864.

26. Freaney R, McBrinn Y & McKenna MJ. Secondary hyperparathyroidism in elderly people:combined effect of renal insufficiency and vitamin D deficiency. *Am J Clin Nut* 1993; 58:187-91.

27. Bender DA. *Introduction to nutrition and metabolism.* UCL Press Ltd, London, 1993.

28. Chandra RK. Effect of vitamin and trace-element supple-

mentation on immune responses and infection in elderly subjects. *Lancet* 1992; 340(8828):1124-7.

29. Middleton E Jr & Kandaswami C. Effects of flavonoids on immune and inflammatory cell functions. *Biochem Pharmacol* 1992; 43(6):1167-79.

30. de Groot LCPG, van Staveren WA & Hautvast JGAJ. EURONUT-SENECA: Nutrition and the elderly in Europe. *European Journal of Clinical Nutrition* 1991; 45 (supplement 3).

31. Horwath CC. *A random population study of the dietary habits of elderly people.* PhD thesis. Dept of Community Medicine, Adelaide University, South Australia, 1987.

32. Horwath CC, Campbell AJ & Busby W. Dietary survey of an elderly New Zealand population. *Nutrition Research* 1992; 12:441-453.

33. Wahlqvist ML, Davies L, Hsu-Hage BB-H, Kouris-Blazos A, Scrimshaw NS, Steen B & van Staveren WS (eds). Food habits in later life: cross-cultural approaches. United Nations University Press, 1994 (in press).

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Long chain polyunsaturated fatty acids in chronic cholestatic liver disease: importance of EFA supplementation including DHA to the patients with biliary atresia

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ABSTRACT

Docosahexaenoic acid (DHA) is believed to be one of the very important long chain polyunsaturated fatty acids (PUFA), particularly in terms of neurofunction in infants. In chronic cholestatic disease, especially extrahepatic biliary atresia (EBA), disturbance of bile excretion often persists even after radical operation, and impairment of intestinal fat absorption causes PUFA deficiency in some patients. Our previous studies indicated that PUFA deficiency may be reversed when PUFA (mainly linoleic acid) are given along with orally administered artificial bile (2 mmol/l of taurocholate) or UDCA (15 mg/kg) (J Pediatr Gastroenterol Nutr 1990; 10:298-32; J Pediatr Surgery, 1994; 29:425-428). In this paper, I will report results of our new study conducted to investigate DHA and other PUFA levels in plasma and red blood cell (RBC) phospholipids of 10 patients with postoperative EBA who had been managed with current approach to supplementation of PUFA (10% Intralipid^{R}, containing 50% linoleic acid and 9% alpha-linolenic acid). The percentages of DHA in both plasma and RBC phospholipids of 5 patients in the jaundiced group were significantly lower in comparison to the normal control group. Five patients in the jaundice-free group had significantly lower levels of DHA and higher levels of linoleic acid in both plasma and RBC in comparison to the normal control group. This study shows that postoperative EBA patients become deficient in DHA even when supplemented with fat emulsions which contains DHA's precursor, alpha-linolenic acid. This demonstrates a deficiency in long chain PUFA desaturase activity in these patients. Therefore, it is recommended that all EBA patients should have small amounts of DHA added to their lipid supplementation.

INTRODUCTION

Docosahexaenoic acid (DHA) is believed to be one of the very important long chain poly-unsaturated fatty acids (PUFA), particularly in terms of neurofunction in infants. In chronic cholestatic disease, especially extrahepatic biliary atresia (EBA), disturbance of bile excretion often persists even after radical operation, and impairment of intestinal fat absorption causes PUFA deficiency in some patients (1). Our previous studies indicated that PUFA deficiency may be reversed when PUFA (mainly linoleic acid) are given along with orally administered artificial bile (2 mmol/l of taurocholate) or UDCA (15 mg/kg) (2,3).

This paper reports result of our new study conducted to investigate DHA and other PUFA levels in plasma and red blood cell (RBC) phospholipids of 10 patients with postoperative EBA.

PATIENTS AND METHODS

Patients

Ten patients were enrolled in the study and divided into two groups according to the serum total bilirubin levels: i.e. the jaundiced group (levels more than 1.0 mg/dl) and the jaundice-free group (levels below 1.0 mg/dl). The jaundiced group consisted of 5 cases, aged 8 months to 16 months (median: 11.8 months) and the jaundice-free group consisted of 5 cases, aged 9 months to 17 months (median: 13.4 months) (Table 1). The patients had been taking solid food from around 6 months of age, one to three times daily depending on the stage of weaning and whether or not they were ingesting 400-500 ml of so-called follow up formula daily. They also were supplemented with 1 ml (1.1 kcal)/kg of 10% Intralipid (containing 50% linoleic acid and 9% alpha-linolenic acid- Ohtuka, Japan), which is widely used in

Table 1. Subjects' features

Group & Case	Sex	Age at Study	Serum Total Bilirubin (mg/dl)
Jaundiced			
1	F	13mo	1.9
2	F	10mo	3.5
3	M	8mo	11.3
4	F	12mo	5.4
5	F	16mo	4.7
		(median : 11.8mo)	(5.3 ± 3.1)
Jaundice-Free			
1	F	9mo	0.7
2	F	14mo	0.8
3	M	11mo	0.5
4	M	17mo	0.9
5	F	16mo	0.7
		(median : 13.4mo)	(0.7 ± 0.1)

total parenteral nutrition as a source of EFA. This supplementation was given enterally because the emulsified fat has a fine particle size (a mean of below 0.3 mm) and has been found to be well absorbed by EBA patients.

Patients were also routinely given UDCA (Tokyo, Tanabe, Japan), 15 mg/kg per day, and Taurine (Taisho, Japan), 100 mg/kg per day, both orally in three divided doses. This was done because UDCA therapy has been proven to be effective in improving fat absorption in EBA patients (3). The normal controls selected were 3 infants and 3 toddlers ranging 8 to 18 months in age (median 12.4 months).

Blood Samples

Fasting blood samples were collected in heparinized tubes and centrifuged to separate the RBCs and plasma.

Analysis

The fatty acid of DHA and other PUFA levels in plasma and red blood cell membrane phospholipids were quantified by gas chromatography.

All data are expressed as means ± SD. Values between the three groups were compared using the unpaired Student's t test. A value of $p<0.05$ was considered statistically significant.

RESULTS

The fatty acid composition of plasma and RBC phospholipids is given for both the experimental and control groups in Tables 2 and 3 respectively.

Table 2. Plasma Phospholipid Fatty Acid Composition

Fatty Acid	Biliary Atresia Patients		Controls	Statistics (p value)	
	Jaundiced	Jaundice-Free		between controls vs. Jaundiced	Jaundice-free
n-6 series					
18:2	16.9 ± 6.0	25.6 ± 5.2	16.9 ± 1.1	NS	< 0.05[b]
18:3	0.3 ± 0.1	0.1 ± 0.4	0.8 ± 0.5	NS	NS
20:2	0.5 ± 0.2	0.4 ± 0.5	0.2 ± 1.0	NS	NS
20:3	0.5 ± 0.7	2.6 ± 0.5	2.7 ± 0.5	< 0.01[a]	NS
20:4	8.2 ± 2.2	7.6 ± 3.2	9.4 ± 1.1	NS	NS
22:4	0.4 ± 0.1	0.2 ± 0.2	0.4 ± 0.2	NS	NS
n-3 series					
18:3	0.2 ± 0.6	0.2 ± 0.6	0.2 ± 0.4	NS	NS
20:5	0.5 ± 0.3	1.0 ± 0.6	2.9 ± 3.2	NS	NS
22:5	0.7 ± 0.4	0.9 ± 0.3	1.3 ± 0.4	< 0.05[a]	NS
22:6	3.8 ± 1.6	5.4 ± 2.4	9.0 ± 1.9	< 0.01[a]	< 0.05[a]

Values are expressed as g/100g (means ±SD)
[a] the value was lower than that of controls
[b] the value was greater than that of controls.
NS = not significant

Table 3. Phospholipid Fatty Acid Composition

Fatty Acid	Biliary Atresia Patients		Controls	Statistics (p value)	
	Jaundiced	Jaundice-Free		between controls vs. Jaundiced	Jaundice-free
n-6 series					
18:2	10.4 ± 2.8	13.2 ± 2.5	11.1 ± 1.7	NS	< 0.01[b]
18:3	0.2 ± 0.4	0.9 ± 0.1	0.2 ± 0.2	NS	NS
20:2	0.4 ± 0.9	0.4 ± 0.9	0.3 ± 0.7	NS	NS
20:3	2.5 ± 0.7	1.9 ± 0.3	1.6 ± 0.5	NS	NS
20:4	15.3 ± 2.4	15.5 ± 2.6	15.6 ± 1.2	NS	NS
22:4	2.8 ± 0.5	2.6 ± 1.2	2.1 ± 0.4	< 0.01[b]	NS
n-3 series					
18:3	0.2 ± 0.1	0.1 ± 0.3	0.6 ± 1.0	NS	NS
20:5	0.5 ± 0.3	1.2 ± 0.8	1.3 ± 0.4	NS	NS
22:5	1.9 ± 0.5	2.4 ± 0.5	2.1 ± 0.5	NS	NS
22:6	5.9 ± 1.2	6.8 ± 2.1	9.1 ± 1.6	< 0.01[a]	< 0.05[a]

Values are expressed as g/100g (means ±SD)
[a] the value was lower than that of controls
[b] the value was greater than that of controls.
NS = not significant

1. Plasma phospholipids

(a) Jaundiced group. A significant decrease in the percentage of 20:3 n-6, 22:5 n-3 and DHA in the plasma phospholipids was found in the experimental group.

(b) Jaundice-free group. Patients in this group had significantly lower levels of DHA and higher levels of linoleic acids in comparison to the control group. No significant differences in the percentages of other fatty acids analyzed were consistently found between controls and either experimental group.

2. RBC phospholipids

(a) Jaundiced group. The percentage of DHA in the RBC phospholipids of patients in this group was significantly lower but that of 22:4 n-6 was significantly higher in comparison to controls.

(b) Jaundice-free group. Patients in this group had significantly lower levels of DHA and higher levels of linoleic acid in comparison to controls. No significant differences in the percentages of the remaining fatty acids analyzed were found consistently between controls and either the jaundiced or jaundice-free groups.

DISCUSSION

It is well known that EFA deficiency readily develops in EBA patients who have had a Kasai operation, when the surgery fails to establish sufficient bile flow from the liver to the intestine (1). Our previous studies, however, indicated that EFA deficiency may be reversed when EFA (mainly linoleic acid) are given along with orally administered artificial bile (2 mmol/l of taurocholate) or UDCA (1,2). Recently, our institute has routinely given UDCA and/or oral fat emulsions (Intralipid usually given intravenously) on a daily

basis to prevent EFA deficiency in postoperative EBA patients. The results of this study demonstrate that linoleic acid and arachidonic acid (20:4 n-6) contents in phospholipids of both plasma and RBC membranes are not significantly lower than those of controls, even in jaundiced patients. The authors believe this can be attributed to the treatment regimen described above. It is also striking that the DHA level is low in both plasma and RBC membrane phospholipids of patints in both the jaundiced and jaundice-free groups while simultaneously the level of linoleic acid is markedly elevated in plasma and RBC membrane phospholipids of patients in the jaundice-free group. A likely explanation for this is that they are consuming a supplement which contains a large amount (50%) of linoleic acid and a relatively small amount (9%) of alpha-linolenic acid.

DHA is derived ultimately from alpha-linolenic acid after a series of desaturations ($\triangle 6$, $\triangle 5$, $\triangle 4$ desaturation) and elongations. We evidence that the desaturases act on the n-3 fatty acids preferentially to n-6 fatty acids. However, excess linoleic acid may inhibit the desaturation of n-3 fatty acids (4). Thus, even the provision of substantial amounts of alpha-linolenic acid does not promote DHA synthesis (5) and study results in infants indicate that dietary DHA is more important than alpha-linolenic acid in determining membrane DHA levels (6).

In contrast, linoleic acid increases supraphysiologic levels in RBC membrane phospholipids, the liver and brain of infants receiving i.v. lipids (7). Furthermore, it has been confirmed that DHA deficiency leads to increased accumulation of n-6 series fatty acids (8). The mean ages of the jaundiced and jaundice-free groups in this study were 11.8 and 13.4 months respectively. By that age one should expect that the saturation and elongation enzymes should have developed to such a point that metabolism would proceed smoothly. This study, however, indicates that the activity of these enzymes is low in postoperative EBA patients who have varying degrees of liver dysfunction. However, bile secretion capacity relative to fat absorption is substantial in unjaundiced patients and can even result in increased accumulation of linoleic acid in the RBC membrane if excessive supplementation of the fatty acid occurs. This presents some problems in the nutritional management of post-operative EBA patients who have low stores of DHA, particularly in early infancy, when levels of most brain lipids rapidly increase.

To our knowledge, no one has previously investigated n-3 fatty acid status, particularly DHA, in postoperative EBA patients, and little attention has been paid to the neurofunctional abnormalities mentioned above. Clearly a great many questions remain to be answered about the role of membrane DHA levels. However, the authors feel that current evidence supports a decision to prevent DHA deficiency or correct it as soon as possible.

Accordingly, the authors recommend and conclude the following:

1. Excessive linoleic acid intake should be avoided lest it inhibit alpha-linolenic acid metabolism.

2. All postsurgical EBA patients should be monitored closely neurofunctionally with an eye to early detection of any EFA deficiency syndrome.

3. All EBA patients should have small amounts of DHA added to their lipid supplementation.

REFERENCES

1. Yamashiro Y, Shimizu T, Morioka A, Miyano T, Suruga K & Hayasawa H. Essential fatty acid deficiency and its management in survivors of biliary atresia. In *Proceedings of the 4th International Symposium on Biliary atresia. Tokyo, Professional Postgraduate Services*, 1987, pp 234-238.

2. Shimizu T, Yamashiro Y, Yabuta K, Miyano T & Hayasawa H. Prostaglandin and fatty acid metabolism in patients with extrahepatic biliary atresia. *J Pediatr Gastroenterol Nutr* 1990; 10:298-302

3. Yamashiro Y, Ohtsuka Y, Shimizu T, Nittono H, Urao M, Miyano T, Kawakami S & Hayasawa H. Effects of ursodeoxycholic acid treatment on essential fatty acid deficiency in patients with biliary atresia. *J Pediatr Surg* 1994; 29:425-428.

4. Rahm JJ & Holman RT. Effect of linoleic acid upon the metabolism of linolenic acid. *J Nutr* 1959; 84:15-19.

5. Innis SM. Effect of total parenteral nutrition with linoleic acid-rich emulsions on tissue n6 and n-3 fatty acids in the rat. *Lipids* 1986; 21:132-138.

6. Carlson SE, Rhodes PG, Rao Vs & Goldgar DE. Effects of fish oil supplementation on the n-3 fatty acid content of red blood cell membranes in preterm infants. *Pediatr Res* 1987; 21:507-510.

7. Martinez M & Ballabriga A. Effects of parenteral nutrition with high doses of linolte on the developing human liver and brain. *Lipid* 1987; 22:133-138.

8. Carlson SE, Carver JD & House SG. High fat diets varying in ratios of polyunsaturated to saturated fatty acid and linoleic to linolenic acid: A comparison of rat neural and rat cell membrane phospholipids. *J Nutr* 1986; 116:718-726.

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A double blind study of milk tolerance in inflammatory bowel disease, in relation to lactose malabsorption

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ABSTRACT

Twenty-two adults with inflammatory bowel disease, all but one originating from northern Italy, underwent an oral lactose tolerance test and, 18 of them, a double blind trial with increasing quantities (125, 250, 500, 1000 ml) of four types of milk with regular or low lactose and fat content. They were questioned on their milk drinking habits and gave a sample of venous blood to determine total Ig E, milk-protein-specific and egg-protein-specific Ig E. Results were compared with those previously obtained by the same methods in healthy adults from northern Italy. Similar frequencies of lactose malabsorption and of positive reactions to milk protein were found in subjects with inflammatory bowel disease and in healthy subjects; although the former habitually drink less milk than the latter, tolerance to milk proved similar in the two groups. The most important determinant of milk intolerance proved to be lactose. Lactose-reduced whole fat milk is recommended for lactose malabsorbers with inflammatory bowel disease, as it was tolerated best.

INTRODUCTION

Primary hypolactasia is a genetically determined condition found in most adult mammals, including man. Intestinal lactase becomes greatly reduced at a variable age, after weaning. For lack of intestinal lactase, dietary lactose is not split into glucose and galactose, it is not absorbed, and symptoms of lactose intolerance appear after eating milk or milk products. These symptoms include osmotic diarrhea, abdominal pain, bloating and flatulence.

The frequency of lactose malabsorption varies greatly in different human populations, the

main reason being that for some people, like nomadic pastoralists, milk and milk products have been essential sources of water and other nutrients for a very long time, and this led to a better survival and reproduction of individuals who were able to absorb lactose also as adults.

The study of lactose malabsorption and intolerance is of particular interest in subjects affected by inflammatory bowel disease, as their diet is already limited by intolerance to several foods, varying from one subject to another.

Several studies have been conducted on lactose malabsorption in ulcerative colitis and Crohn's disease (1-11). Most of these found that the frequency of lactose malabsorption was not significantly different in subjects with inflammatory bowel disease (IBD) compared to non-affected controls (3, 4, 7, 8, 11). Other studies have produced conflicting results (2, 12). This lack of agreement, however, may be due to differences in the ethnic origin of cases and controls, which makes the two groups not comparable when studying the prevalence of lactose malabsorption. Moreover, reduced lactase activity has been found in the acute stages of ulcerative colitis and Crohn's disease (2, 8, 9, 10). Temporary hypolactasia caused by active disease can contribute to increase the number of lactose malabsorbers among subjects with IBD.

These findings suggest that for studying the prevalence of lactose malabsorption in patients with IBD and comparing it with the prevalence in healthy controls, care must be taken to ensure that the two groups have the same ethnic origin and that the affected subjects are in a phase of clinical remission of the disease.

The tolerance to milk of subjects with IBD has been studied by several authors with conflicting results (1, 2, 4, 7, 13, 14, 15, 16, 17, 18, 19). Symptoms of intolerance were not always related to lactose malabsorption, nor was there a consistent finding of positive antibody reactions to milk protein to explain why some subjects don't tolerate milk.

Given the existing controversy on the frequency of lactose malabsorption in IBD and on the role played by lactose malabsorption and allergy to milk protein in causing intolerance to milk, we carried out a study with the following objectives:

1. To assess the prevalence of lactose malabsorption and lactose intolerance in subjects with inflammatory bowel disease, compared to healthy subjects, in Northern Italy;

2. To assess the tolerance to 4 types of milk of lactose malabsorbers and absorbers, affected by inflammatory bowel disease, compared to that of healthy subjects;

3. To assess the role of allergy to milk protein in causing intolerance to milk, in subjects with and without inflammatory bowel disease.

SUBJECTS AND METHODS

Subjects

The subjects who took part in this study were 11 patients affected by ulcerative colitis and 11 affected by Crohn's disease of the colon. They were all in a phase of clinical remission.

The area of origin of the participants was defined as northern Italy on the basis of the place of birth of at least three of the proband's grandparents, a definition which eliminates cases or recent internal migration. According to this definition, 21 of the 22 participants originate from the province of Parma and neighbouring provinces.

The definition of the subjects' area of origin is important because the prevalence of lactose malabsorption varies according to ethnic and geographical origin.

Lactose tolerance test and milk drinking questionnaire

The 22 subjects mentioned above underwent a standard oral lactose tolerance test (LTT), according to a method we had used previously in a similar study on healthy subjects (20).

Following the most commonly used criterion for the diagnosis of lactose malabsorption, subjects were classsified as lactose malabsorbers (LMs) if maximum increase in blood glucose concentration above their fasting value was less than 20 mg/dl, and lactose absorbers (LAs) if this was equal to or greater than 20 mg/dl.

The appearance and the intensity of the four most common symptoms of lactose intolerance were investigated at the end of the LTT and 24 hours later by the physician in charge of the study, according to a previously tested methodology (22, 23, 20). A standard method of scoring was used for the intensity of diarrhea, while the intensity of the other three symptoms was recorded as absent (=0), mild (=1), moderate (=2) or severe (=3), on the basis of the proband's judgement. The total score obtained, by adding the four symptom scores, can range from 0 - 12.

Before undergoing the LTT probands answered a questionnaire, previously used also in our study on healthy subjects (20), regarding their milk drinking habits.

Milk Tolerance Tests

Eighteen of the 22 probands who underwent the LTT agreed to undergo double blind tests with four types of cow's milk containing different amounts of lactose and fat, to establish if one or some of these are better tolerated than others. Ten of these subjects were affected by Crohn's disease of the colon, and 8 by ulcerative colitis.

The four types of milk, in a long-life preparation, were given to probands to take home together with questionnaires to be filled in daily, indicating if they experienced diarrhea, abdominal pain, bloating or flatulence, during the 24 hours following the intake of milk, and if so, whether each of the symptoms was mild, moderate or severe in intensity, according to the same method adopted for the LTT.

Probands were asked to avoid consuming other milk and milk products during the trial period, and to note on the questionnaire - if they could not avoid them - the kind and quantity of these foods consumed. Each type of milk had to be consumed for four consecutive days, in increasing quantities, from 125 ml to 1 litre per day, over the four days period.

Tests of allergy to milk protein

Twenty-one of the 22 subjects with IBD and 21 controls free from gastrointestinal diseases, who had already undergone the LTT, accepted to also give a sample of venous blood, to determine Ig E levels, as Ig E - mediated allergy to milk protein could influence milk tolerance as well. Total Ig E, milk-protein-specific Ig E and egg-protein-specific Ig E were measured, the last one to compare the frequency of hypersensitivity to milk protein with the response to another common food allergen.

The healthy probands needed as "controls" for the allergy tests were chosen from a group of 89 healthy adults originating from northern Italy who participated in the previously-mentioned study (20), matching them with the IBD subjects by LM/LA state, and by age group. The results of the LTTs and the answers to the milk drinking questionnaire of the subjects affected by IBD were compared with those of all the 89 healthy adults (20). The results of milk tolerance tests were compared with those reported by 71 of the 89 healthy adults, who also underwent double blind tests with the four types of milk (21).

RESULTS

The main results of the study are the following.

Frequency of lactose malabsorption among subjects affected by the two intestinal diseases compared to healthy subjects

73% of subjects with ulcerative colitis and 55% of those with Crohn's disease of the colon were LMs. This difference is not statistically significant ($p > 0.50$). The frequency of lactose malabsorption in these two groups of subjects is also not significantly different from that found in 89 healthy adults from northern Italy (52%) (20).

This finding confirms that the frequency of hypolactasia is not greater in subjects with IBD, when they are studied during a non-active phase of the disease, and compared with subjects of the same ethnic and geographical origin.

Symptom response to the LTT in subjects with IBD compared to healthy subjects

After the LTT, LMs with IBD reported intestinal symptoms more frequently than LAs with IBD (93% versus 50% of cases, p close to 5%).

These results are similar to those obtained in our previous study on healthy adults from northern Italy, in which 85% of LMs and 37% of LAs reported symptoms after the LTT.

The mean total score for symptoms after the LTT was higher in LMs affected by IBD than in

healthy LMs. This finding is consistent with a greater sensitivity of subjects with IBD to intestinal challenges of different kinds.

Response to the milk drinking questionnaire

No significant differences were found between lactose malabsorbers and absorbers in the answers provided to the milk drinking questionnaire, as was found previously in healthy subjects.

Significant differences were found only when comparing IBD and healthy subjects independently of LM/LA state. More healthy subjects drank milk regularly than subjects with IBD (91% vs 41%, $p < 0.001$). This is in spite of the fact that symptoms after drinking milk were not reported more frequently by subjects with IBD than by healthy subjects.

Milk drinking was interrupted in adulthood more often by subjects with IBD than by healthy subjects (84% vs 32%, $p < 0.01$).

It is important to note that 70% of IBD cases stopped drinking milk not because of symptoms of intolerance, but because they were advised to do so by their physician, or because they thought it may help to reduce intestinal symptoms.

Results of tests of allergy to protein

The frequency of high milk-protein-specific Ig E values was not significantly different between IBD and healthy subjects ($p = 0.60$). Similar results were found for high egg-protein-specific Ig E values and high total Ig E values.

Allergy to milk protein therefore appears not to have influenced the milk tolerance or the ability to drink milk of either IBD or healthy subjects.

Results of milk tolerance tests

A total of 249 milk tolerance tests were carried out by 18 subjects: 12 were LMs and 6 were LAs. Milk was not taken in 39 cases, corresponding to 14% of the total number of tests planned.

The main results are the following.

1. LMs suffered intestinal symptoms more often than LAs (as occurred in healthy subjects).

2. IBD subjects who are lactose malabsorbers tolerated low-lactose milk better than the full-lactose types.

3. If the fat content of milk affected symptoms, it was in the sense of increasing the tolerance to milk of LMs.

   Although these results only approach the level of statistical significance, they suggest that milk fat may increase the tolerance to lactose of IBD subjects who are lactose malabsorbers. The mechanisms of this could be that milk fat, by decreasing the rate of gastric emptying, may reduce the rate of lactose transit in the intestine and therefore reduce the effects of the lactose challenge.

4. As daily milk intake increased, so did the incidence of intestinal symptoms.

   This was found both in LMs and in LAs affected by IBD, but the statistical significance of the finding was greater for LMs.

   The type of milk which caused more symptoms at the higher doses was normal-lactose/skim milk, while the one which caused less symptoms was the low-lactose/whole fat type.

5. With regards to the taste of milk, fat appears to be more important than lactose. The types of milk preferred were: regular-lactose/whole fat milk, followed by low-lactose/whole fat. Last came low-lactose skim milk and regular-lactose skim milk.

CONCLUSIONS

The main points of interest can be summarised as follows.

1. The habit of drinking milk regularly was twice more frequent in the healthy subjects than in the IBD ones, independently of LM/LA state. This seems mostly due to the fact that subjects affected by IBD stopped drinking milk after the onset of the intestinal disease, not because they had symptoms after drinking it or because they didn't like it, but because they thought, or they had been told, that milk would have an adverse effect on them.

   From the point of view of clinical practice we would like to stress the usefulness of diagnosing lactose malabsorption in subjects with IBD because of its association with intolerance to milk, particularly at the higher doses (500 and 1000 ml/day). Lactose malabsorp-tion is found in 50% of the population of northern Italy and even more frequently in many other parts of the world.

   In subjects with IBD and diagnosed lactose malabsorption, low lactose whole fat milk is recommended, as it tends to be better tolerated. Milk drinking should not be discouraged in IBD patients, unless intolerance to milk can be demonstrated, because their chances of suffering intestinal symptoms due to milk, in this study, are similar to those of healthy subjects, at least when the disease is inactive. If they are LMs, they should be encouraged to drink low-lactose milk.

2. Our findings are in agreement with most previous studies as regards the lack of a significant difference in frequency of lactose malabsorption in patients with IBD - examined when the disease is inactive - compared to healthy subjects. A different ethnic composition of the two groups of healthy and affected subjects, or the activity of the disease, are likely to be responsible for the difference in frequency of lactose malabsorption found by some authors.

3. With regards to the role played by milk allergy in determining intolerance to milk, our results agree with those of the authors

who found no positive correlation between the two.

The reason why high titres of antibodies to milk protein have been found more often in patients with ulcerative colitis than in healthy subjects in some studies is not clear. There may be an association of IBD with a predisposition to allergies in certain ethnic groups: the origin of the subjects studied must therefore always be taken into account. Environmental factors that contribute in generating allergies, such as early weaning from the breast, should also be considered (24).

REFERENCES

1. Binder HJ, Gryboski JD, Thayer WR & Spiro HM. Intolerance to milk in ulcerative colitis. A preliminary report. *Am J Dig Dis* 1966; 2:858-864.

2. Cady AB, Rhodes JB, Littman A & Crane RK. Significance of lactase deficit in ulcerative colitis. *J Lab & Clin Med* 1967; 70:279-286.

3. Chalfin D & Holt PR. Lactase deficiency in ulcerative colitis, regional enteritis and viral hepatitis. *Am J Dig Dis* 1967; 12:81-87.

4. Newcomer AD & Mc Gill DB. Incidence of lactase deficiency in ulcerative colitis. *Gastroenterology* 1967; 53:890-893.

5. Littman A, Cady AB & Rhodes J. Lactase and other disaccharidase deficiencies in a hospital population. *Israel J Med Sci* 1968; 4:110-116.

6. Gudmand-Hoyer E, Dahlqvist A & Jarnum S. Specific small intestinal lactase deficiency in adults. *Scand J Gastroent* 1969; 4:377-386.

7. Gudmand-Hoyer E & Jarnum S. Incidence and clinical significance of lactose malabsorption in ulcerative colitis and Crohn's disease. *Gut* 1970; 11:338-343.

8. Pena AS & Truelove SC. Hypolactasia and ulcerative colitis. *Gastroenterology* 1973; 64:400-404.

9. Gudmand-Hoyer E, Binder V & Soltoft J. The small intestinal disaccharidase activity in ulcerative colitis. *Scand J Gastroent* 1975; 10:209-212.

10. Dunne WT, Cooke WT & Allan RN. Enzymatic and morphometric evidence for Crohn's disease as a diffuse lesion of the gastrointestinal tract. *Gut* 1977; 18:290-294.

11. Kirshner BS, De Favaro MV & Jensen W. Lactose malabsorption in children and adolescents with inflammatory bowel disease. *Gastroenterology* 1981; 81:829-832.

12. Simoons FJ. The geographic hypothesis and lactose malabsorption. A weighing of the evidence. *Dig Dis* 1978; 23:963-980.

13. Wright R & Truelove SC. A controlled therapeutic trial of various diets in ulcerative

colitis. *Brit Med J* 1965; 2:138-141.

14. Wright R & Truelove SC. Circulating antibodies to dietary proteins in ulcerative colitis. *Brit Med J* 1965; 2:142-144.

15. Taylor KB & Truelove SC. Circulating antibodies to milk protein in ulcerative colitis. *Brit Med J* 1961; 2:924-929.

16. Gray J. Antibodies to cow's milk in ulcerative colitis. *Brit Med J* 1961; 2:1265-1266.

17. Davidson L. Milk proteins in ulcerative colitis. *Brit Med J* 1961; 2:1358.

18. Dudek B, Spiro HM & Thayer WR. A study of ulcerative colitis and circulating antibodies to milk proteins. *Gastroenterology* 1965; 49:544-547.

19. Sewell P, Cooke W, Cox E & Meynell M. Milk intolerance in gastrointestinal disorders. *Lancet* 1963; 2:1132-1135.

20. Cavalli-Sforza LT, Strata A, Barone A & Cucurachi L. Primary adult lactose malabsorption in Italy: regional differences in prevalence and relationship to lactose intolerance and milk consumption. *Am J Clin Nutr* 1987; 45:748-754.

21. Cavalli-Sforza LT & Strata A. Double blind study on the tolerance of four types of milk in lactose malabsorbers and absorbers. *Hum Nutr: Clin Nutr* 1987; 41C:19-30.

22. Stephenson LS &, Latham MC. Lactose intolerance and milk consumption: the relation of tolerance to symptoms. *Am J Clin Nutr* 1974; 27:296-303.

23. Veale Jones D, Latham MC, Kosikowski FV & Woodward G. Symptom response to lactose-reduced milk in lactose-intolerant adults. *Am J Clin Nutr* 1976; 29:633-638.

24. Acheson ED & Truelove SC. Early weaning from the breast in the etiology of ulcerative colitis. *Brit Med J* 1961; 2:929-933.

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Effect of daily calcium supplementation on the incidence of hypertensive disorders of pregnancy: a study protocol

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ABSTRACT

Hypertensive disorders of pregnancy encompass a wide spectrum of disorders ranging from asymptomatic elevated blood pressure to life-threatening eclampsia. An observation of the labour room records at the Maternity Hospital, Kuala Lumpur showed that of approximately 2000 deliveries conducted each month, about 5% are associated with varying degrees of severity of this problem.

The consequences of hypertension in pregnancy include multiple antenatal admissions, prolonged post-natal stay in hospital, use of expensive non-teratogenic drugs, repeated laboratory tests, prolonged CTG monitoring and of course increased maternal and foetal morbidity and mortality to name a few.

Some studies done in America, Argentina and Equador suggest a significant decrease in incidence of this problem when 1 or 2 grams of elemental calcium is given from about the twentieth week of pregnancy until delivery.

This paper presents the protocol of a proposed study to be conducted in the Maternity Hospital Kuala Lumpur, to determine if the implementation of calcium supplementation in pregnancy will significantly reduce the incidence of hypertensive disorders of pregnancy.

INTRODUCTION

Hypertensive disorders of pregnancy include a wide spectrum of conditions from asymptomatic elevation of blood pressure to life-threatening eclampsia. Its etiology is still an unsolved mystery. The consequences of this condition are many, including the following:

1. Increased maternal and foetal morbidity and mortality;

2. Multiple antenatal admissions are inconvenient to the patient and increases expenses of hospital stay.

3. Prolonged post-natal stay in hospital for the mother as well as the need to use Special Care Nursery (SCN) facilities for some of the newborns.

4. Anti-hypertensive drugs also cause increased expenses as well as the inconvenience of having to take these drugs several times a day.

5. There is a need for additional visits to the antenatal clinic for close monitoring.

6. Additional laboratory tests are required for early detection of complications arising from pregnancy-induced hypertension.

Some studies conducted in America, Ecuador and Argentina suggest that daily supplementation of a pregnant lady with calcium from about the twentieth week of pregnancy until delivery can decrease the incidence of hypertensive disorders of pregnancy to a significant extent. Epidemiological studies have demonstrated an inverse relationship between calcium intake and preeclampsia (1). It has also been shown that calcium supplementation appears less effective in subjects with increased urinary calcium losses. It has been suggested that a dietary calcium intake of at least 2g / day during pregnancy is necessary to maintain a positive calcium balance.

It is interesting to note that calcium supplementation has been reported to lower blood pressure in pregnant and nonpregnant women.

It has also been observed that the largest reduction in blood pressure in pregnant women given calcium supplements was seen in those with low pretreatment serum calcium levels.

An observation of the labour room records at Maternity Hospital Kuala Lumpur over a span of 30 days showed that of the 1989 deliveries, 93 were associated with varying degrees of hypertensive disorders of pregnancy.

OBJECTIVE OF THE STUDY

To determine the effect of daily calcium supplementation on the incidence of hypertensive disorders of pregnancy.

METHODS

1 Study Design

a. Subjects

The subjects taking part in this study are pregnant ladies attending antenatal clinics. A questionnaire will be used to obtain information on past medical, surgical and family history of each subject. Dietary calcium intake will be determined for 250 subjects by the food frequency method. Written informed consent will be obtained from all subjects, giving them the right to withdraw from the study at any time they choose.

Inclusion Criteria

i. Blood pressure of 120/80 mm Hg or less.

ii. Age of not more than 35 years at the beginning of the study.

iii. Duration of gestation of 18 to 22 weeks at the beginning of the study.

iv. Healthy - free of any illness.

v. Planning follow-up and delivery at the Maternity Hospital Kuala Lumpur.

Exclusion Criteria

i. Presence of renal, hepatic, cardiac disorders or glycosuria in the absence of medication.

b. Sampling Frame

This consists of pregnant women attending two large antenatal clinics in Kuala Lumpur as well as those attending the antenatal clinic at the Maternity Hospital Kuala Lumpur. Only women planning to deliver at Maternity Hospital Kuala Lumpur, a hospital that conducts about 2000 deliveries per month, will be chosen for this study. The duration of the study will not exceed 18 months. The sample size as determined by Kelsey L.J.'s method is 900.

c. Selection Criteria

Blood pressure will be recorded at the time of selection of subjects for the study and this recording will be used as the pre-supplementation blood pressure value.

The first subject will be assigned to one of the two groups by drawing lots. Subsequent subjects will be assigned to one of the two groups alternately.

Blood pressure will be recorded again at 24, 28, 30, 32, 34 and 36 weeks of gestation and again immediately after delivery. Readings are to be taken with the subject in a sitting position by a doctor, a staff nurse or a trained midwife.

Those assigned to the treatment group will each receive 2 g of elemental calcium daily until they deliver. The control group subjects will receive identical placebo tablets for the same duration.

d. Laboratory Procedures

5 ml of venous blood will be collected from each of the subjects before commencement of the supplementation, to be analysed at the Department of Biochemistry of the Institute for Medical Research to study the pre-supplementation levels of serum calcium, serum ionised calcium, serum phosphorus, serum magnesium and serum albumin.

A second 5 ml sample of venous blood will be collected during the antenatal visit at 28 weeks of gestation for analysis of the earlier mentioned parameters to observe any changes, since the beneficial effect of calcium supplementation has been found to be apparent as early as the 28th week of gestation.

A third 5 ml sample of venous blood will be collected and all the earlier tests repeated immediately after subjects deliver at the

Maternity Hospital Kuala Lumpur's labour room.

e. Compliance

Compliance will be determined by pill counts at each visit as subjects will be asked to bring along their pill bottles for each visit.

f. Drop-Outs

Subjects developing gestational hypertension (demarcated by a pressure of 140/90 mm Hg or more), preeclampsia (gestational hypertension with albuminuria and ankle edema) or eclampsia (hyperreflexia with or without convulsions) will receive immediate medical treatment and their participation in the incidence study will end.

2 Data Analysis

The 't' test will be used for analysis of data obtained to determine any differences in the mean systolic and/or diastolic blood pressures of the two groups.

The x^2 (chi square) analysis will be used to compare the proportions in the two samples who develop hypertensive disorders of pregnancy.

REFERENCES

1. Belizan JM, Villar J, Gonzalez L, Campodonico & Bergel E. Calcium supplementation to prevent hypertensive disorders of pregnancy. *N Engl J Med* 1991; 325:1399-405.

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Intractable ulcerative colitis: a case for dietotherapeutic intervention

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ABSTRACT

Ulcerative colitis is a frustrating disorder characterized by persistent loose bloody stools with mucus that defies nearly all pharmacological intervention. A case study is presented from a middle-aged Malay female with intractable ulcerative colitis who had been on steroidal therapy for over 3 years. She sought advice from the author for an alternative route of management via naturopathic or nutritional therapy.

A detailed history-taking on her psychological state, stress levels, occupation, medication etc. suggests dietary intolerance may be one of the aggravating factors. She was put on a semi-fasting programme of fruit & vegetable juices, followed by a low-fibre, low-fat diet, supplemented by low-dose multi-vitamin-mineral capsules to maintain proper nutrition and electrolyte balance. There was little change in her status after a month of dietary adjustment. The programme was reviewed with further advice on a gluten-free & milk-free diet. Further supplementation with yeast-free and milk-free acidophilus capsules and 500 mg herbal medication (Ulmus fulva) were given three times a day to augment the treatment. This was given for another month. A log-book was kept by the patient to monitor her own progress. Significant clinical improvement was observed on this regime at the end of the 65 weeks trial. There was a 60% reduction in the diarrhoeal episodes, with only a little mucus, and no blood.

The case is being followed up at monthly intervals with a view for an independent sigmoidoscopic evaluation by her gastro-enterologist at post-management stage. Dietary manipulation as an aetiological consideration should be the first line of management in ulcerative colitis where drug intervention alone fails.

INTRODUCTION

A number of inflammatory bowel diseases have been associated with ulceration of the colon. Besides bacillary and amoebic dysenteries and tuberculous enterocolitis, non-specific chronic conditions include Crohn's disease which may affect both the large and the small bowels; the other, affecting only the colon, is ulcerative colitis.

The aetiology of ulcerative colitis is largely unknown. Food hypersensitivity and an allergic reaction has been suspected (1,2,3,4). IgG and IgM antibodies to cow's milk protein in particular, were found to be increased in patients with ulcerative colitis (5). The temporary withdrawal of milk and milk products from the diet seems to improve the diarrhoeal attacks in some patients. The deleterious effects of milk in some of these patients may also be from lactose intolerance due to the development of secondary alactasia other than sensitivity to milk proteins. It has also been suggested that a familial tendency may be involved, with increased incidence among relatives of the patient. It is seen in all ages but is more commonly seen between the ages of 20 to 40 years, with female preponderance. Among some of the aetiological considerations, there is some evidence showing the presence of antibodies to certain strains of E. coli, suggesting an abnormal immune response to faecal bacteria.

Evidence in favour of an autoimmune process is the isolation of anticolon antibodies in the serum of some patients with colitis. It has also been found that patients with ulcerative colitis showed emotional and psychological disturbances, the characteristic personality of many of them are often those who are extremely fussy, tidy, meticulous, and emotionally immature individuals. The disease is also characteristic of people who have a hurried and restless life-style.

The tendency of this disease to remit and relapse again irrespective of what treatment is prescribed is notorious. Treatment-wise there is no satisfactory drug for controlling diarrhoea. Codeine phosphate 30-60 mg, 3-6 hourly, may be tried; alternatively, an anticholinergic such as propantheline may be prescribed. Sulphasalazine is of value in reducing the inflammation of the colon and hence the degree of diarrhoea and in reducing the relapse rate, after an acute attack has been controlled by corticosteroid therapy. However this has some disadvantage (6) unless supplemented with folic acid (7). For those who fail to respond to conservative treatment, and for those who relapse frequently, ileostomy and colectomy are usually the second line of management.

CLINICAL FINDINGS AND THERAPY

This is a case study of a Malay female, aged 35 years, married with one child. She is 1.562m (5'1 1/2") tall, and weighs 43.6 kg (96.0 lbs). This is about 20% underweight for her height. She is a medical technologist by occupation, and she leads a hurried, anxious and agitated life-style.

She presented with a history of bloody diarrhoea with mucus for 7 years. She complains of fatigue with progressive weight loss, and lower abdominal discomfort. Her persistent bloody diarrhoea went into remission during her last pregnancy 5 years earlier. Her diarrhoea resumed after the birth of her only child, and there has been no remission since then.

On examination, there was mild tenderness over the lower quadrants of her abdomen. She had tachycardia (100-110 beats/minute) and irregular cardiac rhythm (ectopic beats). She appeared significantly underweight and wasted. She had undergone a series of investigations by gastroenterologists years earlier, including barium enema, sigmoidoscopy, colonoscopy as well as biopsy, to rule out other bowel disorders. Examination suggested she was anaemic, but there were no signs of secondary complications of chronic ulcerative colitis. There was also no evidence of toxic megacolon from the colonic examination done years earlier.

A detailed dietary history was taken over a period of a week, and it was found that her mean protein intake was about 75 gm (150% RDA) per day, with fat contributing to about 30% of the total energy, half of which was derived from carbohydrates. Breakfast usually consisted of milk-based beverages. Lunch was usually taken outside, and comprised mainly of rice, curries, fish, chicken and vegetables. Afternoon teas usually included kuih, cakes or

Table 1. Example of food intake of ulcerative colitis patient

Food intake	Nutrient intake/day				
	wt (g)	protein (g)	fat (g)	CHO (g)	Kcal
Breakfast					
Horlicks	50	2.1	2	6.4	50
Lunch					
Rice	250	5.8	0.3	75	325
Fried fish	90	35.4	15.9	3.2	298
Fried tau-kua	45	7.7	6.8	1.7	99
Apple	150	0.5	0.3	13.7	59
Afternoon tea					
Curry-puff	40	1.9	5.6	17.3	128
Dinner					
Rice	250	5.8	0.3	85	325
Chicken	60	13.4	11.9	2.2	170
Fried sawi	50	1.1	10.4	1.8	105
Sambal ikan bilis	10	2.8	2.1	0.4	32
Total	955	76.5	55.6	196.7	1591
% RDA		186.6	–	–	79.6
% of total energy		19.2	31.4	49.4	–

currypuffs. Dinner was taken at home, and it included the usual rice or wheat-based noodles, chicken, fish, vegetables of different varieties, *ikan bilis*, *balacan*, or *sambal*. She had an occasional cup of tea or a *kuih* at night for supper. A typical food intake pattern randomly taken is shown in Table 1.

The patient was advised to go on a semi-fast diet of fruit and vegetable juices for 5 days (physiological fasting). The total volume of the fruit juice was between 0.8 - 1.2 L/day. At the end of the physiological fast (bowel rest), a little well-cooked soft cereals, consisting of porridge with a half-boiled egg was introduced for another 10 days or until improvement was observed. The quantity of food was increased to about 180 gm (6.4 oz) with fish or skin-free chicken added for another 2 weeks. Energy intake was further increased with the introduction of low-fibre bread with jam or honey. Only fruit and vegetable juices or herbal teas were allowed with the scattering of meals into small feeds. In any case, the fat intake was restricted to 20% of the total energy, together with an initial protein limitation to 20 gm daily, and building up gradually to about 40-50 gm per day.

This was derived mainly from skinless chicken, fish, a little soya products and rabbit's meat if possible. The patient was advised to avoid mucosa-irritating foods and drinks such as curries, spicy preparations, tea, coffee and alcohol, and to restrict foods containing high osmotic gradient ingredients such as excessive salt, monosodium glutamate, and sugars which are likely to draw water and exudates from the colon.

She was also counselled about the need to avoid moderate to high-salicylate foods such as apples, apricots, guavas, raisin, alfalfa, carrots, dates, broccoli and green beans, spinach and tomatoes. Foods with high content of sugars and saturated fats, cholesterol, trans-fatty acids and low in vitamins and minerals, likely to block the formation of anti-inflammatory prostaglandin-1, derived from essential fatty acids, were also to be avoided.

Her physician had prescribed codeine phosphate 30-60 mg q.d.s, propantheline 15 mg b.d. and low-dose steroid (prednisolone). When no improvement was observed, all medication was stopped by the time the author saw the patient. It was unfortunate that when she sought dietary advice from her doctor she was told to eat liberally on a normal diet.

In addition to dietary constraints she was also provided with broad-spectrum multivitamin and mineral tablets to be taken 2-3 times daily post-cibum to prevent vitamin and mineral deficiencies during the period of her dietary treatment. Cod-liver oil at a dose of 15ml daily post-cibum was given as a prostaglandin-2 modulator. In addition, evening primrose oil containing 10% gamma-linoleic acid was given at a dosage of 500 mg t.i.d. post cibum. Zinc complex tablets containing 15 mg elemental zinc were also supplemented to her daily diet.

RESULTS & DISCUSSION

The above treatment was given

over a period of 65 weeks. In the pre-treatment stage the diarrhoeal episodes were about 10 times per day. There was also a lot of mucus and some blood, initially. Haemoglobin level was about 8.2 gm/dL, and the fasting blood sugar was 5.5 mmol/L.

Blood urea and serum electrolyte were low. Clinically, the patient felt very weak before starting on the dietetic approach. She remained very weak and lethargic for a month even after initiation of the diet. Improvement was observed when her treatment programme was reviewed. The patient was then put on a gluten-free and a milk-free diet.

She was also provided with Lactobacillus acidophilus capsules, in which each capsule contained more than 3,000 million live Lactobacilli derived from non-dairy sources. These were administered 3 times a day to establish normal gut flora in addition to 500 mg of powdered Ulmus fulva tablets. Ulmus fulva or slippery elm assists by coating and protecting the entire gastroenteric tract with a non-irritating mucilaginous astringent. On the sixth week from the initial treatment, the frequency of diarrhoea was reduced from 10 to 8 times a day. The volume of loose stool was also reduced, and there was much less mucus.

There was also only a little blood. Although the haemoglobin level had not changed much, symptomatically the patient felt much better and less lethargic. She said she was more active than before. As dietary modification was maintained for 8 - 16 weeks, diarrhoeal episodes were further reduced to a third of the original quantity. There was also very little mucus observed. What was more significant was that visible blood (chemical analysis for traces of blood in the stool was not done) was not seen for the first time since 7 years. Her Hb level had also progressively climbed from 8.5 to 9.0, 9.8 and 10.4 gm./dl on the 6th, 8th, 12th and 16th weeks. Fasting blood sugar was also higher towards normal at 6.0 mmol/L. The plasma sodium level on the 12th week was 132 mmol/L and the potassium level was 3.8 mmol/L. Urea and serum electrolytes, including chloride, calcium and PO4, monitored 4 times throughout the dietary treatment, were found to be fairly normal, although slightly on the low side during the pre-treatment stage, and also during the first month of dietary rehabilitation.

From the 30th week onwards till the 65th week, there was progressive decline in the frequency of diarrhoea to just 3-4 times a day, compared to 10 times during the initial stages. Although the presence of mucus persisted throughout the period, the amount was estimated to be very much less, about one-third as much. However, blood in the mucus was visually absent from the 8th week onwards till the end of the trial (65th week). The volume of watery stools also showed marked decline. From the 16th week, the patient also recorded a slow but steady weight gain of 1.3 kg. She felt much more active, and did not complain of being easily tired, although she felt a "little weak" when she was followed up on the 64th week. The results of her response to dietary treatment are given in Table 2.

Table 2. Response to dietary and other treatment in a patient with ulcerative colitis

Profile	Pre-treatment	Weeks of treatment								
		4	6	8	12	16	30	60	64	65
Body weight (kg)	43.6	43.5	43	42.8	43.2	44	44.3	45	45	45.3
No. diarrhoeal episodes/24 hrs	10	10	8	8	6	5	4	4	3	4
Vol. of stool (dl)	35	30	20	10	10	10	5	10	5	5
Mucus	+++	+++	++	++	+	+	+	+	+	+
Blood	++	+	+	–	–	–	–	–	–	–
Hb (g/dL)	8.2	8.6	8.5	9	9.8	10.4	10.5	10.6	10.8	–
FBS (mol/L)	5.5	5.8	5.6	–	–	6	–	6.2	6.6	–
BUSE (mmol/L)	low	low	–	–	fair	–	–	NAD	–	–
Subjective response	very weak	very weak	fair	fair	fair good	good	good	good	weak	fair

Observations recorded during this period suggested that there may be a case for dietary intervention as part of the management of chronic ulcerative colitis. A number of food suspects should be considered and excluded from the diet. These include wheat, shell-fish, spicy foods, eggs, corn, coffee, citrus fruits, cured meat, dairy products, tea, red meat and brinjal. They may be part of food intolerance and food sensitivity to some individuals. The fact that mucus is excreted in ulcerative colitis suggests that the colon may be trying to protect itself with a natural coat of mucus against food irritants. This was part of the reasons for prescribing bowel rest, and maintaining only fluid and electrolyte balance during the initial stages of dietary management. Low dose multi-vitamin and mineral supplementation may be introduced later.

Like medical management with drugs, dietary approach should only be part of the treatment, since ulcerative colitis is more frequent among those who are easily upset or suffer from some form of psychological disturbance. It also appears that those who belong to Type I personality, i.e. leading a hurried and stressful life-style, are more prone to the disorder. This suggests that the disease may be psychosomatic in origin and stress-related.

Multiple approaches like putting the patient on a stress reduction programme, hydrotherapy, such as alternative hot-cold baths, hot fomentations, or relaxation baths may be beneficial, and these may be as important as medical and dietary treatment. Besides Ulmus vulva (slippery elm) given at a dose of 500 mg t.i.d., Hammelis virginian (witch hazel) at a dose of 250 mg t.i.d. as an anti-inflammatory and an astringent may also be considered as an alternative treatment modality.

Remission has also been noted among pregnant and nursing mothers when breast milk is being formed. Breast milk is known to be rich in gamma-linolenic acid from which beneficial anti-inflammatory prostaglandine-1 are derived. The presence of

gammalinolenic acid in the body may have a protective action against ulcerative colitis, as much as a diet rich in essential fatty acids, eg. linoleic acid. Administration of gammalinolenic acid directly, such as derived from evening primrose oil, may also be considered as another approach in intractable cases.

It is important that patients with ulcerative colitis not responding to standard drug treatment should be considered for dietary intervention (8,9). If the disease remains uncontrolled after a period of 10 years, a number of complications may arise for which surgical measures may be indicated.

CONCLUSION

Prognosis may be good if ulcerative colitis is managed by proper and adequate dietotherapeutic intervention, along with proper medical care, stress management, and other modalities of treatment, but it is usually poor if treatment was solely dependant on anti-diarrhoeal medication, or anti-inflammatory corticosteroidal and immunosuppressive therapies.

Nevertheless, the results given here were drawn from only one case study, and this means they may not be duplicated precisely in larger studies. Proper placebo-controlled double-blind studies on a larger number of subjects would be needed for meaningful statistical analysis. Notwithstanding the difficulty of collecting sufficient cases, this case findings may serve as a pointer on what to expect from a larger scale study.

REFERENCES

1. Siegel J. Inflammatory bowel disease: another possible facet of the allergic diathesis. *Ann Allergy* 1981; 41:92-94.

2. Mee AS & Jewell DP. Reaginic hypersensitivity in inflammatory bowel disease, In: Pepys J, Edwards AM, eds. The Mast Cell. London, Pitman, 1979; pp. 638.

3. Rider JA & Moeller HC. Food hypersensitivity in ulcerative colitis: Further experience with an intramucosal test. *Am J Gastroenterol* 1962; 37:497.

4. Rowe AH & Rowe A Jr. Chronic ulcerative colitis: Atopic allergy in its etiology. *Am J Gastroenterol* 1960; 34:49.

5. Jewell DP & Truelove SC. Circulating antibodies to cow's milk in ulcerative colitis. *Gut* 1972; 13:796.

6. Halsted CH, Gandhi G & Tamura T. Sulfasalazine inhibits the absorption of folates in ulcerative colitis. *N Engl J Med* 1981; 305(25):1513-17.

7. Carruthers LB. Chronic diarrhoea treated with folic acid. *Lancet* 1946; 1:849.

8. Wright R & Truelove SC. A controlled therapeutic trial of various diets in ulcerative colitis. *Brit Med J* 1965; 2:138.

9. Wright R & Truelove SC. A controlled therapeutic trial of various diets in ulcerative colitis. *Am J Dig Dis* 1966; 11:858.

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Relationship between dietary intake and pregnancy-induced hypertension among Malay pregnant mothers

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ABSTRACT

The purpose of the study is to compare the intake of calcium, protein, and calorie between pregnant mothers with pregnancy-induced hypertension (PIH) and the normotensive pregnant women. A total of 68 women aged between 19 to 35 who were attending antenatal clinics were selected from the attendance records for the study. They consisted of two groups: the first group comprised 33 pregnant women with PIH (blood pressure: 130/80 to 140/100mm Hg) and the other group consisted of 35 normotensive pregnant mothers (blood pressure: 90/60 to 120/80mm Hg) as control. The results showed that 39.3% of the pregnant women with PIH and 17.1% of the women in the control group obtained low scores in nutrition knowledge respectively. Analysis by t-test showed that nutrition scores of the PIH group were significantly lower than the normotensive control ($t=2.54$, $p< 0.05$). The analysis of calcium, protein and calorie from 24-hour dietary recall and food frequency data showed that the mean intake of calcium for the normotensive group was 1112.1 mg while the mean intake for the PIH group was 994.4 mg and it was significantly different ($p<0.05$). The intake of protein between the two groups was significantly different ($p<0.05$) where the mean intake of protein for the PIH group was 48.4 g and that for the normotensive group was 44.2 g. There was no difference in the intake of calorie between the two groups. The findings suggest a higher dietary intake of calcium may be preventive against the development of pregnancy-induced hypertension in pregnant women.

INTRODUCTION

Hypertensive disorders adversely affect a small percentage of pregnant women. Without proper dietary management and rest in severe cases, it can lead to maternal and fetal death. Hypertensive disorders include the presence of chronic hypertension prior to pregnancy and the development of specific conditions referred to as pregnancy induced hypertension (PIH). PIH refers to the progression of symptoms from pre-eclampsia to eclampsia. The term pregnancy-induced hypertension (PIH) has been adopted by the American College of Obstetricians and Gynecologist to replace the terms pre-eclampsia and eclampsia (1).

PIH usually develops after the twentieth week of pregnancy and is characterized by hypertension with protein urea and/or edema. The etiology of PIH is poorly understood but it is felt to involve interactions between nutritional intake and physiologic adjustments associated with pregnancy. Some epidemiolgic studies on PIH had shown a relationship between calcium intake and blood pressure.

Several studies conducted in South America have shown an inverse relationship between maternal calcium intake and the occurrence of PIH. An observation made in Guatemala showed that poor pregnant women with an overall low nutrient intake but relatively-high calcium intake, had a low incidence of PIH (2). Some clinical studies (3,4) also found an inverse relationship between calcium intake and blood pressure. Calcium supplementation has been reported to decrease blood pressure in normotensive (5) and hypertensive humans (6,7). In another case control clinical trial (7) on 30 normotensive and 20 hypertensive pregnant women, supplementation with 1 gm of calcium per day showed a significant ($P<0.05$) inverse relationship between intake and blood pressure in the hypertensive group.

Studies on PIH in pregnant women in Malaysia are few and incidence of PIH among pregnant women in Malaysia is also not known. Those pregnant women diagnosed with pre-eclampsia are usually given bed rest till the blood pressure returned to normal. A low salt diet or no salt added in the diet is usually recommended.

OBJECTIVES

This study attempts to look at the general profile of the pregnant women diagnosed with having pregnancy-induced hypertension and to determine the relationship between dietary intake of calcium with pregnancy-induced hypertension. The study also determines the difference in calcium intake between the hypertensive group and the normotensive control.

METHODOLOGY

A total of 68 women between 19 to 35 years of age, without symptoms of previous chronic diseases were enrolled for the study. The respondents were volunteers who were in the 15 to 35 weeks of gestation. Thirty-three of the women made up the first

group with PIH (blood pressure 138/80 - 140/100) and the other thirty-five were the normotensive control with blood pressure between 90/60 - 120/80. The subjects were systematically sampled from the attendance records. The required data were recorded from prenatal record cards, and through interviews by using pre-prepared questionnaire. The questionnaire was divided into 4 sections which included background information of the respondents, their health condition, nutritional knowledge and dietary intake. The data was analysed by using SPSS-X.

RESULTS AND DISCUSSIONS

The background information of the respondents are presented in Table 1. A higher percentage (42.4%) of the pregnant women diagnosed as having PIH were between 19 to 25 years old. In studies conducted in United States and South America, women younger than 20 years old were found to have symptoms of PIH.

Table 1. Background informations of the respondents n = 68

Control (%)	Case (%) n = 33	Control (%) n = 35
19–25	42.4	40.0
26–30	24.2	25.7
31–35	33.3	34.2
Education		
Primary school	18	28.6
Lower secondary school	39.4	40.0
Higher secondary school	30.3	20
Pre-U	12.1	11.4
Employment		
Professional	3.0	14.3
Clerical	12.1	5.7
Skill worker	21.2	8.6
Semi skill worker	21.2	25.7
Housewife	42.4	54.3
Income		
< RM350	21.2	14.3
RM350 – RM650	3.3	34.3
RM651 – RM950	18.2	25.7
RM951 – RM1250	18.2	25.7
> RM1250	9.1	11.4

In this study the women in both groups were mostly from the lower educational status and lower income group. Generally those from the higher income groups seek treatment at private hospitals for their illnesses. Therefore it is not surprising that the percentage of women from the lower income group in this study was higher.

The pregnancy-induced hypertensive women were asked on how their condition was detected (Table 2). About 82% knew that they had PIH through regular antenatal check up while 12.1% knew through routine clinical examinations. Thus an early antenatal check up is important to the success of the pregnancy as well as the health of the mother.

From Table 3, it can be seen that a higher percentage of women with PIH were primigravidae and pre-eclampsia as a primary disorder is more likely to occur in

Table 2. Detention of hypertension n = 33

Type of Examination	Percentage
Antenatal	81.8
Routine clinical examination	12.1
Headache, short of breath	6.10
Total	100%

Table 3. Parity of the Respondents n = 68

Parity	Case (%) n = 33	Control (%) n = 35
0	42.4	42.8
1 – 3	30.3	28.6
4 – 6	27.3	28.6
Total	100	100

Table 4. Percentage of respondents having hypertension according to trimester (n = 33)

Trimester	Percent
1st trimester (4 – 12 weeks)	18.1
2nd trimester (13 – 24 weeks)	60.6
3rd trimester (25 – 36 weeks)	21.2
Total	100

primigravidae than in multigravidae and usually they are in the younger age group. The results also showed that as the number of pregnancies increased the incidence decreased. The percentage of pregnant women that showed symptoms of PIH were highest in the second trimester as compared to the other two semesters (Table 4). Earlier epidemiological studies carried out on PIH found that the condition usually occurs after 20 weeks of pregnancy.

In Table 5, the mean difference in the score of nutrition knowledge between the case and the control groups are shown. The results

Table 5. Mean difference in the score of nutrition knowledge between cases and control

Group	Mean score	t value	p value
Case	10 ± 135	2.54	0.013
Control	15 ± 2.08		

showed that most of the PIH women obtained low scores in nutrition knowledge. T-test analysis showed that nutrition scores were significantly different between the case and the normotensive group ($t = 2.54$, $p<0.05$).

With regards to daily food intake (Table 6 and Table 7), it was found that a higher percentage of the mothers with PIH ate less calcium-rich foods such as fresh fish (75.8%) and anchovies (36.4%) compared to normotensive controls with 85.7% and 54.2% respectively. Data in Table 7 shows that the case group consistently ate less calcium-rich vegetables compared to the control group, with the exception of cabbage.

Daily nutrient intake was obtained by using 24-hour recall method. The nutritional contents were determined by using the 'Nutrient Composition of Malaysian Foods' (8). Group means of nutrient intake were compared by T-test analysis (Table 8).

The results showed that calcium and protein intake were significantly different between the two groups ($p<0.05$). Intake of foods high in calories such as rice can act as a vehicle for other high density nutrient foods. Those who

Table 6. Frequency of intake of food with high calcium

Type of Food		Frequency					
		Once a day	4–6 times/ week	1–3 times/ week	2–3 times/ week	Once a month	Never
Anchovy	Case	36.4	3.0	15.2	15.2	30.3	0
	Control	54.2	11.4	25.7	5.7	0	2.8
Eggs	Case	27.3	33.3	27.3	9.1	0	3.0
	Control	37.1	22.8	31.4	0	0	8.0
Shell fish	Case	3.0	0	15.2	9.1	57.6	15.2
(Kerang)	Control	2.8	5.7	17.1	5.7	22.8	50.0
Fresh	Case	75.8	12.1	0	0	3.0	3.0
fish	Control	85.7	8.6	2.8	0	0	2.8

Table 7. Frequency of intake of vegetable

Types of vegetables		Percent					
		Every-day	4–6 times/ week	1–3 times/ week	2–3 times/ week	Once a month	Never
Spinach	Case	9.1	18.2	45.5	18.2	0	9.1
	Control	22.8	11.4	40.0	2.8	5.7	17.1
Sawi	Case	51.4	12.1	12.1	6.1	3.0	0
	Control	66.7	11.4	14.3	8.6	2.8	11.4
Kangkung	Case	42.4	3.0	9.1	6.1	27.3	9.1
	Control	80.0	0	14.2	8.6	2.8	11.4
Cabbage	Case	6.1	6.1	27.3	6.1	12.1	42.4
	Control	2.8	–	20.0	8.6	17.1	51.4
Tomato	Case	6.1	24.2	39.4	6.1	12.1	12.1
	Control	14.3	14.3	37.1	–	22.8	5.7
Cekur	Case	–	–	9.1	6.1	15.2	69.7
Manis	Control	–	–	11.4	8.5	5.7	68.6

Table 8. Mean difference of nutrient intake between case and control (24 hours recall)

	Calories	Protein	Calcium
Case n = 33	2199	44.2 g	994.4 mg
Control n = 35	2272	48.4 g*	112.1 mg*
	t = 1.98	t = 2.98	t = 3.28
	p = 0.052	p = 0.004	p = 0.002

ate less of cereal foods might get less of other nutrients too. This study shows that the respondents in the case group took in less calorie as well as protein and calcium.

CONCLUSION

In conclusion, women with pregnancy-induced hypertension are at risk to adverse pregnancy outcomes as compared with normotensive women and correlates with age, duration of gestation, and parity. For nulliparous women who develops PIH in the middle of pregnancy, the only major modifiable factor that may reduce the severity of the condition is diet. Therefore, a well-programmed diet for pregnant women with or without health conditions will ensure a successful pregnancy from beginning till delivery.

REFERENCES

1. Willis SE. Hypertension in pregnancy. *Am J Nursing* 1982; 82:792.

2. Belizan JM, Villar J. The relationship between calcium intake and edema proteinuria and hypertension - gestosis: an hypothesis. *Am J Clin Nutr* 1980; 33:2202.

3. Mc Carron DA 1982. Low serum concentration of ionized calcium in patients with hypertension. *N Engl J Med* 1982; 307:226-228.

4. Grobee D.E. Hofman A. 1986. Effect of calcium supplementation on diastolic blood pressure in young people with mild hypertension. *Lancet* 1986; 2:703-706.

5. Belizan JM, Villar J, Pineda O, et al. 1983. Reduction of blood pressure with calcium supplementation in young adults. *JAMA* 1983: 249:1161-1165.

6. Mc Carron DA, Morris CD. Blood pressure response to oral calcium in persons with mild to moderate hypertension. *Ann Intern Med* 1985: 103:825-831.

7. Knight KB, Keith RE. Calcium supplementation on normotensive and hypertensive pregnant women. Am J Clin Nutr 1992; 55:891-895.

8. Tee ES, Mohd Ismail N, Mohd Nasir A, Khatijah I. Nutrient Composition of Malaysian Foods. ASEAN Sub-Committee on Protein: Food Habits Research and Development, Kuala Lumpur, 1988.

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The effect of Ramadan fasting with trimester of pregnancy on pregnancy outcomes

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ABSTRACT

A historical cohort study was conducted on 622 pregnant women to study the effect of time of exposure of pregnancy to Ramadan fasting and its association with pregnancy outcomes. Depending on the exposure to Ramadan fasting month of 1985, the women are classified into first trimester, second trimester and third trimester exposed. A comparison group comprised the pregnant women whose pregnancy are outside the Ramadan month. Using analysis of variance, the main findings are that time of exposure to Ramadan fasting is not significantly associated with the weekly weight gain of the pregnant women. However, there is a significant association with infant birth weight among the "first-trimester-exposed" when compared to the "third-trimester exposed". In addition, women who were exposed to Ramadan fasting during the third trimester of gestation, had more premature deliveries compared to women who were not exposed to Ramadan fasting at all, when we combine time of exposure to Ramadan fasting and categories of fasting (number of days fasting) to form a new variable "fasting status". The finding that "fasting status" 9 (29th weeks gestation and fasting 26-30 days in Ramadan) is borderline significantly associated with only the gestational age of the infant at $p = < 0.0574$.

INTRODUCTION

Fasting in Ramadan month is one of the 5 pillars in Islam and is compulsory for adult Muslim men and women. During the fasting time they do not drink or eat or even smoke cigarette from sunshine to sunset, which in an equatorial country like Malaysia, is equivalent to 13 hours without food.

There are more than 138 million women in their reproductive age in Asia, Africa and North America (1). At least one third of them are pregnant at any one time. If they fast, depending on their religiosity, they will be exposed to partial starvation for 13 hours daily for 30 days. No such study has been done except for Prentice in Gambia, Africa (2) and Hanafiah Salleh in 1986 in Malaysia. (3).

In the study by Prentice et al., the sample comprised 22 pregnant African Gambian women who were on supplemental diet. Prentice hypothesised that hypoglycemia, especially during the latter part of pregnancy, may give rise to adverse pregnancy outcome, such as lower than average birth weight of the infant. However, there was no comparison group in that study.

Therefore this study attempts to answer the question of whether the differential exposure to Ramadan (in trimester I, II, or III) has a different effect on the health status of the mother and the fetus.

METHOD

All pregnant women with different gestational period, either the first trimester (0 - 14 wks), second trimester (14 - 27 wks) or third trimester (28 - 40 wks) who came for antenatal care in a rural health unit in Parit Jawa area were included in the sample. This list was obtained from the antenatal record attendances between August 1984 and August 1985. Women whose pregnancy was not exposed to Ramadan (19 May to 20 June 1985), were chosen as the comparison group. Only Muslim women are included in the study.

A retrospective survey was conducted on these samples. To reduce recall bias, the critical event technique was used in questions related to the number of days they had fasted. As fasting is a significant annual event among the Muslim, the recall bias is minimal.

Interobserver and intraobsever agreement were in the range of 70 - 90%. Pregnant women were followed up prospectively for their pregnancy outcomes.

RESULTS

Depending on the exposure to fasting, women were classified into first trimester, second trimester and third trimester exposed to Ramadan month of 1985. There is another group which is not exposed, the comparison group.

When we look at the relationship using analysis of variance (Table 1), the finding is that time of exposure to Ramadan is not associated significantly with pregnancy weight gain. However, there is an association with infant birth weight when first trimester exposure is compared to the reference category (third trimester exposure). In addition, women whose pregnancy was exposed to Ramadan in the third trimester had more premature deliveries compared to women who were not exposed to Ramadan at all.

When we combine time of exposure to Ramadan and categories of fasting to form a new variable "fasting status", the finding is that "fasting status" is significantly associated with only the gestational age of the infant with $p = 0.0574$ (Tables 2, 3 & 4).

Table 1. Effect of time of exposure to Ramadan and pregnancy outcomes by analysis of variance

Time exposed	n	mean wt gain (kg)	p	remarks
0 (comparison)	95	0.33	0.5374	n s
first trimester	170	0.37	0.1057	n s
second trimester	183	0.36	0.1176	n s
third trimester	78	0.31	-	base
		mean birth weight of infant (kg)		
0 (comparison)	112	3.16	0.4291	n s
first trimester	191	3.24	0.0207	sig
second trimester	202	3.12	0.8120	n s
third trimester	103	3.11	-	base
		mean duration of pregnancy (days)		
0 (comparison)	112	268	0.0007	sig
first trimester	191	273	0.1521	n s
second trimester	202	275	0.8187	n s
third trimester	103	275	-	base

Table 2. Combined effect of time of exposure and groups of fasting on weight gain by analysis of variance

status*	n	mean wt gain (kg)	p	remarks
0	112	0.35	0.3493	n s
1	29	0.30	0.8971	n s
2	55	0.39	0.1271	n s
3	71	0.37	0.2414	n s
4	27	0.39	0.1854	n s
5	38	0.34	0.4744	n s
6	107	0.37	0.2156	n s
7	13	0.30	0.9965	n s
8	20	0.23	0.2682	n s
9	40	0.30	0.2682	n s

* 0 = nonexposed (comparison) p; 1=1-14 wks exposed & 1-15 days fast; 2=1-14 wks exposed & 16-25 days fast; 3=1-14 wks exposed & 26-30 days fast; 4=15-28 wks exposed & 1-15 days fast; 5=15-28 wks exposed & 16-25 wks fast; 6=16-28 wks exposed & 26-30 days fast; 7=29+ wks exposed & 1-15 days fast; 8=29+ wks exposed & 16-25 days fast; and 9=29+ wks exposed & 26-30 days fast.

n s = not significant

Table 3. Combined effect of time of exposure to Ramadan and days of fasting on birth weight of infants by anova

status*	n	mean birth weight (kg)	p	remarks
0	130	3.135	0.9346	n s
1	29	3.207	0.6819	n s
2	63	3.188	0.6734	n s
3	80	3.316	0.0519	n s
4	28	3.124	0.7423	n s
5	42	3.135	0.7548	n s
6	120	3.113	0.6327	n s
7	19	3.026	0.3345	n s
8	28	3.116	0.9912	n s
9	49	3.154	-	n s

s = not significant

Table 4. Combined effect of time of exposure to Ramadan and days of fasting and gestational days of the infant using anova

status*	n	mean gestational days	p	remarks
0	130	270	0.0574	sig
2	29	274	0.7549	n s
3	63	275	0.9518	n s
4	80	274	0.1486	n s
5	42	277	0.5230	n s
6	120	274	0.8304	n s
7	19	274	0.5526	n s
8	26	275	0.5614	n s
9	49	277	-	n s

n s = not significant
sig = significant

CONCLUSION

This study found that when third trimester pregnant women fasted in Ramadan their infant birth weight was less by 130-162 g compared to those infants born by first trimester pregnant fasting women. Statistically this difference is significant. But clinically it is only significant if the birth weight of the infant is on the lower side, thus this further lowering effect may make it worse. However, there is a need for caution in the practise of fasting in Ramadan for third trimester pregnant women.

In addition, third trimester pregnant fasting women have infants whose gestational age is 7 day longer compared to infants from the unexposed to Ramadan. This is statistically significant with a p value of 0.05. There is a tendency towards post maturity of infants among third trimester fasting women.

Both these findings suggest that women in the third trimester of pregnancy are not encouraged to fast during Ramadan, especially those having some known pathology like diabetes mellitus, anaemia, malnutrition and the like.

This study also suggests that further study should be done to unravel the physiology of pregnancy during fasting in Ramadan. For example, we need to know if indeed there is a real difference in intake of calories between fasting and non fasting women.

REFERENCES

1. Hoffmann MS (editor). Third world almanac and books of facts, pp 340, World Almanac, New York, 1987.

2. Prentice A, Prentice A, Lamb W, Lunn PB & Austin S. Metabolic consequence of fasting during Ramadan in pregnant and lactating women. *Human Nutr Clin Nutr* 1983; 370-393.

3. Hanafiah MS. Ramadan fasting among pregnant women in Muar District, Malaysia and it is association to health outcomes. *Malaysia J Reprod Health* 1989; 7(1):69-83.

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Serum lipids in chronic progressive renal diseases

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ABSTRACT

Chronic renal diseases are associated with a variety of lipid and lipoprotein abnormalities especially in diabetic nephropathy and nephrotic syndrome. That the highest cause of mortality in CRF patients is due to cardiovascular events and the link between hyperlipidaemia and increased risk of cardiovascular morbidity and mortality has been well established. Recent evidence in animal models has implicated the possible role of serum lipids contributing to progressive renal injury. However, the link between hyper lipidaemia and chronic renal diseases in humans is unclear. A retrospective study was conducted and data will be presented.

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Serum albumin and death risk in patients on continous ambulatory peritoneal dialysis (CAPD)

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Objective — To describe the survival experience of CAPD patients in relation to risk factors adversely affecting survival.

Design — Observational cohort study.

Subjects and setting — Inception cohort comprising 207 patients accepted for CAPD in Hospital Kuala Lumpur between 1984 and 1992.

Main outcome measures — Patient characteristics, diabetic status, blood pressure cardiovascular disorder at starting CAPD, serum albumin, serum triglyceride, serum cholesterol, peritonitis rate, patient survival.

Results — Overall acturial survival of CAPD patients was 70%, 76% and 68% at 1, 2 and 3 years. Cardiovascular events accounted for 61% of deaths. Cox's proportional hazards regression analysis identified the following significant predictors for survival : Serum Albumin less than 30g/L (relative risk (PR 4.6), cardiovascular disorder (RR 3.8) and diabetes mellitus (RR 2.3). Other factors like age, hypertriglyceridaemia, elevated blood pressure and peritionitis rate were not significant. 25% of CAPD patients has serum albumin below 30g/L.

Conclusion — Malnutrition as assessed by serum albumin level was the most important predictor of death in CAPD patients. This has not previously been reported. Unlike the other risk factors, it is potentionally avoidable and correctable.