



The Medical Journal of Malaysia

Editorial Board

Editor:

A.A. Sandosham, LMS, AM, MD,
PhD, FLS, FRES, FZS, FRMS.

Surgeon:

G.A. Sreenivasan, JSD, MBBS,
AM, FRCS, FRACS

Physician:

R.P. Pillay, PSD, SPMK, DPMT,
JMN, PJK, MBBS, AM, FRCP,
FACP, FCCP, FACCP.

Obstetrics:

S. Lourdenadin, LMS, AM, DCH,
FRCPI, FRCOG.

Public Health:

Paul Chen, MBBS, MPH, MSc.

Northern Branch

Representative:

V. Thuraisingham, KMN, PKT,
MBBS, AM, MRCP, FRCPE,
FRCP(Lond.)

Sub-Editor & Southern Branch

Representative:

Lim Kee Jin, DPMJ, KMN, PIS,
MBBS, AM, FRCPE, FRCP.

Malay Section:

Mahmood Merican, MBBS, AM,
FRCS, MCh. Orth. FICS.

Vol XXX No. 3.

March, 1975

CONTENTS

	Page
1) Editorial - The case for a study of coronary disease by V. Thuraisingham.	156
2) Malaria - The end of a cycle? Further clinical and laboratory experiences of malaria in Seremban - during the four years 1970-73 by Donal R.O'Holohan.	157
3) Serum haptoglobin levels and types in normal Malaysians by J. Ganesan, Wong Pui Wang and Lie-Injo Luan Eng.	163
4) Serum Tocopherol (Vitamin E) status of Malaysian by T.K.W. Ng and Y.H. Chong.	169
5) Breastfeeding in a rural area in Malaysia by Teoh Soong Kee.	175
6) Cataract extraction in West Malaysia by Then S.M. and Chandran S.	180
7) Ecological Assessment of the vitamin A status of primary school children in Ulu Trengganu by N. Chandrasekharan.	187
8) The management of residual bile duct calculi by Hussein bin Mohamaed Salleh.	195
9) Problems in the early diagnosis of genital tuberculosis by A. Puraviappan, Ng Keng Hing and Wong Wai Ping.	202
10) Acute myocardial infarction in systemic lupus erythematosus by K.L. Khoo and Pillay R.P.	206
11) Catapres in the management of hypertension by Narinderpal Singh and V. Menon.	209
12) Lorazepam in patients with mixed psychic and somatic symptoms by K. Sundram.	214
13) Salmonella typhi meningitis - A case report and family investigation by. Gooi Hock Chye and Sia Tuan Hong.	219
14) Ablaton - Single intramuscular injection to suppress lactation by K.B. Kuah.	223
15) Accidental vaccinia infection - A case report by K.L. Lam, V.J.L. How and S.K. Lam.	227
16) Lipoma : An unusual case with a brief review of the literature by Yan Kor Lee.	231
17) An infant oesophageal stethoscope by Robert P.C. Liew, Yeo Keat Him and Cheah Ui Jin	234
18) Book Review.	235

THE CASE FOR A STUDY OF CORONARY DISEASE

by *V. Thuraisingham*

There is today in Malaysia an increased awareness and fear of coronary disease. This feeling is not entirely due to the rising incidence and dramatic nature of the disease itself but to the advertising publicity given by the pharmaceutical and food industries as they seek to promote their 'cures' and preventive agents. Our population now living to an older age is being subjected to new ways of life with trends towards westernization, urbanization and industrialization. These changes create new stresses and strains which some claim, predispose to coronary disease on individuals in the Society. The WHO has warned that coronary disease has now reached epidemic proportions in some parts of the world, but, where do we stand?

For a long time, doctors in this country have been diagnosing and treating patients with coronary disease by conservative methods at home or hospital but now coronary care units are very much in vogue. Mobile coronary care ambulances are also being contemplated. In the U.S.A., the approach is even more aggressive. Coronary artery surgery with saphenous venous bypass is very common and infartectomy is considered not too radical! Results attained with all these approaches have in general been good but yet not satisfying and many now wonder whether we are proverbially forgetting the woods in our quest for the trees! Thus renewed attention and interest are being increasingly directed to preventive aspects of coronary disease.

In this country, we have not had the chance to jump on the band wagon of any particular expensive fad in coronary care or treatment, simply because we have sadly not been able to afford the equipment or the manpower! However, as we see and hear the

glamorous progress and claims of results from abroad, there is the temptation to embark on piecemeal isolated efforts to set up such facilities. Though in the interests of research, medical science and progress, we may bemoan our cardiac care facilities, one must first be convinced of the need for such expensive sophisticated forms of patient care in the context of the magnitude of the problem. This, therefore, should motivate us in the profession to make useful and reliable studies on the true incidence, morbidity and mortality of coronary disease in this country.

The diagnosis of coronary disease is primarily based on a good history, electrocardiogram and enzyme studies. All practitioners would have access to the first but, with some effort, an ECG could be easily obtained. The Serum Transaminase and Lactic Dehydrogenase can also be requested. Even simple epidemiological data such as age, sex, ethnic origin, occupation, mode of presentation, association of other diseases eg. Hypertension, Diabetes, Obesity, Smoking Habits etc. could provide useful information in the assessment of this disease in our Community. The College of General Practitioners of Malaysia, which appears to be a robust 'baby' in this country, could perhaps launch a nationwide co-operative study. A Cardiac Society could be formed to co-ordinate all interested bodies to work with the College. The time has come for such organizations to take the initiative in launching properly conducted local surveys and studies without falling back on the Ministry of Health for all data on health matters. The Ministry will not only welcome but probably support all such attempts to collect data which could lead to valuable knowledge regarding disease trends as it affects our own communities.

MALARIA – THE END OF A CYCLE? FURTHER CLINICAL AND LABORATORY
EXPERIENCES OF MALARIA IN SEREMBAN – DURING THE FOUR YEARS 1970–73.

By

Donal R. O Holohan, M.B., F.R.C.P. (Irel.)
P.O. Box 170, Seremban, N.S., West Malaysia.

Introduction:

This is a further, short, factual report of the author's experiences of malaria in a medical practice in the town of Seremban in the State of Negeri Sembilan, Peninsular Malaysia. This report covers the four years period which commenced on 1st January, 1970 and concluded on 31st December, 1973. The years 1970 – 1971 have already been reported elsewhere, O Holohan and Matthews (1972), but are included in order to give a broader perspective and again the figures for the first report have been modified by applying stricter criteria for malaria episodes rather than episodes of parasitaemia. Finally a special study of children aged 2 years and under has been made over the whole four year period.

As in our previous report we are only concerned here with parasitologically proven malaria in patients attending the writer's clinic or discovered on domiciliary visits. Malaria episodes occurring on Rubber and Oil Palm Estates (total population over 20,000 persons) visited by the authors are not included in this report.

The objects of the report are to put on record the number of parasitologically proven cases of malaria in a particular busy practice, in a particular locality over a given period. The practice has not changed in character, either in the number of patients seen year by year or in the ethnic, social, regional, distribution of the patients who attend it. It is

therefore suggested that any changes (in malaria pattern) which have or have not occurred over this four years period can reasonably be assumed to reflect similar changes in similar practices in the immediate neighbourhood.

This is not the report of a widescale survey of a chosen area nor is it a study of a stable population such as is found on a rubber plantation, farming community or a group of kampungs. In such cases the investigators go to the subjects and study them in their own environment – the area where their infection is most likely being obtained and transmitted. Our role is more that of an observation post waiting for the subjects to come our way if, when and as often as they themselves chose to do so. Our subjects will of necessity be a group with diverse backgrounds. Some will have come direct to us either as old patients (who return) or completely new patients who may have been to other practitioners, hospitals or district health centres. Some of the latter group may have already had some antimalarial therapy either after blood examination or on clinical grounds.

Our study therefore has its limitations on purely epidemiological grounds but if our opening remarks on the objects of our report are borne in mind it is believed that this study will stimulate medical practitioners to be more malaria conscious and make more frequent use of the microscope in the diagnosis of febrile illness.

The work of Huehne et al. (1967) emphasises that as most malarial statistics in West Malaysia are derived from hospitals and estates reports (and certain controlled study schemes) the overall incidence of malaria in the true rural areas are grossly underestimated. The findings of Toh and Yeo (1971) in Singapore, which at the time was believed by many to be malaria free, that only 48% of their subjects had been clinically suspected of malaria and in 24% the disease was not even considered a possibility and was only discovered during routine haematological investigations prompted these authors to suggest – “that the degree of diagnostic accuracy can be greatly enhanced through increased awareness of its presence here.”

The timing of this report is opportune as it coincides with the start of Phase One of the Malaria Eradication Programme in the State of Negeri Sembilan.

Materials and Methods:

All patients attending the clinic (including patients attended on domiciliary visits) were closely questioned to elicit a history suggestive of malarial infection and blood slides taken for examination in suspected cases. During the height of the maximum malaria transmission season, all patients who were willing to co-operate had blood examination. From mid-April to mid-July, relatives who accompanied patients were also examined where possible. In cases where the physician felt that malaria was clinically the most likely diagnosis, the blood tests were repeated if initially negative.

Thick films, using Field's quick staining method was the standard procedure – when pressure of work was less heavy, thin films were also examined. Where a second examination was called for to establish the diagnosis both thick and thin films were employed and 200 microscopic fields examined in each.

TABLE I
BLOOD EXAMINATIONS 1970 – 1973

No. of Slides Examined:	27,537
No. of Episodes of Malaria:	6,049 in 5,297 Individuals.
Males:	3251 53.7%
Females:	2798 46.3%

In this report (over the 48 months period commencing 1st January, 1970 and ending 31st December, 1973) we have attempted to be more specific as to the number of episodes. We do not include episodes of malaria parasitaemia in the follow-up period after treatment. Any episodes of parasitaemia of the same species occurring within sixty days is counted as one and the same episode of malaria. Some fresh infection after successful treatment may thus not be counted but it reduces the inclusion of recrudescences (especially *P. vivax*) as separate episodes of malaria. Many of the total number of examinations were repeated tests before the parasite was discovered and also many were follow-up tests after treatment.

TABLE II
INCIDENCE IN ETHNIC GROUP – 4 YEARS

		%
Malay	2780	46.0
Indian	1708	28.2
Chinese	1420	23.5
Others	141	2.3
Total	6049	

As can be seen in Table II, the greatest incidence was among Malay patients – all but a very few of whom came from the rural areas, i.e. kampungs and land development schemes. While some of the Indians came from the town areas, the majority came from rubber or oil palm estates. Many of the Chinese came from Seremban town and its environs, others from rubber estates, small villages or even logging camps in the rural area. When it is appreciated that Indians and others form only 15% of those attending the practice (a constant percentage year by year) the incidence in this community is therefore high. The overall incidence over the four years reflects the yearly incidence very closely.

TABLE III
AGE DISTRIBUTION 1970 – 1973

			%
Children:	2 years and Under	671	11.0
	3 to 5 years	481	8.0
	6 to 12 years	766	12.7
	>12 and Adults	4131	68.3
		6049	=====

While we have only divided our subjects into two age groups, i.e. under 12 years, and over 12 years, we found, as others have, that malaria has a predilection for the young and most of our cases were under 35 years of age.

Our youngest patient was 18 days old – our oldest was 80 years. We had an average of about 10 cases of cerebral malaria per year in children under 12 years – ranging from behaviour disorder (aggression, hostility, mutism and altered mood) to stupor and semi-coma. Hyperpyrexia (highest record temperature 108°F.) was a not infrequent problem and required immediate and persistent therapeutic efforts to lower the temperature as hyperpyrexia itself can be lethal to young children and infants. We have learned to keep patients with us for at least two hours after successfully lowering the hyperpyrexia as a sudden resurgence of pyrexia is not uncommon within half to one hour.

TABLE IV
ALLOCATION OF CASES ACCORDING TO AREA

	1970	1971	1972	1973
	%	%	%	%
Negeri Sembilan Total:	1434	1553	1447	1163
N.S. Outside Seremban:)	761	963	1027	923
Seremban Town Board:)	673	590	420	240
Selangor:	68	107	61	48
Other States:	70	52	24	22
Total: >	1572	1712	1532	1233

It can be seen here that there are some differences in the 1970 – 1971 figures from our previous report. This is due (see above) to a more ruthless elimination of possible recrudescences of malaria and including some previous ‘cases’ as single ‘episodes’. Most cases naturally come from Negeri Sembilan. As the rate in the Seremban Town Board area fell the rest of Negeri Sembilan showed a proportionately higher malaria rate. However this higher level in the rural area was more apparent than real – there was in fact little change over the years in the rural rate. Selangor is mentioned specifically as we share a long common border (ranging 16 – 20 miles from Seremban Town) and most of the “other States” were in fact cases from the timber areas of Pahang who came to us through Kuala Pilah.

FIGURE 1
ALL MALARIA EPISODES IN N.S.
&
SEREMBAN TOWN BOARD AREA

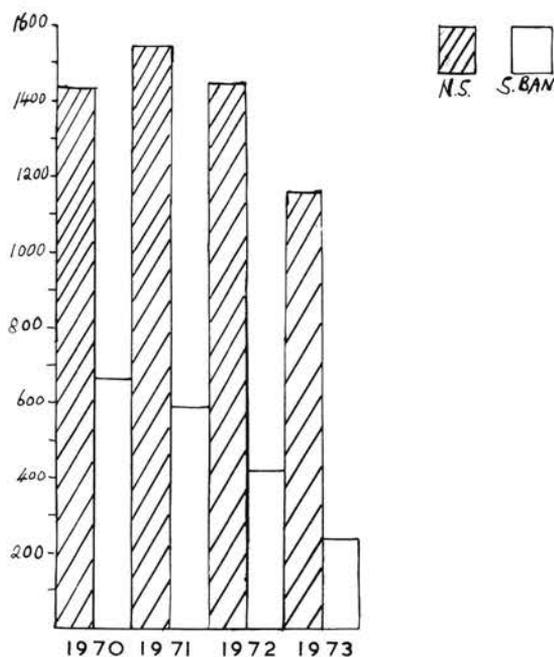
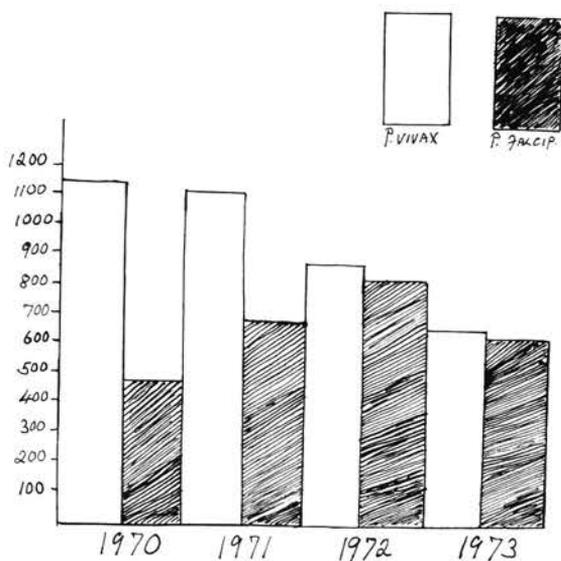


Figure 1 shows the Negeri Sembilan picture (over 90% of all our malaria cases) quite clearly. There is little significant difference in malaria incidence over the four years outside of Seremban Town Board area. The Town Board area shows a steady fall year by year — most marked after 1972.

FIGURE 2
YEARLY VIVAX & FALCIP.



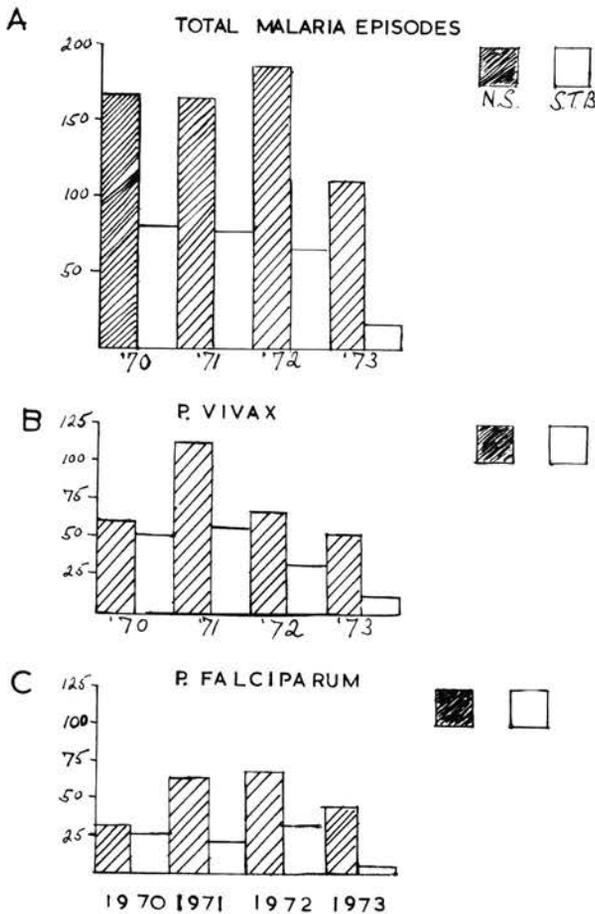
There is little significant difference between the overall malaria in 1970 and that of 1973. However it does appear that falciparum is certainly not on the wane. This may be due to an increase in Chloroquine resistant falciparum - many of whom end up at our clinic because of our known interest in malaria. As we have tried to exclude recrudescences in this series this may reduce our figures for vivax (but the same criteria were applied to the earlier years also) but some of the apparent drop in P. vivax cases could be due to a greater awareness of malaria and thus such cases are now vigorously treated on clinical grounds in this area without resort to the microscope.

TABLE V
STUDY OF CHILDREN AGED 2 YEARS AND UNDER

In	there were	172 Episodes in	110 Children	11.0 of all malaria
1970	"	"	"	"
"	"	179	165	10.5
"	"	202	182	13.2
1973	"	118	99	9.6
Total:	671	556	110	11.1

Table V shows the absolute figures from all areas year by year. There is a definite drop in 1973. This age group we studied in some detail as they are too young to be (very) chronic in regards to P. vivax and they certainly act as pointers to fresh transmission each year, especially of P. falciparum.

FIGURE 3
CHILDREN 2 YR ... N.S. & SEREMBAN



In this age group Figure III (A) it can be seen that there was little overall change both in the whole State of Negeri Sembilan and in the Seremban Town Board area up to the end of 1972. The overall incidence was less for the State in 1973 but the Town Board area showed a dramatic and significant drop in the same year.

Figure III (B & C) show that again throughout the four years the incidence of both vivax and falciparum did not significantly change in this age group except in the Seremban Town Board area where there were only 6 episodes of falciparum malaria in 1973.

These graphs suggest that fresh malaria transmission was taking place at about the same rate throughout the State year by year but that in the Seremban Town Board area a change had taken place and transmission was brought to a very low level in 1973. This was due to vigorous anti-malarial measures undertaken by the Seremban Town Board Health Officers.

Some Notes on the Clinical Presentation:

In our previous report on this subject (ibid) we dealt in some detail with our clinical experiences and will not repeat them here. However, in a recent study (O'Holohan 1974) based on these experiences some interesting facts emerged on studying 1000 subjects in close detail.

In a close examination of 1334 episodes of malaria in 1000 subjects it was found that at the time the parasite was discovered 49% of the patients were afebrile i.e. had a temperature of 99°F. or less. (This did not preclude pyrexia either before or after the discovery of the parasite.) This is mentioned as many clinicians appear to wait for a rise in temperature before taking blood for examination.

Toh and Yeo (1971) found that presenting symptoms (in 87 subjects) in decreasing order of frequency were fever, chills, rigors, headaches and sweats. These were followed by vomiting, the passing of dark urine and non specific complaints like bodyache and gastroenteric disturbances.

We studied 200 episodes of malaria (100 *P. vivax*, 100 *P. falciparum*) to establish what the presenting complaint (i.e. the symptoms which prompted the patients to seek medical attention) was and found the following (Table VI).

TABLE VI
presenting symptoms in 200 CASES OF MALARIA

	P. vivax (100)	P.falciparum (100)
Classical (i.e. chills, fever, sweats – all 3)	6%	17%
Fever & Chills	46	52
Fever only	23	10
Fever & Sweats	1	2
Fever with Diarrhoea/Vomiting	4	4
Cough	11	5
Body pains	7	4
Abdominal pain	–	3
Chills only	2	–
Sore throat	–	2
Cerebral	–	1
	-----	-----
	100%	100%
	=====	=====

In the matter of chemotherapy a recurrent problem was that of inadequate Chloroquine therapy. It has been established that the loading dose of Chloroquine is most important (Covell et al. 1955). Many practitioners appear to fear the unpleasant side effects of Chloroquine (such as nausea and vomiting) and attempt to minimize these side effects by giving smaller doses over a longer period. The 4 – Aminoquinolines are rapid blood schizonticides but they must be given in adequate dosage and the initial loading dose is all important. In our experience the side effects are not always dose related and even inadequate doses can cause severe vomiting and depression with a continuing parasitaemia. It was a not uncommon experience to be presented with patients who had patent asexual parasitaemia including (*P. vivax*), evidence of Chloroquine in the urine and severe vomiting who required parenteral therapy. Many such patients appear to show increased sensitivity to the phenothiazine derivatives used to control vomiting and present a therapeutic problem. 50 mg. of Promethazine Hydrochloride by intramuscular injection to patients above the age of 12 years (and proportionally less for younger age group) was found to be most effective.

Conclusion:

If our practice can be accepted as reasonably representative of similar such practices in the area of

Seremban (always bearing in mind that patients from all over the State tend to seek medical attention in the State Capital) then the pattern of malaria as portrayed here should give some idea of the overall picture throughout the State. We have here no recorded data prior to 1970 (clinical impressions are unreliable) but the picture we have displayed could suggest that there has been a persistent level of malaria for some years. Month to month figures are so dependent on local climatic conditions that they are unreliable and tend to give rise to later clinical impressions that there were periods of intense malaria acting alternating with little or no malaria. The overall figures show that there has been in fact no epidemic – rather a state of endemic malaria.

The figures for the two years old age group show that fresh transmission has been taking place throughout but that there has been dramatic curtailment of such transmission in the Seremban Town Board area. The figures for the Negeri Sembilan rural areas suggest that this change in the Seremban Town Board area was not part of a general decline in malaria but the result of interference in transmission.

REFERENCES

- COVELL, G., COATNEY, G.R., FIELD, J.W. and SINGH, J. (1955).
Chemotherapy of Malaria. W.H.O. Monograph Series No. 27.
- HUEHNE, W.H., MOHAMED DIN A. and LING, D.S. (1967).
Malaria a Primary Health Problem in Rural West Malaysia Med. J. Malaya, 22: 2. 60.
- O'HOLOHAN, D.R. and HUGOE-MATTHEWS, J. (1972).
Clinical and Laboratory Experiences of Malaria In a Seremban Medical Practice During the Two Years: 1970–1971. Med. J. Malaysia, 27:1. 52-56.
- O'HOLOHAN, D.R. (1974).
The Clinical Presentations of Malaria: An Analysis of One Thousand Subjects With Malaria Parasitaemia.
Proceedings 13TH SEAMEO-TROPED Seminar on Tropical Medicine and Public Health, Saigon, June 1974.
- TOH, K.K. and YEO, K.L. (1971).
The Present Trend of Malarial Infection in Singapore S'pore Med. J., 12: 1. 2.

SERUM HAPTOGLOBIN LEVELS AND TYPES IN NORMAL MALAYSIANS

By

J. GANESAN

M.B.B.S., D.C.P., D.Path.,

WONG PUI WAN

and

LIE-INJO LUAN ENG

M.D., Ph. D. D.T.M. & H.

Divisions of Haematology and Blood Genetics, Institute for
Medical Research, Kuala Lumpur.

This work was supported by the University of California International Center for Medical Research (ICMR) with Research Grant A1-10051 from the National Institutes of Health, US Public Health Service.

Polonovski and Jayle (1938)¹ first detected the presence in the serum of a protein having the property of binding haemoglobin. Subsequently these authors² characterized the binding substances as an α_2 glycoprotein and gave it the name of haptoglobin (HP). The ability of haptoglobin to bind haemoglobin serves to prevent haemoglobin released into the plasma from being excreted by the kidney, through the formation of a larger molecule, the haemoglobin-haptoglobin complex.^{3,4} This haemoglobin-haptoglobin complex is cleared from the plasma much more rapidly than free haptoglobin, so that marked hypohaptoglobinaemia is a concomitant of haemolysis.^{3,4} If all the available haptoglobin has been consumed in forming this complex, as in cases of severe haemolysis, then the unbound haemoglobin in the plasma is free to pass into the urine, and haemoglobinuria will be observed. This state exists until the liver is able to produce sufficient haptoglobin to combine with and surpass the haemoglobin present in the plasma. This process takes about 38 hours but normal levels are not reached until about 4 – 7 days after a haemolytic episode.⁵

In 1955 Smithes⁶ showed on starch gel electrophoresis that there were 3 main types of

haptoglobin. He designated them Hp 1 – 1, Hp 2 – 1 and Hp 2 – 2; and subsequently several different sub-types have been demonstrated.

A number of clinical conditions have been shown to cause a rise or fall in the serum haptoglobin level. But the normal serum haptoglobin level in Malaysians has not so far been determined. We therefore set out to determine the normal range of serum haptoglobin in the three different racial groups in Malaysia. At the same time we determined the haptoglobin types in the same individuals so as to see whether the serum haptoglobin level is related to the genetic haptoglobin type, as has been reported previously.^{7,8,9.}

MATERIALS AND METHODS

The serum haptoglobin level was determined in 240 male Malaysian blood donors of whom 79 were Malays, 81 Chinese and 80 Indians. Their ages ranged between 18 and 57. They had a haemoglobin level of over 13 gm %. A haemoglobin analysis was done on all these donors and this included alkaline denaturation for haemoglobin F, haemoglobin A₂ quantitation and electrophoresis of haemoglobin on starch gel. Persons found to have an abnormal haemoglobin were excluded from the series. We also excluded those found to have increased levels of Hb

A₂ or F; thus persons with — thalassaemia trait were as far as possible excluded. Motulsky's test for G6PD deficiency was also done on all these donors and those with G6PD deficiency were excluded.

The serum haptoglobin level was measured by the method of Owen *et al.*¹⁰ This is based on the fact that the complex formed by the combination of serum haptoglobin with methaemoglobin has a much greater peroxidative activity than free methaemoglobin; the peroxidative activity of the complex is

measured with a spectrophotometer and the concentration of haptoglobin determined by reference to a calibration curve. The values are expressed in terms of bound methaemoglobin as mg per 100 ml of serum.

The haptoglobin types were determined by starch-gel electrophoresis by the method of Poulik.¹¹ A highly sensitive benzidine solution was used to stain the haemoglobin-haptoglobin complex.

RESULTS

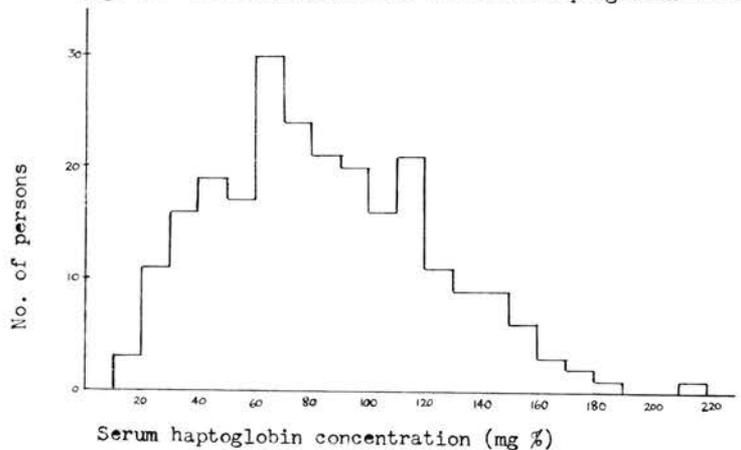
Table 1
Serum haptoglobin levels in normal Malaysians

Race	No. of subjects examined	Serum haptoglobin concentration (mg/100ml)		
		Mean	S.D.	Actual range
Malays	79	89.0	37.1	18.0 — 212.5
Chinese	81	84.8	38.7	17.2 — 176.6
Indians	80	82.0	37.3	21.7 — 169.7
All three races	240	85.3	37.0	17.2 — 212.5

Table 2
The relationship of the serum haptoglobin level to the haptoglobin type.

No. examined.	Haptoglobin type	Serum haptoglobin concentration (mg/100ml)		
		Mean	S.D.	Actual range
12	1-1	103.3	43.2	26.8 — 158.0
88	2-1	100.6	33.3	25.1 — 212.5
140	2-2	74.1	36.0	17.2 — 176.6

Fig. 1. The distribution of the serum haptoglobin levels.



The results of the serum haptoglobin estimation in each of the three main racial groups in Malaysia, i.e. the Malays, Chinese and Indians, and the results for the group as a whole are presented in table 1. The difference between the means for the Malays and Chinese was not significant ($p>0.25$) and neither were those between the means for Malays and Indians ($p>0.1$) or Indians and Chinese ($p>0.25$).

The frequency distribution of the serum haptoglobin levels in the whole group is shown in fig. 1.

Table 2 shows the relationship of the serum haptoglobin level to the haptoglobin type. The difference between the means for Hp 1-1 and 2-2 was significant ($p<0.05$) and that between 2-1 and 2-2 was highly significant ($p<0.001$) while that between 1-1 and 2-1 was not significant ($p>0.25$).

DISCUSSION

It can be seen from the results that the range of serum haptoglobin in our normal population is very wide. This has in fact been so in most of the published series. Smith and Owen⁷ whose method we have used had similar findings in 152 Caucasian blood donors: mean 93, S.D. 40 and actual range 4-220. Nyman⁸ using the peroxidase-iodide method of Jayle¹² found again in Caucasians a mean value of 110 with a S.D. of 41 and an actual range of 20-250. In a recent report of the haptoglobin level in 200 normal Thais¹³ using the method of Owen et al, the mean was found to be 90.61 with a S.D. of 26.5 and an actual range of 41.50 to 170.40. The range of values obtained in the Thais was therefore not as wide as that found by us in Malaysians or that found in the earlier mentioned series in Caucasians.

In various population surveys, it has been found that the average serum haptoglobin level as indicated by the hb-binding capacity depends on the haptoglobin phenotype: it has been found to be highest for the Hp 1-1 phenotype and lowest for the Hp 2-2; the Hp 2-1 phenotypes have intermediate levels.^{7,8,9} Smith and Owen, whose method we have used, reported that the values for the group of Caucasian donors that they examined were:-

Haptoglobin type	Mean	S.D.	Actual range
1-1	104	34	21-155
2-1	102	37	28-220

2-2	72	38	14-193
All	93	40	14-220

Two of their sera contained so little haptoglobin (4 and 11 mg/100 ml) that it was not possible to determine the haptoglobin type.

Our findings, shown in table 2, are in agreement with the above reports that the serum haptoglobin level in terms of the haemoglobin-binding capacity depends on the genetic haptoglobin type. The lowest values for the serum haptoglobin level in our series were 17.2 and 21.7 mg/100 ml and at these levels we could still determine the haptoglobin type by starch gel electrophoresis although the pattern was faint and both these sera showed the pattern of Hp 2-2.

Like Smith and Owen, with the same photometric method, we also failed to find any normal serum completely lacking in haptoglobin. Several reports¹⁴⁻¹⁹ have been made of Hp 0 in different populations. Kirk *et al.*¹⁸ when examining serum samples from Malaysians (made up of approximately equal numbers of Malays, Chinese and Indians) by starch gel electrophoresis found a frequency of Hp 0 of 8 in 622 people. But Kirk *et al.* and the other authors did not examine only healthy persons and they did not screen them for abnormal haemoglobins,

- thalassaemia trait and G6PD deficiency as we have done. Also most of these authors used only starch-gel electrophoresis to determine the frequency of Hp 0. And as was pointed out by Kirk *et al.* it is difficult to determine the Hp 0 phenotype with certainty using the starch gel method as in many cases the amount of the haptoglobin present in the Hp 2-2 individuals is so slight that it can readily escape detection.

Because the normal range of serum haptoglobin is so wide, an isolated observation of a low haptoglobin level in any patient may not be of much value. Complete anhaptoalbuminaemia however would still be significant. Also the haptoglobin level remains fairly constant in any healthy individual.^{20,8} Thus observation of a marked rise or fall usually has some clinical significance. Haptoglobin measurement can be helpful in confirming that an acute haemolytic episode has taken place even when there is no longer any demonstrable free haemoglobin or methaemalbumin in the plasma, because the

haptoglobin level does not return to its usual level for 4–7 days after complete depletion unless the patient has a disease associated with increased Hp synthesis. However, as has already been pointed out above, while complete anhaptoalbuminaemia is significant, interpretation of a low haptoglobin level in terms of increased haemolysis is only reliable if a specimen obtained before the haemolytic episode is available for comparison. In chronic haemolytic disease there is a continuous release of haemoglobin into the circulation, and the serum haptoglobin level is continuously depressed and the renal threshold for haemoglobin is lowered.

The serum haptoglobin reaches normal adult levels by the age of one year.²¹ By far the most common cause of low serum haptoglobin is an increased Hb turnover. This may be the result of increased haemolysis of circulating red cells,^{3,4} or of the increased destruction of red cell precursors before their release into the circulation, so-called ineffective erythropoiesis. As an example of the latter, in pernicious anaemia, although red cell survival time is not markedly shortened, plasma haptoglobin is consistently low, and upon specific treatment with vitamin B₁₂ it rises to normal levels before the shortened survival time is corrected.^{22,23} A lower concentration or complete absence of serum haptoglobin has also been reported in liver cell failure;²⁰ such patients are usually jaundiced and it is not known whether the low values are due to impaired synthesis by the damaged liver or to increased haemolysis which frequently accompanies severe hepatocellular disease.

An increased serum haptoglobin level has on the other hand been found in a variety of disorders associated with inflammation or tissue destruction and the serum haptoglobin level has been used as an index of activity of such disorders. Thus elevated levels occur in acute and chronic infection,^{24–27} burns and trauma,²⁸ collagen disease,^{29–31} scurvy, amyloidosis, biliary obstruction, renal disease, neoplasms and in lymphomas, leukaemias, Hodgkins disease and myeloma.^{32,33}

It can be seen from the above that a number of conditions can cause alteration of the serum haptoglobin level. The normal serum haptoglobin is the result of a balance between the factors which tend to raise the haptoglobin level and those that

lower it. Thus the serum haptoglobin is usually decreased in uncomplicated haemolysis, the decrease depending on the extent of increased haemolysis. But if the haemolytic disease is complicated by a condition giving rise to an increase of haptoglobin, the increased synthesis of haptoglobin as a response to this condition may offset the increased removal of haptoglobin from the plasma as a result of haemolysis and the haptoglobin value may then be normal, or even raised. Therefore it may be said that lowered values in the absence of hepatic disease indicate haemolysis but that normal values do not exclude haemolysis especially in the presence of systemic disorders eg. infection or malignancy.

SUMMARY

The serum haptoglobin level was determined in 240 male Malaysian blood donors of whom 79 were Malays, 81 Chinese and 80 Indians. These donors all had a haemoglobin level of over 13 gm % and haemoglobin analysis and Motulsky's test for G6PD deficiency were done on all of them and those with abnormal haemoglobin, β – thalassaemia trait or G6PD deficiency were excluded from the series. The serum haptoglobin level was determined by the photometric method of Owen *et al.* and the result showed: in the Malays, a mean value of 89 mg/100ml with a S.D. of 37.1 and an actual range of 18.0 – 212.5 mg/100ml; in the Chinese a mean value of 84.8 mg/100 ml, with a S.D. of 38.7 and an actual range of 17.2 – 176.6 mg/100 ml; and in the Indians a mean value of 82.0 mg/100 ml with a S.D. of 37.3 and an actual range of 21.7 – 169.7 mg/100 ml. The haptoglobin type was also determined for all these donors and it was seen that the serum haptoglobin level, as indicated by the haemoglobin binding capacity depends on the haptoglobin phenotype; it was highest for Hp 1–1, and lowest for Hp 2–2; Hp 2–1 had intermediate levels. The value of serum haptoglobin estimation in clinical practice is discussed.

ACKNOWLEDGEMENTS

We wish to thank Dr. C.G. Lopez, Director of the National Blood Transfusion Centre for providing the blood specimens.

We also wish to thank Dr. Bhagwan Singh, Director of the Institute for Medical Research for permission to publish our data.

REFERENCES

1. Polonovski, M and Jayle, M.F. (1938) Existence dans de plasma sanguin d'une substance activent l'action peroxydasique de l'he'moglobine. C.R. Soc. Biol. 129 : 457
2. Polonovski, M and Jayle, M.F. (1940) Sur la preparation d'une nouvelle fraction des protein plasmatiques, b'haptoglobine. C.R. Acad Sei. 211, 517.
3. Allison, A.C. and AP. Rees, W (1957) The binding of haemoglobin by plasma protein (haptoglobin). Brit. Med. J. 2 : 1137.
4. Laurell, C.B., and Nyman, M. (1957) Studies on the serum haptoglobin level in haemoglobinemia and its influence on renal excretion of haemoglobin. Blood 12 : 493.
5. Noyes, W.D. and Garby, C. (1967) Rate of haptoglobin synthesis in normal man. Scand. J. Clin. Lab. Invest. 20 : 33.
6. Smithes, O. (1955) Zone electrophoresis in starch gels : Group variations in serum proteins of normal human adults. Biochem. J. 61: 629.
7. Smith, H. and Owen, J.A. (1961) The determination of haptoglobin in normal human serum. Biochem. J. 78 : 793.
8. Nyman, M. (1959) Serum haptoglobin Methodological and clinical studies. Scand. J.Clin. Lab. Invest., 11 (Sypl. 39).
9. Planas, J., Vinas, J., Castro, S, Orribas, J.M. and Martin-Matro, M.C. (1965) The values of haptoglobin and their relation to the genetic type in a group of donors. Rev. Esp. Fciol. 21 : 15
10. Owen, J.A., Better F.C. and Hoban J. (1960) A simple method for the determination of serum haptoglobins. J.Clin. Path., 13, 163.
11. Poulik, M.D. (1957) Starch gel electrophoresis in a discontinuous system of buffers. Nature 180, 1477.
12. Jayle, M.F. (1951) Method de dosage de l'haptoglobine serique. Bull. Soc. Chim. biol., 33 : 876 - 880.
13. Areekul, S and Chantachum, Y (1972) Serum haptoglobin level in normal Thais. South East Asian J. Trop. Med. Pub. Hlth. 3:2 86-287.
14. Sutton, H.E., Neel J.V., Binson G, & Zuelzer. W.W. (1956) Serum protein differences between Africans and Caucasians. Nature 178, 1287.
15. Allison, A.C., Blumberg, B.S., & AP Rees, W. (1958) Haptoglobin types in British, Spanish Basque and Nigerian African populations. Nature 181, 824.
16. Harris, H., Robson, E.B. & Siniscalio M. (1958) Atypical segregation of haptoglobin types in man. Nature 182, 1324.
17. Kirk, R.L., Lai, L & Hogben, D.L. (1960 a) Haptoglobin groups of white Australians. Med. J. Aust. 1, 45.
18. Kirk, R.L., Lai L.Y.C., Mahmood S. and Singh R.B. (1960b) Haptoglobin types in South-East Asia. Nature 183, 185.
19. Lie-Injo L.E., Bolton J.M. and Fudenberg H.H. (1967) Haptoglobin, transfermin and serum gammaglobulin types in Malayan aborigines . Nature 215 : 777
20. Jayle, M.F. and Boussier, G. (1955) See seromucoïdes du sang. leur relations avec mucoproteïnes de la substance fondamentale du tissu conjunctiv.
21. Bergstrand, C.G.Czar B & Tarukoski P. H. (1961) Serum haptoglobin in infancy. Scand. J.Clin. Lab. Invest. 13, 576.
22. Nyman, M. (1957) Haptoglobin in pernicious anaemia. Scand.J.Clin. Lab. Invest 9 : 168.
23. Owen, J.A., Carew, J.P., Cowling, D.C., Boban, J.P., and Smith, H. (1960) Serum haptoglobins in megaloblastic anaemia. Brit.J.Haemat. 6:242.
24. Bovornkitti, S. (1962) Serum protein changes in tuberculosis with particular reference to alpha-2 globulin. Amer. Rev. Resp. Dis. 85 : 56
25. Schwantes, A, Salzano, E, Castro, I. et al (1967) Haptoglobins and Leprosy. Acta Genet. (Basel) 17 : 127.
26. Bogdanovich L (1968) Serum haptoglobin as an index of the activity of pulmonary tuberculosis. Probl Tuberk 46 : 65.
27. Murray, R., Robinson, J. Dublin, T., et al (1966) Haptoglobin and rheumatic fever. Brit. Med. J. 3490 : 762.
28. Neuhaus, O. (1964) Biochemical significance of serum glycoproteins 3. Hepatic production of alpha-1 and alpha-2 globulins responding to injury. Proc. Soc. Exp. Biol Med. 117 : 244.
29. Turowska, B. (1969) The value of haptoglobin level determination in synovial exudates in the

- diagnosis of rheumatic disease. *Rheumatologia* 7 : 57.
30. Kobiela, J., Turowska B, Baniowski, A. (1966) The level of haptoglobins in serum of patients with rheumatoid arthritis. *Pol.Med.J.* 5:1004.
 31. Boottiger, L, Malmquist, E, Olhagen, G. (1964) Serum protein-bound carbohydrates in rheumatic disease. II Evaluation of activity in rheumatoid arthritis. *Ann Rheum. Dis* 13:495.
 32. Owen, J.A., Smith, H.Padanyl, R.and Martin, J. (1964) Serum haptoglobin in disease. *Clin. Sci.* 26 : 1.
 33. Gurda, M. (1971) Haptoglobin level in blood serum in Leukaemia patients. *Folia Hamatol., Liepzig* 95, 1, 5.37 – 41.

Serum Tocopherol (Vitamin E) Status of Malaysians.

T.K.W. NG and Y.H. CHONG

Division of Nutrition,
Institute for Medical Research,
Kuala Lumpur.

INTRODUCTION

Recently there has been a renewal of interest in vitamin E. This is partly due to reports in the popular press and magazines extolling the benefit of vitamin E supplements in the prophylaxis of cardiovascular disorders, skin conditions and athletic performance. Although none of these claims have been proven on firm scientific foundations, it cannot be denied that such reports stemmed primarily from the proceedings of scientific forums or conferences dealing with vitamin E which are yet to make their appearance in print.

Until the exact roles of vitamin E are ascertained, human daily vitamin E requirements are put at 5 – 30 mg. Recently, the Food and Nutrition Board, National Academy of Sciences U.S.A. recommended a daily dietary allowance of 10 mg for a healthy adult (*Am. J. Publ. Hlth.*, Vol. 63, 1973). However, when relatively large amounts of polyunsaturates are consumed as in the treatment of primary hyperlipoproteinaemia, opinions are divided as to whether there is an increased need for vitamin E (Horwitt, 1962; Jager, 1972; Briggs and Briggs, 1974).

Owing to the complete lack of information on vitamin E nutriture in Malaysians, we thought it worthwhile to undertake some fundamental studies in this connection.

The objectives in this study are therefore as follows:—

- (i) to obtain some baseline data on serum tocopherol status of Malaysians in apparent good health.
- (ii) to compare the vitamin E status of the above subjects with patients treated for primary hyperlipoproteinaemia with a low-cholesterol, polyunsaturates-rich diet.
- (iii) to study the effect of a daily supplementation of alpha-tocopherol on serum tocopherol status

and the levels of serum beta-lipoproteins, total serum lipids, serum cholesterol and serum triglycerides.

MATERIALS AND METHODS

Subjects

a. **Subjects in apparent good health:** These consisted of 63 Malaysian blood donors and subjects undergoing routine medical examination. Their ages ranged from 7 to 55 years with a mean age of 34 years. The majority were males and consisted of an approximately equal number of Malays, Chinese and Indians.

b. **Hyperlipoproteinaemic patients on a modified diet:** These consisted of 63 patients of Malay, Chinese and Indian origin, aged 7 to 55 years with a mean age of 39 years. The majority were out-patients found to have primary hyperlipoproteinaemia (mostly Type II) and had been instructed to avoid cholesterol-rich foods such as eggs and organ foods and to use corn oil for cooking purposes instead of other edible oils. Hyperlipoproteinaemia was diagnosed when beta-lipoproteins exceeded 700 mg/100 ml serum, cholesterol exceeded 260 mg/100 ml serum and triglycerides (fasting) over 200 mg/100 ml serum, occurring singly or in combination.

c. **Hyperlipoproteinaemic subjects on a normal diet:** These consisted of 56 subjects of various races, aged 11 to 69 years with a mean age of 43 years. They were not known to be on drug or diet therapy at the time of investigation.

d. **Subjects on vitamin E supplementation:** These comprised 3 healthy, non-obese laboratory personnel, aged 24, 26 and 28 years. They were given 100 mg dl-alpha-tocopherol acetate daily (except Sundays) after meals for a total of 5 weeks.

During the period of the study, they were instructed to adhere to their normal eating habits.

Methods

Single venous samples were obtained usually after an over-night fast and for the vitamin E supplementation experiment, weekly fasting venous samples were obtained before, during and after the 5-week supplementation period. The sera were analysed for total tocopherol, beta-lipoproteins, total lipids, total cholesterol and triglycerides.

Serum total tocopherol was estimated by the Emmerie and Engel reaction which involved the reduction by vitamin E of ferric ions to ferrous ions, the latter forming a red colour with dipyrindyl (Baker and Frank, 1968). n-Heptane was used as the serum extractant (Hashim and Scuttringer, 1968). Tocopherol levels were expressed as mg per 100 ml serum and also as mg per gram total serum lipids, referred to henceforth as Horwitt's ratio (Horwitt et al, 1972).

Serum beta-lipoproteins were determined by a turbidimetric method involving the specific precipitation of beta-lipoproteins by dextran sulphate in the presence of calcium ions at pH 9.0 (B.D.H. beta-lipoproteins kit).

Serum total lipids were estimated using a turbidimetric method (Huerga et al, 1953). The concentration of lipids was read from a standard curve obtained by plotting the total serum lipid levels determined gravimetrically (Friedman, 1968) against turbidimetric readings of corresponding samples. Aliquots from the same chloroform-methanol extract of serum were used to obtain the turbidimetric and gravimetric values.

Serum total cholesterol was determined by the method of Abell et al (1952) which involved a preliminary saponification, extraction with petroleum ether (B.P. 40-60°C) and colorimetry by the Liebermann-Burchard reaction.

Serum triglycerides were determined essentially by the method of Van Hendel et al (1957) as modified by Harding et al (1967); phospholipid-free sera extracts were obtained by adsorption onto 'Florisil'. The samples were saponified and the glycerol liberated was oxidised to formaldehyde which reacted with chromotropic acid forming a purple colour. Triglycerides were expressed as mg tripalmitin per 100 ml serum.

All readings were read on a Coleman 44

spectrophotometer.

RESULTS AND DISCUSSION

The serum tocopherol levels (expressed as mg/100 ml serum) for the various categories of subjects are summarised in Table I.

Table I
Mean \pm S.D. and range of serum tocopherol in the various categories of subjects

Subjects	No. of samples	Mean \pm S.D. (mg/100ml serum)	Range (mg/100ml serum)
Subjects in apparent good health	63		0.30-2.07
Malays		0.83 \pm 0.39	
Chinese		0.92 \pm 0.36	
Indians		0.98 \pm 0.32	
Means of all races		0.92 \pm 0.36	
Hyperlipoproteinaemic patients on a modified diet	63	1.20 \pm 0.38	0.34-2.10
Hyperlipoproteinaemic subjects on a normal diet	56	1.21 \pm 0.30	0.69-2.12

No significant difference was observed between the mean values for Malays, Chinese and Indians; the overall mean of all races was 0.92 mg/100 ml. This is slightly lower than the mean of serum tocopherol obtained by other investigators (Harris et al, 1961; Bieri et al, 1964) but higher than values reported by others using chromatographic procedures for the estimation of serum alpha-tocopherol (Dayton et al, 1965; Christiansen and Wilcox, 1973). However, higher tocopherol values were apparent in the patients with hyperlipoproteinaemia.

We observed that the levels of serum tocopherol correlated positively with serum beta-lipoproteins, cholesterol and triglycerides (Figs. 1-3). This corroborates the findings of others who reported similar associations (Davies et al, 1969; Rubenstein et

al, 1969). Consequently, the expression of tocopherol in terms of mg per 100 ml serum is of little value particularly when there is concurrent hyperlipoproteinaemia or hypolipoproteinaemia. Thus it can be argued that a high level of serum tocopherol may be secondary to lipid disorders and need not reflect vitamin E nutriture.

To overcome this, Horwitt et al (1972) suggested the use of the expression serum tocopherol : total serum lipid ratio (i.e. mg tocopherol per gram total serum lipids). These values for our subjects are now shown in Table II.

Table II
Serum tocopherol : total serum lipid ratios and incidence of vitamin E deficiency in the 3 groups of subjects

Subjects	No. of samples	(Horwitt's ratio) mg tocopherol per g total lipids (Mean \pm S. D.)	% subjects <0.8 mg tocopherol per g total lipids
Subjects in apparent good health	63	1.32 \pm 0.34	5
Hyperlipoproteinaemic patients on a modified diet	63	1.29 \pm 0.35	8
Hyperlipoproteinaemic subjects on a normal diet	56	1.26 \pm 0.29	2

It is evident from Table II that when expressed in this fashion, there was little difference in the serum tocopherol status of the 3 groups of subjects which differed when the levels were expressed in mg tocopherol per 100 ml serum.

Thus while none of our subjects had serum tocopherol levels below 0.3 mg/100 ml, a level below which Leonard and Losowsky (1969) considered indicative of serious vitamin E deficiency, when expressed as Horwitt's ratio it may be seen that 5% of the normal healthy subjects and 8% of the primary hyperlipoproteinaemic patients on the modified diet had ratios below 0.8, a ratio suggested as representing minimal vitamin E adequacy (Horwitt et al, 1972).

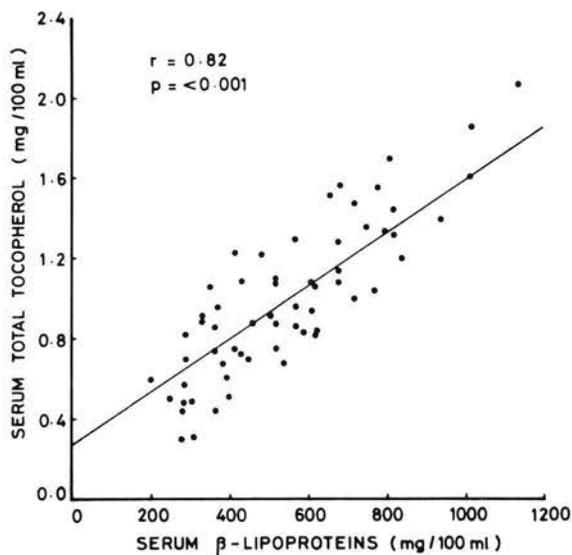


Fig 1
Correlation between serum tocopherol and serum beta-lipoproteins.

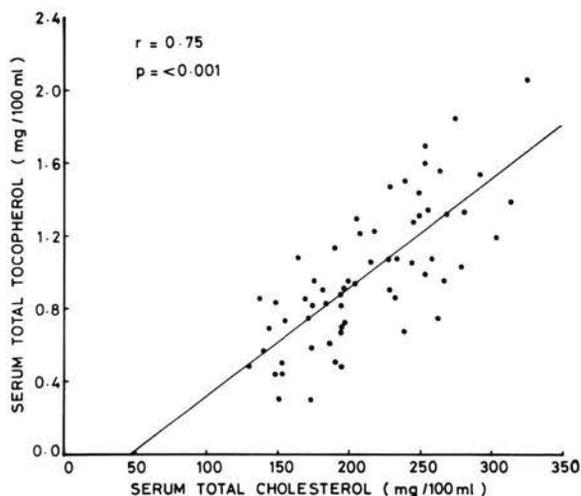


Fig. 2.
Correlation between serum tocopherol and serum total cholesterol.

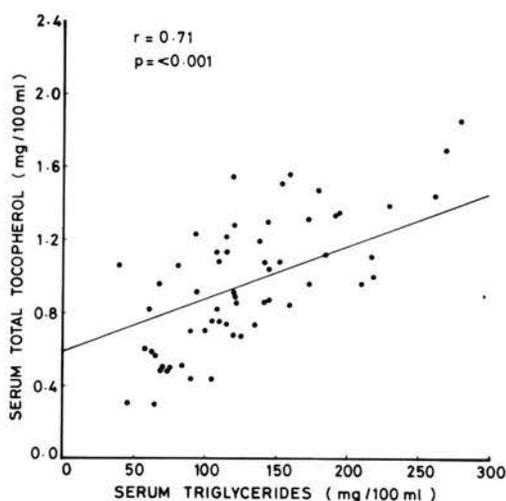


Fig. 3
Correlation between serum tocopherol and serum triglycerides.

This slight difference in the incidence of vitamin E inadequacy however, is of no statistical significance. But it would appear that expression of serum tocopherol in terms of the tocopherol : serum lipid ratio not only gives a truer picture of vitamin E status but it also possesses the added advantage of a greater sensitivity in predicting vitamin E insufficiency.

The highly significant correlation between the levels of serum tocopherol expressed as mg/100 ml and the various serum parameters e.g. beta-lipoproteins, cholesterol and triglycerides (see Figs. 1-3) prompted us to investigate the levels of these substances with daily supplementation of vitamin E.

The effect of a daily supplementation of 100 mg dl-alpha-tocopherol acetate for a period of 5 weeks on the levels of serum tocopherol, serum beta-lipoproteins, total serum lipids and serum lipid fractions in the 3 human volunteers is shown in Tables III-VI.

Table VI shows that only serum tocopherol levels, expressed either as mg/100 ml or mg per g total serum lipids, were altered significantly during the period of vitamin E supplementation. No significant changes could be observed in the levels of serum beta-lipoproteins, total serum lipids and serum lipid fractions. This is in agreement with the observations

Table III
The effect of alpha-tocopherol supplementation on the level of serum constituents in subject A.

Serum constituents (mg/100ml unless otherwise stated)	Before supplementation (Mean of 3 consecutive samples)	During supplementation (Mean of 5 consecutive samples)	After supplementation (Mean of 3 consecutive samples)
Tocopherol	0.70	1.45	0.99
Tocopherol (mg per g total lipids)	1.10	2.15	1.36
Beta-lipoproteins	422	427	533
Total lipids	613	653	708
Total cholesterol	196	218	224
Triglycerides (fasting)	117	92	131

Table IV
The effect of alpha-tocopherol supplementation on the level of serum constituents in subject B

Serum constituents (mg/100ml unless otherwise stated)	Before supplementation (Mean of 3 consecutive samples)	During supplementation (Mean of 5 consecutive samples)	After supplementation (Mean of 3 consecutive samples)
Tocopherol	0.61	1.19	0.68
Tocopherol (mg per g total lipids)	1.06	1.97	1.18
Beta-lipoproteins	217	271	258
Total lipids	575	583	563
Total cholesterol	171	180	168
Triglycerides (fasting)	72	95	125

Table V
The effect of alpha-tocopherol supplementation on the level of serum constituents in subject C.

Serum constituents (mg/100ml unless otherwise stated).	Before supplementation (Mean of 3 consecutive samples)	During supplementation (Mean of 5 consecutive samples)	After supplementation (Mean of 3 consecutive samples)
Tocopherol	1.45	1.79	1.34
Tocopherol (mg/g total lipids)	1.45	1.85	1.50
Beta-lipoproteins	920	905	840
Total lipids	948	932	862
Total cholesterol	324	307	279
Triglycerides (fasting)	219	234	231

Table VI
Statistical Analysis of effect of Vitamin E supplementation on the levels of serum tocopherol, serum beta-lipoproteins and serum lipids

Serum constituents	During supplementation vs before		
	subject A	subject B	subject C
Tocopherol (mg/100ml)	S p=<0.001	S p=<0.001	raised but N.S.
Tocopherol (mg per g total lipids)	S p=<0.001	S p=<0.001	S p=<0.001
Beta-lipoproteins	N.S.	N.S.	N.S.
Total lipids	N.S.	N.S.	N.S.
Total cholesterol	N.S.	N.S.	N.S.
Triglycerides	N.S.	N.S.	N.S.

S = significant; N.S. = not significant

of Harman (1960) and suggests that supplementation with vitamin E has no direct effect on the levels of serum lipoproteins and lipids.

SUMMARY

1. Normal, healthy Malaysians had a mean serum tocopherol level of 0.92 ± 0.36 mg/100 ml with a range of 0.30 - 2.07 mg/100 ml.
2. The mean serum tocopherol levels of healthy subjects appeared significantly lower than those of hyperlipoproteinaemic subjects either on a normal or modified diet. However, when expressed as mg tocopherol per gram total serum lipids, no difference was observed between healthy subjects and patients suffering from hyperlipoproteinaemia.
3. Serum tocopherol when expressed as mg per g total serum lipids (Horwitt's ratio) appeared to be a better indicator of vitamin E nutritional status than the expression in terms of mg per 100 ml serum. The mean Horwitt's ratio for normal, healthy Malaysians was 1.32 ± 0.34 .
4. In 3 human volunteers, alpha-tocopherol supplementation at a daily level of 100 mg for a period of 5 weeks significantly raised the serum tocopherol levels but had no significant effect on the levels of serum beta-lipoproteins, total serum lipids, serum total cholesterol and serum triglycerides.

ACKNOWLEDGEMENTS

We would like to thank Messrs Mohd Noor bin Mohd Yatim and Kanapan Alagapan for kindly consenting to be our subjects in the vitamin E supplementation study.

The sera of patients with primary hyperlipoproteinaemia were those submitted to the Nutrition Laboratory for routine lipid studies by Dr. Khoo Kah Lin, Clinical Specialist of the General Hospital, Kuala Lumpur.

REFERENCES

- ABELL, L.L., LEVY, B.B., BRODIE, B.B., and KENDALL, F.E. (1952)
In *Std Methods of Clinical Chemistry*, Vol. II : 26; edited by David Seligson. Acad. Press Inc., N.Y.
- BAKER, H., and FRANK, O. (1968) In *Clinical*

- Vitaminology, Chap. XII : 169. John Wiley & Sons. Inc.
- B.D.H. CHEMICALS LTD., The Determination of Low-Density Lipoproteins.
- BIERI, J.G., TEETS, L., BELAVADY, B., and ANDREWS, E.L. (1964). Serum Vitamin E Levels in Normal Adult Population in the Washington D.C. area. *Proc. Soc. Exper. Biol. Med.* 177 : 131.
- BIOCHEMICAL PROCEDURES (1961) Vol. 1 USAMRU & Nutr. Lab., 42.
- BRIGGS, M., and BRIGGS, M. (1974) Are Vitamin E Supplements Beneficial? *Med. J. Aust.* 1 : 434.
- CHRISTIANSEN, M.M., and WILCOX, E.B. (1973) Dietary Polyunsaturates and Serum Alpha-Tocopherol in adults. *J. Am. Dietet. Assoc.* 63 : 138.
- DAVIES, T., KELLEHAR, J., and LOSOWSKY, M.S. (1969) Interrelation of Serum Lipoprotein and Tocopherol Levels. *Clin. Chim. Acta.* 24 : 431.
- DAYTON, S., HASHIMOTO, ROSENBLUM, D., and PEARCE, M.L. (1965) Vitamin E Status of Humans During Prolonged Feeding of Unsaturated Fats. *J. Lab. & Clin. Med.* 65 : 739.
- Food and Nutrition Board, Nat. Acad. Sci., Nat. Res. Council; Recommended Daily Dietary Allowances, Revised 1973. *Am. J. Publ. Hlth.* 63 : 82. Edited by Christakis, G.
- FRIEDMAN, H.S. (1968) Quantitative Determination of Total Lipids in Serum. *Clin. Chim. Acta.* 19 : 291.
- HARMAN, D. (1960) Vitamin E; Effect on Serum Cholesterol and Lipoproteins. *Circulation.* 22 : 151.
- HARRIS, P.L., HARDENBROOK, E.G., DEAN, F.D., CUZACK, E.R., and JENSEN, J.L. (1961) Blood Tocopherol Values in Normal Human Adults and Incidence of Vitamin E Deficiency. *Proc. Soc. Exper. Biol., & Med.* 107 : 381.
- HASHIM, S.A., and SCUTTRINGER, G.R. (1966) Rapid Determinations of Tocopherol in Macro- and Micro-Quantities of Plasma. *Am. J. Clin. Nutr.* 19 : 137.
- HORWITT, M.K. (1962) Interrelations Between Vitamin E and Poly-unsaturated Fatty Acids in Adult Men. *Vitamins and Hormones.* 20 : 527.
- HORWITT, M.K., HARVEY, C.C., DAHM JR., G.H., and SEARCY, M.T. (1972) Relationship Between Tocopherol and Serum Lipid Levels for Determination of Nutritional Adequacy. *Ann. N.Y. Acad. Sci.* 203 : 223.
- HUERGA, J.D.L., YESINICK, C., and POPPER, H. (1953) Estimation of Total Serum Lipids by a Turbidimetric Method. *Am. J. Clin. Pathol.* 23 : 1163.
- JAGER, F.C., (1972) Linoleic Acid Intake and Vitamin E Requirement in Rats and Ducklings. *Ann. N.Y. Acad. Sci.* 203 : 199.
- LEONARD, P.J., and LOSOWSKY, M.S. (1967) Relationship Between Plasma Vitamin E and Peroxide Hemolysis in Human Subjects. *Am. J. Clin. Nutr.* 20 : 795.
- RUBENSTEIN, H.M., DIETZ, A.A., and SCRINAVASAN, R. (1969) Relation of Vitamin E and Serum Lipids. *Clin. Chim. Acta.* 23 : 1.

Breastfeeding In A Rural Area In Malaysia

by Dr. Teoh Soong Kee, MBBS.
formerly Medical Officer, Perlis
Now Dept. Obst. and Gynecology
Hospital University, Kuala Lumpur.

INTRODUCTION

The importance of breastfeeding is being emphasised by many medical authorities such as WHO¹, Jelliffe², Wong³ especially in a developing country in relation to protein malnourishment in infants. Whereas in the western countries, the trend is reversing back to breastfeeding, that in the developing countries is directed towards artificial feeding, perhaps with a mistaken feeling of "progress". Studies made in Kuala Lumpur (Dugdale⁴) and Singapore (Willis³, Wong³) have shown a drastic fall in breastfeeding by our urban mothers. This paper is a study of the incidence of breastfeeding in a rural area in relation to various factors and the reasons given by the rural mothers for their choice.

Materials and Method

The area chosen is the state of Perlis in Northern Malaysia. Its small population of 127,000 is mainly rural involved in rice-farming, fishing and tin-mining. The largest town has only 8,700 people. The racial composition is roughly 75% Malays, 20% Chinese, and 5% others (Indians and Siamese) (Source: from Vital Statistics, W. Malaysia 1970).

It is however well served in health facilities for a rural area and being a small compact state, with fairly good communications, attendance at these health clinics is high.

Pregnant mothers who attend the antenatal clinics are asked by the nursing staff about the feeding of their youngest child, provided the child was born between January 1970 and June 1972. A total of 714 eligible patients were asked whether they breastfed, the duration and each was asked to state not more than three main reasons for their choice.

Analysis of the data

The incidence of breast/feeding was calculated in relation to race, age, parity, income, occupation of mother and education of mother.

Race

Whereas 92.5% of Malay mothers breastfeed their child, only 58% of the Chinese mothers breastfeed. Most of the Malays who breast feed do so for more than 6 months (72.8%).

On the whole, 84.1% of the mothers in Perlis breastfeed their child, a figure which compares very well with those in K.L. and Singapore.

Age

There is no significant difference in the incidence of breast feeding in the 3 age-groups studied except for slightly higher percentage in those over 35 years old, who also tend to breastfeed longer.

Parity

It is noted that even those who were bearing their first child in the period under study, 74% of them breastfeed though only 43.5% do so longer than 6 months compared to the multipara (65-68%).

Income

The total family income was taken in case of working wives. Most of the families considered belong to the poorer class and the lower middle class groups. While the poorest class who earn less \$150 (mainly tenant farmers and fishermen) almost always breastfeed (90.4%), only 70% of the other class mothers breastfeed. In those earning more than \$300 a month, only about quarter do so for more than six months.

Mother's Occupation

It is presumed that mothers who are having a full-time occupation of their own seldom breastfeed as is proved by the study. Nearly half do not breastfeed and of those who did, many of them do so only during their puerperium or just after. It was heartening to note that those mothers who had to help their husbands in the fields are able to carry out normal breastfeeding.

Mother's education

Most of the mothers studied have only gone to primary schools and this amount of education has no apparent effect on their choice of infant feeding. However nearly half of those who had gone to secondary schools do not breastfeed or if they did, they did so only during their puerperium.

Reasons for NOT breastfeeding

More than 1/3 of those who feed their babies with powdered milk claimed that they did not have enough breastmilk and nearly a quarter alleged that their babies preferred the bottle to the breast. 74 prefers social convenience than to breastfeed. Only

one considered their figure important enough to avoid breast feeding (these questions were mainly asked by nurses).

Racially, there was no difference in their reasons. As far as the income is concerned it is understandable that about 20% of those with more than \$300 per month felt socially inconvenient but it is surprising that even among the poor, "excuses" of insufficient milk and baby's preference are as common as the higher-income groups.

Reasons for Breast feeding

"Convenience" was the most popular reason, followed closely by "cheapness", "traditional advice" and "baby's preference." Thus 148 mothers have attempted to give artificial feeds but found that their babies prefer their mothers' breasts. 24 mothers intentionally breastfeed to delay a further pregnancy. It is noted that "advice from health staff" has minimal effect on the choice of infant feeding.

Malay mothers found it more convenient, and cheap and were influenced by their elders and their babies' choice. The same pattern was present in the lowest income group.

Table 1. Breastfeeding according to race					
	less than 6 weeks	6 months to 6 months	more than 6 months	Artificial Feeding	Total
Malays	26 (4.8)	78 (14.9)	372 (72.8)	39 (7.8)	514
Chinese	16 (9.0)	28 (15.8)	62 (35.0)	72 (42.0)	178
Others	0	3 (13.6)	16 (72.8)	3 (13.6)	22
Total	41 (5.9)	100 (15.2)	450 (63.0)	114 (15.9)	714

Table 2. Breast Feeding according to age					
	less than 6 weeks	6 months to 6 months	more than 6 months	Artificial Feeding	Total
under 25	22 (6.0)	70 (18.8)	228 (57.5)	63 (17.7)	383
26 – 35	16 (6.0)	31 (11.8)	177 (64.2)	47 (18.0)	271
36+	3 (5.0)	8 (13.0)	45 (75.3)	4 (6.7)	60

Table 3. Breast feeding according to parity					
	less than 6 weeks	6 months to 6 months	more than 6 months	Artificial Feeding	Total
primip	21 (10.5)	40 (20.0)	110 (43.5)	52 (26.0)	223
P 2 – 3	17 (4.5)	61 (17.0)	286 (68.0)	44 (10.5)	408
P 6 +	3 (3.5)	8 (9.8)	94 (65.9)	18 (21.0)	83

Table 4. Breastfeeding according to family income					
	less than 6 weeks	6 months to 6 months	more than 6 months	Artificial Feeding	Total
under \$150	15 (3.0)	69 (14.3)	365 (73.1)	45 (9.0)	494
\$151–300	17 (11.0)	23 (15.0)	69 (44.0)	45 (30.0)	154
\$300 +	9 (14.2)	17 (28.0)	16 (27.8)	24 (30.0)	66

Table 5. Breastfeeding according to mother's occupation					
	less than 6 weeks	6 months to 6 months	more than 6 months	Artificial Feeding	Total
housewife	27 (5.8)	89 (16.7)	329 (60.1)	88 (16.8)	533
help husband	9 (5.7)	14 (8.6)	119 (77.1)	14 (8.6)	166
own occup.	5 (20.0)	6 (24.0)	2 (8.0)	12 (48.0)	25

Table 6. Breastfeeding according to mother's education					
	less than 6 weeks	6 months to 6 months	more than 6 months	Artificial Feeding	Total
nil	8 (4.0)	34 (17.0)	144 (61.9)	35 (17.1)	211
primary	20 (4.3)	56 (13.0)	292 (58.7)	62 (14.0)	430
secondary	13 (20.0)	19 (30.0)	14 (22.3)	17 (27.0)	63

Table 7. Reasons for Artificial Feeding

	Race			Total	Income		
	M	C	O		\$150	\$300	\$300+
1. Social convenience	33	53	5	71	25	20	16
2. Own occupation	13	15	0	28	6	12	10
3. Help husband	35	18	0	53	29	20	4
4. Figure care	1	0	0	1	0	1	0
5. Not enough breast milk	73	72	4	149	88	37	24
6. Baby's preference	43	42	5	90	56	20	14
7. Medical reasons	6	6	1	13	7	5	1
8. Others	7	8	0	15	4	6	5
Total	211	194	15	420	320	129	84

Table 8. Reasons for Breast Feeding

	M	C	O	Total	Income		
					\$150	\$300	\$300+
1. Convenient	170	26	9	205	168	29	8
2. Cheap	134	10	3	147	127	18	2
3. Health for baby	51	16	2	69	43	17	9
4. Health for mother	11	2	0	13	10	2	1
5. Delay pregnancy	17	7	0	24	17	5	2
6. Traditional advice	119	16	6	141	114	19	8
7. Advice from health staff	9	15	0	24	15	7	2
8. Baby's preference	123	17	8	148	123	18	7
9. Others	1	3	0	4	1	3	0
Total	635	112	28	775	618	118	41

Discussion

The sample in this study represents the rural population in Malaysia especially in terms of racial composition, level of income and education. However the area under study has relatively more health facilities compared to other rural areas in the country. But is this an important factor in influencing breast feeding? Few of the mothers who breastfeed did so mainly on advice from health staff as shown by the study. This probably does not mean that our health staff were not doing their job but that most of these mothers were already in favour of breastfeeding because of convenience, economy and tradition. In fact at health centres are found mothercraft nurses giving out samples of milk powder products. The main reasons for breast feeding are easily forgotten, as in the urban areas with better health facilities as soon as the women leave their traditional ties, have higher income and have part-time or fulltime work.

Thus the importance of stress on the effects of breast feeding on the health of both mother and baby. The health staff must be well motivated in order to convince the women otherwise they easily find excuses not to breastfeed. Although infant feeding is a pediatric problem, the motivation must start at the antenatal level i.e. by midwives and nurses in antenatal clinics. Too often this aspect of health education is left till the postpartum period by which time the mothers have seen tempting advertisements on powdered milk, given samples by mothercraft nurses and influenced by their friends on the "inconvenience" of breastfeeding.

The study in this paper fortunately shown that our rural mothers still breastfeed. This is in contrast to studies made in urban centres by Dugdale⁴, Wong³ and Millis⁵. Wong H.B. found in Singapore that in the lower income group only 43% breastfeed at one month and only 5% con-

tinued to do so at 3 months compared to 84.1% and 63.0% respectively in Perlis. In his book, he noted that in U.K. 65% do so at 1 month and 45% remained at it at 3 months.

The study however shown a similar trend in that Chinese, even in a rural area, breastfeeds less. The incidence similarly falls, though not so remarkably, as income and education increases.

Summary

The incidence of breast feeding in a rural community was studied in relation to race, age, parity, income, occupation and education of the mother. The period of study was of children born between 1970 and 1972. The reasons for the choice between breast feeding and artificial feeding were analysed and it was noted that to prevent the trend to artificial feeding as is already present in urban areas, the health staff at MCH clinics should motivate the women even at antenatal periods.

Acknowledgement

I thank Dr. Ahmad Adnan, the state Pengarah, for permission to carry out the study and the Health Matron in Perlis and her staff for their invaluable assistance in collecting the data.

REFERENCES

1. WHO Technical Report Series No. 305.
2. Jelliffe, D.B. Breast Milk and the world protein gap Clin. Pediat. 7:96. 1968
3. Wong H.B. Breast Feeding in Singapore 1971
4. Dugdale A.E. Breast feeding in a South East Asian City Far East Medical J. 6:8 1970
5. Millis, J. Some aspects of Breast Feeding in Singapore Med. J. Malaya 10:157. 1955

Cataract Extraction In West Malaysia

An evaluation of
743 Cataract Extractions
Then S.M. & Chandran S.
Department of Ophthalmology,
Faculty of Medicine,
University of Malaya,
Kuala Lumpur.

INTRODUCTION

Cataract is a common eye affliction of the old and successful surgical removal of the cataractous lens allows the patient to regain good vision. This study is undertaken to evaluate (i) the results of cataract extractions in West Malaysia and (ii) the age group and racial distribution of the cataract subjects.

Only patients with senile and presenile cataracts were included in this series. Cataracts resulting from trauma, uveitis, or associated with other ocular disease and those associated with general disease other than diabetes, were excluded.

MATERIALS AND METHODS

During the period 1968 – 1972, 743 cataract extractions were carried out at the University Hospital, on 671 patients, aged 30 and over. Pre and post-operative visions were recorded. In all cases, the post-operative visual acuity accepted was the latest that was available. This applied to all cases and especially in those following complications, where the final visual acuity was accepted. Chloramphenicol drops were instilled into the conjunctival sac twenty-four hours before operation. Extractions were done under general anaesthesia and only those considered unsuitable for general anaesthesia were done under local anaesthesia. Two types of sections were used.

(a) Graefe Section. This was the technique used on 430 cases operated on between 1968 and

mid 1970. This section was mainly corneal with no conjunctival flap and the incision closed with three to four sutures of 6/0 silk, which were removed between the tenth and twelfth post-operative day.

(b) Ab externo. On 313 cases ab externo section with Bard Parker and corneoscleral scissors with a limbus-based conjunctival flap was employed. The incision was closed with four to five buried sutures of 8/0 virgin silk.

Peripheral iridectomy was done routinely and sector iridectomy in selected cases.

Until mid 1970 the lens was delivered by Aruga's forceps; hypermature lens by erisophake or Smith's expression method. When a cryo extractor was available, this became the method of choice.

From the fourth post-operative day onwards, local steroids were instilled into the operated eye. Those with Graefe section were kept until sutures were removed between tenth and twelfth day and those with buried virgin silk sutures were discharged between fifth and seventh day.

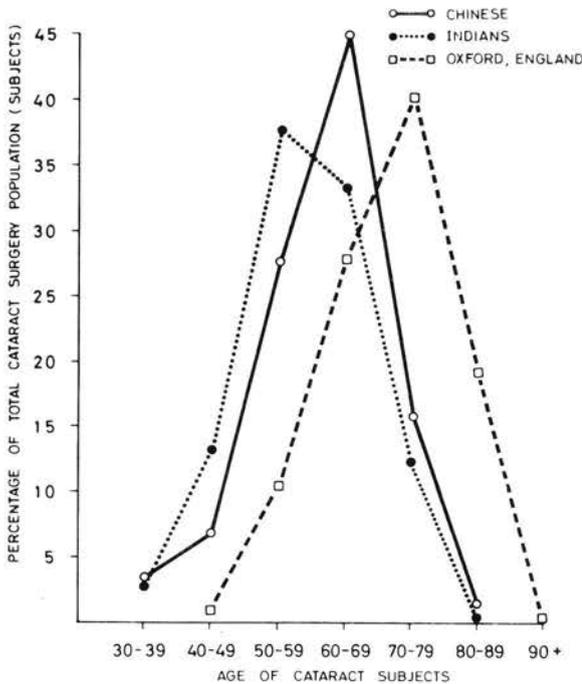
RESULTS

Age and Racial Distribution, Table 1, Figure 1.

The age incidence of cataract extraction shows a peak between fifty and seventy years. This is a decade earlier than the Oxford Group studied by

Caird et al. Among the Indians there was a relatively higher proportion within the 50 – 60 group. Chinese who make up 37% of the population account for 54% of the patients whereas Indians who only make up 12% of the population account for 39%.

FIG. I



Grouping by Morphology, Table II.

The maturity of the cataract was noted pre-operatively. This knowledge was useful during the routine use of capsular forceps. Just over one half were immature and 39% were mature and of these nearly 15% were hypermature.

Operative and Post-operative complications.

Of 743 lens extractions, 599 were intracapsular lens extraction and the rest were extracapsular. In the extracapsular group, 29 were done electively in patients under 35 years old, the remaining 135 were unplanned.

At operation the major complication was vitreous loss and this occurred in 40 cases (Table III). During the early years when cryo extraction was not available, the Smith's expression method and erisophake were used in hypermature cataracts. These methods of extraction resulted in a higher incidence of vitreous loss.

During the early post-operative period there were eighteen cases of hyphaema (Table IV), of which 3 occurred in diabetics, and one was associated with vitreous loss and another with iris prolapse. The latter requiring resuturing. All cases cleared spontaneously with bed rest.

There were seventeen cases of iris prolapse, 14 of which occurred in cases done with Graefe section technique.

There were 14 cases of marked anterior uveitis, which required subconjunctival steroids and mydriatics. Three cases required systemic therapy. Nine of these cases had extracapsular extraction, and one was associated with iris prolapse.

There were 42 cases of loss or shallowing of the anterior chamber making a total of 5.5%. 28 of these cases recovered spontaneously, while 14 or over 1/3 required surgical intervention. In the group that recovered spontaneously, 3 were due to choroidal detachment, 2 due to air in the posterior chamber and 9 followed the removal of corneoscleral sutures. The surgical methods employed for reforming the anterior chamber were as follows:- with air only (6); air plus iridectomy (5); and incision of anterior hyaloid face (3).

Post-operative endophthalmitis occurred in 2 cases. Coagulase-positive staphylococci was isolated in one but none in the other. The final visual acuity was P.L. in the former and 6/60 in the latter. These cases occurred during the first two years of the period of study.

Of the late complications, glaucoma developed in 11 cases. Four of these cases were the result of flat anterior chamber, and one was associated with uveitis, and another with post-operative hyphaema. There were three cases of retinal detachment, three cases of corneal dystrophy and two cases of epithelial invasion of the anterior chamber.

POST-OPERATIVE VISUAL ACUITY

Our follow-up rate was high. All but 19 of the 743 eyes were refracted by us. Over 80% had a preoperative vision of 6/60 or less. The post-operative visual results are discussed under 3 headings.

(a) Series as a whole (Table V)

Post-operatively corrected vision of 6/18 and better was achieved by 85% and vision of 6/6 and above was obtained by 35%. This latter group could have been larger had there been closer co-operation between the patient and the refractionist. In this multi racial/dialect society there is often a communication difficulty and the patient who is refracted to 6/6 usually communicates easily with the refractionist.

(b) Cases with operative complications (Table VI)

The poorest results came from the group that required surgical reformation of the anterior chamber (14 cases). Nine ended up with vision of less than 6/60 and the rest had vision no better than 6/24. Those with vitreous loss fared better and 29 of these had 6/18 and better while five had vision of less than 6/60. In the group that developed glaucoma, 5 had vision of 6/24 to 6/60 and 4 had vision of less than 6/60.

(c) Cases with fundal complications

Fundal complications were seen in 24 cases. These consisted of senile macular degeneration (8), myopic degenerative changes (5), diabetic retinopathy (8), and optic atrophy (3), most of these had a vision of 6/24 or less.

DISCUSSION

In this retrospective study the results of 743 cataract extractions performed over a five year period are evaluated. These extractions were done by six ophthalmologists with varying surgical experience and a small number by the trainee staff. No attempt has been made to separate the results of these two groups in this study.

The overall incidence of vitreous loss of 5.4% compares unfavourably with other surveys (Vail

1965 3.7%). Before cryo extraction, attempts to remove hypermature lens intracapsularly by Smith's expression resulted in vitreous loss in 3 out of the 11 cases when the Erisophake was used occasionally for mature and hypermature lens, there was a loss of vitreous in 3 out of 41 cases (7%). Vectis had to be resorted to on 8 occasions when the lens became subluxated or lying free. Our incidence of vitreous loss with cryo extractions is 3.7%. Cryo extraction has reduced the chief operative complication of vitreous loss. This has been found to be the case in many retrospective studies (Seedorf 1968, Croll 1968).

Of all the postoperative complications those with flat anterior chambers which required surgical intervention, were responsible for the poorest visual results. There were 42 cases with shallowing or loss of the anterior chamber, an overall incidence of 5.5%. 14 of these required surgical intervention. In E. Cotlier's Study on aphakic flat anterior chambers (1972) the incidence was 7.58% in a series of over 8,500 extractions; one out of five requiring surgical intervention. The visual results in our 14 cases are analysed in Table VI. It is noteworthy that all these 14 cases had wound sections with the Graefe technique, with no conjunctival flap using 6/0 silk sutures. The sutures were removed around the 10th post-operative day. Removing these sutures in uncooperative patients were not without danger and 9 cases developed shallowing of the anterior chamber after suture removal. Of 17 cases of iris prolapse, 14 followed Graefe section. There is no doubt that in our series, the complications arising from poor wound healing were more frequently encountered with the Graefe technique than the ab externo technique. In the latter half of this series, the former technique was abandoned and now ab externo is routinely used. Since then, flat aphakic anterior chambers and iris prolapse are very infrequent complications.

This series of cataract extractions involved the 3 main ethnic groups, namely: Malays, Chinese and Indians. But as only 6% of the extractions were Malays, the following discussion is confined to Chinese and Indians.

The Chinese made up 54% of the total extractions, and the Indians contributed to 39%. 72% of these patients who had cataract extractions were between the ages of 50 and 70 years old. This peak age group is a decade earlier than the peak age group for cataract extractions in patients studied by Caird et al (1965) (Table 1, Figure 1). Our patients are not only younger but they also come to operation when their vision is markedly impaired. Over 80% had a preoperative vision of 6/60 or less, and 38% of the cataracts were mature at the time of operation. Patients over the age of 70 represented only 15% of our extractions. 45% of Chinese extractions were in the 60's while 28% were between 50 and 59 years. In the Indians only 33% were in the 60's while 38% were between 50 and 59. All these points are demonstrated in the graph, which shows a shift to the left for the Malaysian, with the shift being more marked in the Indians than in the Chinese. Indians are relatively younger when they had a cataract extraction. However, we have as yet no evidence that cataracts are more prevalent in Indians though they contribute to 39% of our extractions when in the general population they form a mere 12%. The Indians predominate possibly because they prefer to attend public hospital rather than seek private treatment. Nevertheless, there is an impression that cataracts appear to be more prevalent among the Indians.

SUMMARY

The results of 743 cataract extractions in West Malaysia have been evaluated. 6/18 or better vision was obtained in 84% of extractions, out

of which 35% achieved a vision of 6/6 or better. The poorest visual results were seen in those cases which developed post-operative flat anterior chambers which required surgical intervention. The majority of this group had a final visual acuity of less than 6/60 and the best vision obtained was no better than 6/24. Compared with the Graefe section method post-operative complications such as flat anterior chamber, iris prolapse, were fewer with the ab externo method. The peak age group incidence of cataract in Malaysians was a decade earlier than the Oxford series and this shift is more marked in Indians than the Chinese.

ACKNOWLEDGEMENT

We wish to thank the Department of Medical Illustration, University of Malaya, and Mrs. T.C. Lai for assisting in the preparation of this paper.

REFERENCES

1. Caird, F.I. Hutchinson M., & Pirie (1965) "Cataract Extraction in an English Population" *Brit. J. Prev. Soc. Med.* 19, 80-84.
2. Cotlier E., (1972) "Aphakic Flat Anterior Chamber" *Arch. Ophthalmol.* 87 119-123.
3. Croll M., Croll L.J., (1968) "Cryo extraction of cataracts in 351 consecutive cases" *Amer. J. Ophthalmol.* 66, 875-880.
4. Seedorf H.H., B. Lawaety, (1969) "Intracapsular Extraction by the cryo technique and other methods" 47, 761-773.
5. Vail, D. (1965) "After effects of vitreous loss" *Amer. J. Ophthalmol.* 59, 573-586.

AGE AND RACIAL DISTRIBUTION

Age	Chinese	%	Indians	%	Malays	Total	%
30-39	15	3.4	8	2.7	1	24	3.2
40-49	24	6.7	39	13.3	3	66	8.9
50-59	111	27.6	110	37.7	16	237	31.9
60-69	184	45.0	98	33.4	12	294	39.7
70-79	62	15.8	36	12.5	14	112	15
80+	9	1.5	1	0.4		10	1.3
	405	100.0	292	100.0	46	743	100.0

TABLE II

GROUPING OF CATARACT BY MORPHOLOGY

Type	No.	% of Total
Immature	402	54
Mature	243	33
Hypermature	41	5
Uncertain	57	8

TABLE III

METHOD OF LENS DELIVERY AND VITREOUS LOSS

Method	No.	% of the total	No. of vitreous total	% of the loss
Capsule forceps	398	53.5	24	6.0
Cryo-extractor	264	35.5	9	3.7
Erisophake	41	5.5	3	7.2
Elective extra capsular	29	3.9	1	3.4
Smith (Expression)	11	1.5	3	27.2
	743	100.0	40	5.4

TABLE IV
COMPLICATIONS OF OPERATION

Complications	No.	Percentage
Total No. of operation	743	
Operative		
Vitreous loss	40	5.0
Early Post-operative		
Hyphaema	18	2.4
Iris Prolapse	17	2.3
Anterior Uveitis	14	1.9
Flat Anterior Chamber	14	1.9
Infection	2	0.3
Late Post-operative		
Glaucoma	11	1.4
Retinal Detachment	3	0.4
Corneal Dystrophy	3	0.4
Epithelial downgrowth	2	0.3

TABLE V
VISUAL RESULTS AFTER CATARACT
EXTRACTION
(Series as a whole)

Visual Acuity	No. of eyes	% of Total
Defaulters	19	2.6
No P.L.	7	0.9
Less than 6/60	46	6.2
6/60 to 6/24	49	6.6
6/18 to 6/9	364	49.0
6/6 & better	258	34.7
	743	100.0

TABLE VI
VISUAL RESULTS OF COMPLICATED
CASES

Visual Acuity	Iris Prolapse	Flat Anterior Chamber	Anterior Uveitis	Vitreous Loss	Glaucoma
No P.L.	—	2	2	1	2
Less than 6/60	—	7	5	4	2
6/60 to 6/24	6	5	2	6	5
6/18 to 6/9	8	—	5	20	2
6/6 & better	3	—	—	9	—
	17	14	14	40	11

Ecological Assessment Of Vitamin A Status Of Primary School Children In Ulu Trengganu

by
N. Chandrasekharan, B.Sc., M.B.,B.S., Ph.D.,
Associate Professor
Department of Biochemistry
Faculty of Medicine, University of Malaya,
Kuala Lumpur, Malaysia.

Hypovitaminosis A is a well known problem in South and East Asia (Oomen, McLaren and Escapini, 1964) and it has been suggested as an important cause of blindness (Patwardhan, 1969). Prolonged deficiency of the vitamin may have serious effects on growth and development, besides affecting resistance to infection (Hayes, 1971). In Malaysia vitamin A deficiency is often encountered in certain parts of Trengganu, especially amongst pre-school and school going children (Soni, 1971, Chong, Mckay and Lim, 1972 and Chen, 1972).

An understanding of the factors contributing to vitamin A deficiency is very essential for any effective therapeutic or public health programmes aimed at combatting this nutritional problem. The present work gives an account of some nutritional and biochemical investigations for elucidating the multifactorial etiology of vitamin A deficiency amongst children in the district of Ulu Trengganu. It also discusses the interrelationships of various factors affecting the availability and utilisation of vitamin A and its precursors in foods. Such information has considerable bearing on the prophylactic measures for the prevention of this condition. A preliminary account of this work was reported earlier (Chandrasekharan, 1973).

Materials and Methods

Ten primary schools located in different parts of the district of Ulu Trengganu were selected randomly. The children attending these schools were drawn from surrounding villages in some cases up to a radius of 3-5 miles. The enrollment in the schools ranged between 30 and 200 and consisted

of both boys and girls. For the purpose of this study, all children in the schools were examined clinically for evidence of vitamin A deficiency and the following categories of children were picked out for detailed nutritional and biochemical investigations. All those (a) who complained of night blindness or had an history of diminished vision at night (b) who appeared to be malnourished clinically (c) with xerotic changes in the eye and pigments in the conjunctive (d) with hyperkeratosis of the skin. This condition can also be due to causes other than vitamin A deficiency (Kamel, 1973). By this procedure about 10% of the children examined were selected. The sample studied could be considered as representative of the primary school population of Ulu Trengganu. For comparative studies the children attending the primary school in Pulau Perhentian Kechil were investigated.

Blood samples were collected in the morning using vacutainer tubes and the serum was separated from the cells by centrifugation. Serum retinol and β carotene levels were determined by the trifluoroacetic acid method (Gyorgi and Pearson, 1967). Total serum protein concentration was determined with a refractometer (American Optical Co., Buffalo, U.S.A.) and the serum albumin estimated by electrophoresis on cellulose acetate (Chandrasekharan, 1969).

The homes of all students were visited for a detailed enquiry into the family's food habits and food consumption - by the 24 hour recall of the food consumed as well as data on foods purchased in a week. This process was greatly facilitated by trained medical students and school teachers

drawn from the locality, who were very familiar with local conditions and had the confidence of the community investigated. The daily food consumption per individual was calculated and the nutrient intake was computed from food composition tables available for this country (Olivero, 1955, DHEW and FAO, 1974).

Results

The places visited for this study in Ulu Trengganu are shown in Fig. 1. The schools were accessible in most cases by road. Many of the homes had to be approached by foot paths and in some cases by boats. Most of the houses visited had home gardens. Poultry in small numbers were seen in some houses. Some possessed cattle, but fresh milk consumption was practically nil, as the cows were not milked at all. Thus a good source of protein and preformed vitamin A is made unavailable. The majority of the families visited made a living from agriculture. Except for the town of Kuala Brang, there was no electricity or piped water supply in the other places surveyed. Mobile health clinics served these areas periodically. There was no regular school feeding programmes in the schools investigated.

Table I shows the average intake of calories,

carbohydrate, protein, fat and vitamin A by the subjects investigated. Fig. 2 shows the percentage contribution of calories from carbohydrates, proteins and fats in the diets of the children studied. More than 75% of the calorie intake was in the form of carbohydrates.

Only about 10% of the calories were accounted for by fats. The protein intake averaged about 39g per day of which only 35% was animal origin, against the national intake of 49g. The daily consumption of fat was particularly low, fats and oils accounting for only 21g compared with the national figure of 40.6g. (FAO-1971). The fats were mostly of vegetable origin, mainly coconut oil with practically no animal fat.

Consumption of foods rich in preformed vitamin A was very low and infrequent. In fact the only source was fish eaten in small amounts once or twice a week. As fish liver was not generally eaten, a concentrated form of vitamin A is lost. Over 95% of the vitamin A consumed was in the form of the provitamin from vegetables and fruits. The average daily intake of vitamin A in terms of retinol equivalence was 205µg which is inadequate when compared to the recommended allowance of 488µg for the age group under investigation (Van Veen and Van Veen, 1973).

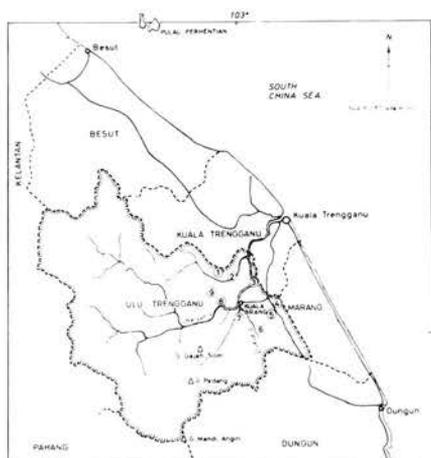


Fig. 1. Map of Ulu Trengganu showing the locations of schools which were surveyed. (1) Tengkwang (2) Matang (3) Tanggol (4) Bukit Apit (5) Bukit Diman (6) Kua (7) Bukit Gemuroh (8) Kuala Dura (9) Tapah and (10) Kuala Brang. Scale: 1" = 16 miles

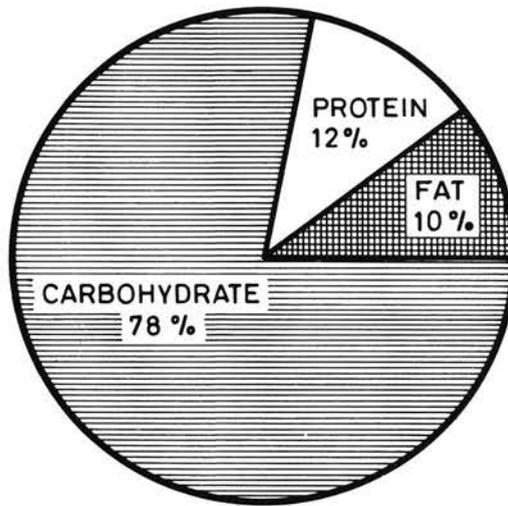


FIG. 2. % CALORIES FROM CARBOHYDRATES, PROTEINS AND FATS IN THE DIETS OF PRIMARY SCHOOL CHILDREN IN ULU TRENGGANU.

Table I

Average daily nutrient intakes of primary school children Ulu Trengganu

Locality	No. of homes visited	Total No. of individuals	Calories		Protein				Fat(g)		Vitamin A 'Retinol Retinol(%) Equivalence'		
			Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean
1. Tengawang	7	40	1580	98	39	5	35	6	19	5	209	13	4.0
2. Matang	16	93	1647	326	43	7	34	13	18	9	203	4	1.3
3. Tanggol	20	132	1571	429	41	15	33	13	20	10	202	2	0.7
4. Bukit Apit	14	96	1605	247	44	9	42	16	21	9	202	2	1.0
5. Bukit Diman	19	117	1550	289	40	9	36	9	22	8	205	9	1.8
6. Kua	10	65	1571	164	36	6	26	8	23	6	202	2	0.7
7. Bukit Gemoroh	21	131	1566	238	40	8	33	8	20	7	210	11	3.4
8. Kuala Dura	8	85	1441	305	37	9	35	18	21	5	207	8	3.0
9. Tapah	3	15	1140	244	27	3	33	16	18	7	205	5	2.3
10. Kuala Brang	25	161	1560	218	42	10	39	12	23	11	205	6	2.8
Average for Ulu Trengganu			1528	147	39	5	35	4	21	2	205	5	2.1
Recommended National Allowance ^(a)			2095		40						488		20

(a) IMR Report No. 64 (1964) Kuala Lumpur

For the purpose of expressing the provitamin A (β carotene) intake in terms of "retinol equivalence" the following factors have been taken into consideration:- The availability of carotenes in diets is 33% and the efficiency of conversion of β carotene into retinol is only 50%. So in man μ g of β carotene in the diet is taken to have the same biological activity as 0.167 μ g of retinol (W.H.O.,1967)

Table 2 shows the serum levels of protein, retinol and β carotene in primary school children. The total serum protein and albumin levels could be considered to be within accepted limits. However the retinol and β carotene levels were lower than those reported for supposedly healthy children from other parts of the country (ICNND, 1964). The serum level of retinol was higher in children from Pulau Perhentian, and the β carotene levels lower than those from Ulu Trengganu. This could be attributed to the greater availability and higher

consumption of fish and other sea foods in the island, which is mainly habited by a fishing community.

Fig. 3 shows the percentage distribution of children examined who could be considered to have a vitamin A nutrition problem based on the criteria of the Pan American Health Organisation (1970). The population is considered to have a vitamin A nutrition problem when 15% or more of the persons surveyed have serum retinol values less than 20 μ g/100ml and/or 5% or more present serum values less than 10 μ g/100ml.

Discussion

The present study provides us with information on dietary intake of some nutrients and the vitamin A status of selected primary school children in the district of Ulu Trengganu.

Table II
Serum protein, retinol and B-carotene levels amongst primary school children in Ulu Trengganu

Locality	No. Examined	Total Protein (g/100ml)		Serum Albumin (g/100ml)		Serum Vitamin A (μ g/100ml)		B-carotene	
		Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
1. Tengawang	17	6.40	0.39	3.7	0.45	16	7	41	14
2. Matang	20	6.20	0.65	3.7	0.39	21	13	42	13
3. Tanggol	22	6.20	0.60	3.5	0.40	25	17	50	26
4. Bukit Apit	20	6.40	0.55	3.7	0.40	26	13	45	14
5. Bukit Diman	23	6.30	0.49	3.6	0.36	25	7	35	17
6. Kua	20	6.10	0.57	3.6	0.47	25	8	37	11
7. Bukit Gemeroh	22	6.50	0.59	3.8	0.41	25	11	49	23
8. Kuala Dura	20	6.30	0.50	3.5	0.35	19	11	39	13
9. Tapah	8	6.90	0.71	3.6	0.48	18	7	42	12
10. Kuala Brang	50	6.30	0.65	3.7	0.48	26	10	48	14
Pulau Perhentian	27	6.80	0.50	3.5	0.37	32	17	29	18
Average for Ulu Trengganu		6.36		3.6		22	4	44	5
Normal School Children ^(b)						29		76	

(b) From ICNND Survey: Federation of Malaya (1962) Interdepartmental Committee on Nutrition for National Defence, Washington, D.C.

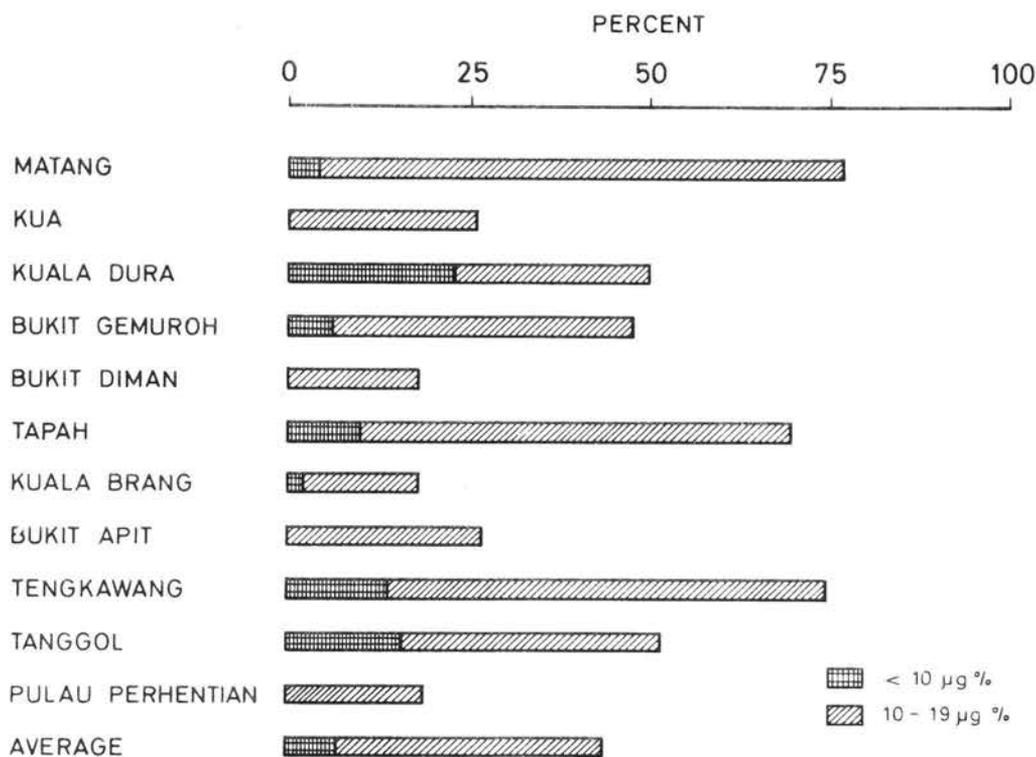


Fig. 3. Percentage distribution of children with vitamin A deficiency in Ulu Trengganu based on serum retinol concentration determinations

The principal source of vitamin A was green vegetables and fruits, the β carotene in them contributing to over 95% of the total daily vitamin A intake. This is much higher than that reported for a rural area in the West Coast of Peninsular Malaysia (Tco, 1973). In most developing countries carotenoids in the diet provide over 60% of the total vitamin A activity ingested (Oomen et al., 1964). A number of dietary factors such as food source, fat and protein intake are known to affect the utilisation of carotenes (Rodriguez and Irwin, 1972). Similarly the utilisation and metabolism of vitamin A are interrelated with several other nutrients in the diet. So in assessing the intake and requirements of vitamin A, one has also to consider the intakes of calories, total protein, animal protein and fat in the diet.

Protein deficiency impairs intestinal absorption, transport and metabolism of retinol and de-

presses conversion of carotene to retinol. It has been reported that there may be an optimal protein intake for maximum carotene utilisation in the gut (Deshmukh and Ganguly, 1964, Mahadevan, Malathi and Ganguly 1965, and Roels and Mack, 1971). Experiments in rats have shown that a high protein intake leads to storage of vitamin A in the liver (Rodriguez and Irwin, 1972). The level of dietary protein in addition to affecting utilisation of vitamin A may also be directly related to the requirement for vitamin A. Vitamin A appears to be required for normal growth, definitely in association with protein utilisation and weight gain (Hayes, 1971). A high protein diet promotes growth and this in turn requires a high rate of expenditure of vitamin A (Moore, 1969).

Adequate serum and dietary proteins are necessary for the mobilisation of retinol from the liver and its transport in the blood. Retinol circulates

in plasma mainly associated with a transport protein called retinol binding protein (RBP). The synthesis of RBP may be affected by dietary deficiencies of protein (Moore, 1969). The quantity and quality of protein consumed cannot be considered to be entirely satisfactory. However the serum levels of protein and albumin do not suggest any protein malnutrition in the children investigated. Increments of dietary proteins may result in increased mobilisation of retinol from the liver and deplete the liver stores faster, if there is no simultaneous increase in the intake of vitamin A. It has been demonstrated that nutritional status with regard to dietary protein and calories may strongly influence vitamin A metabolism by affecting the metabolism of the retinol transport proteins (Smith, Goodman, Zaklama et al., 1973).

The absorption and utilisation of β carotene is also dependent upon the amount of dietary fat and its normal absorption. However, dietary lipids do not appear to be as important for utilising the preformed vitamin A as they are for the pro-vitamins. β carotene is converted to vitamin A by the intestinal epithelial cells and some is also absorbed unchanged (Goodman, Blomstrand, Werner et al., 1966). Animal experiments suggest that both the quantity and quality of fat have a definite effect on carotene utilisation (Rodriguez and Irwin, 1972). Very low intakes of dietary fat may diminish the availability of β carotene. The amount of carotene absorbed from the diet does not depend directly on the amount of carotene it contains, but on the amount of fat with which it is associated. Unsaturated fatty acids are essential for assimilation of vitamin A in animals. In the present study the amount of fat in the diet was relatively low and judging from the nature of oils and fats in the diet could also be considered as poor in unsaturated fatty acids.

The level of carotenoids in plasma are believed to vary and are affected by the preceding intake of carotenoid rich foods. Dietary intake is the only source of carotene in man and in contrast to retinol, it is not stored in the body and dietary deficiency can deplete serum levels in three to four weeks (Goodman, Blomstrand, Werner et al., 1966).

One of the satisfactory ways of determining the extent of vitamin A deficiency problem in population groups resulting from inadequate intake of vitamin A is by the estimation of plasma retinol concentration. The level of retinol has generally been considered as an indicator of vitamin A nutrition. Retinol content of liver influences its serum concentration.

It is known that 90% of the body stores of vitamin A is in the liver. Only when the liver stores of retinol are exhausted, does the level of plasma retinol begin to fall. The low levels of serum retinol are indicative of low liver reserves. This could in turn be attributed to poor utilisation of the pro-vitamin as a result of inadequate intakes of protein and fat, both in terms of quantity and quality. The low intake of both preformed and provitamins could be an additional factor.

Children with low levels of serum retinol represent a very vulnerable group in terms of health and can develop serious clinical lesions of the eye. The ideal long term measure for preventing the occurrence of vitamin A nutrition problem would be the improvement of the diets of all affected and vulnerable groups. An adequate diet in all respects promotes adequate storage of retinol in the liver. As preformed vitamin A is relatively expensive, because it is derived from animal sources, dependence on plant sources is likely to prevail for a long time to come. Increase in the consumption of high quality proteins as well as increase in the intake of fats and oils may facilitate the increased utilisation of the pro-vitamin from plant sources.

In this country the red palm oil is a potent source of β carotene and in view of its associated fat content - the efficiency of utilisation of β carotene is likely to be higher. Palm oil has a β carotene concentration of 4100 μ g/g (Hartley, 1967). In fact red palm oil has been successfully used in the prevention of vitamin A deficiency in West Africa and Indonesia and a considerable degree of protection can be accorded by its use (Roels, Trout and Dujaequier, 1958; Roels, Djaeni Trout et al., 1963; Lian, Tie, Rose et al., 1967). Trials with palm oil after suitable modification are likely to be rewarding. Its use in the prevention of vitamin A deficiency deserves much consideration.

Apart from the long term measures of improving the diet of the vulnerable groups, immediate measures should be taken to supplement their diets with vitamin A preparations. Fortunately for us today, high potency preparations of retinol derivations are available at relatively low prices (Bauernfeind, 1973). In terms of cost for one child's annual requirement of vitamin A as the ester, it would be around 25 cents (twenty five cents). These are very useful in the prevention and treatment of vitamin A deficiency and its clinical manifestations. One massive dose of vitamin A consisting of 100mg or 300,000 I.U. as retinyl palmitate given orally can maintain satisfactory blood levels for between 4-12 months. The side effects, if any, from the administration of such massive doses are usually minimal and are not manifested after 24 hours (Oomen, 1972 and Oomen, 1973). The massive doses would build up liver reserves of the vitamin. Alternatively it is also feasible to give periodic doses of the vitamin in smaller amounts if facilities are available.

Conclusion

The consequences of prolonged deficiency of vitamin A are very serious and incapacitating. "To be able to see is the most precious gift that nature has given us." As such the problem of vitamin A deficiency should be recognised and treated early and appropriate prophylactic measures taken to reduce their occurrence and progress in this country. It would be very unfortunate if we fail to tackle this problem despite the low cost of the vitamin.

Acknowledgement

This work was supported by a grant from the 'F' vote, University of Malaya, Kuala Lumpur. The cooperation of the Health and Education Departments, Trengganu are gratefully acknowledged. It is a pleasure to thank the many students and teachers who cheerfully assisted in this study. Special thanks to Miss Choy Sow Kuen for carrying out the analytical procedures, and Mr. Pikaraju and Mr. Munusamy for field assistance.

Summary

The magnitude of the problem of vitamin A deficiency and the role of various dietary factors

in the etiology of hypovitaminosis A was investigated amongst children attending 10 primary schools in Ulu Trengganu district in Trengganu State.

The dietary intake of various nutrients was obtained by the recall of foods consumed over 24 hours and longer periods. Serum levels of retinol, β carotene and proteins were determined in all children. The protein and fat contributed to 12% and 10% of the total calorie intake respectively. The proteins were mostly of vegetable origin and the fats were of the saturated type. β carotene accounted for over 95% of the vitamin A activity of the diets. Total vitamin A intake was inadequate by recommended standards and serum levels of retinol and β carotene were low, partially due to poor utilisation of the dietary provitamins. The utilisation of the provitamins depends upon many factors amongst which are an adequate supply of dietary protein and fat, both in terms of quantity and quality.

The primary school population is considered to have a vitamin A nutrition problem. Suggestions are made for both short and long term preventive and therapeutic measures to overcome the problem, which if untackled may lead to serious consequences.

REFERENCES

- Bauernfeind, J.C. (1973). In, Vitamin A, Xerophthalmia and Blindness. vol. III p.25. Agency for International Development, U.S. Department of State, Washington, D.C.
- Chandrasekharan, N. (1969). *Far East Med. J.* 5:25
- Chandrasekharan, N. (1973). *Proceedings of the 8th Singapore Malaysia Congress of Medicine* 8:482
- Chen, P.C.Y. (1972). *J. Trop. Med. Hyg.* 75:231
- Chong, Y.H., McKay, D.A. and Lim, R.K.H. (1972). *Bull. Publ. Hlth. Soc.* 6:55
- Deshmukh, D.S. and Ganguli, J. (1964). *Ind. J. Biochem.* 1:204
- Food and Agricultural Organisation (1971) *Production Year Book* 25:435. FAO. Rome

- Goodman, D.S., Blomstrand, R., Werner, B., Huang, H.S. and Shiratori, T. (1966). *J. Clin. Invest.* 45:1615
- Gyorgi, P. and Pearson, W.N. (1967). In *The Vitamin* 6:181, Academic Press, New York
- Hartley, C. (1967). *The Oil Palm*, Longmans, London.
- Interdepartmental Committee on Nutrition for National Defence:(ICNND) Federation of Malaya. Nutrition Survey 1962. N.I.H. Bethesda Maryland U.S.A.
- Kamel, W.W. (1973), In *Vitamin A. Xerophthalmia and Blindness*, vol. I p.41. Agency for International Development, U.S. Department of State, Washington D.C.
- Lian, O.K., Tie, L.T., Rose, C.S., Prawiranegara D.D. and P. Gyorgi (1967). *Am. J. Clin. Nutr.* 20:1267
- Mahadevan, S., Malathi, P. and Ganguli, J. (1965) *World Rev. Nutr. Diet* 5:209
- Moore, T. (1969) *Am. J. Clin. Nutr.* 22:1095
- Oliveiro, C.J. (1955) *Proc. Alumni Assoc. Malaya.* 8:105
- Comen, H.A.P.C., McLaren, D.S. and Escapini, E. (1964). *Trop. and Geog. Med.* 4:271
- Comen, H.A.P.C. (1972). *Tropical Doctor.* 2:169
- Comen, H.A.P.C. (1973). *Xerophthalmia Club Bulletin*, No. 3 May 1973
- Pan American Health Organisation (1970). *Hypovitaminosis A in the American Region*. Regional Office of the World Health Organisation, Washington, D.C.
- Patwardhan, V.N. (1969). *Am. J. Clin. Nutr.* 22:1106
- Rodriguez, M.S. and Irwin, M.I. (1972). *J. Nutr.* 102:909
- Roels, O.A., Trout, M.E. and Dujaeuquier, R. (1958). *J. Nutr.* 65:115
- Roels, O.A., Djaeni, S., Trout, M.E., Lauw T.G., Health, A., Poey S.E., Tarwotji, M.S. and Sahardi, B. *Am. J. Clin. Nutr.* 12:380
- Roels, O.A. and Mack (1971). *Proc. Am. Chem. Soc. Annual Meeting*
- Smith, F.R., Goodman, D.S., Zaklama, M.S., Gabr, M.K., Maraghy, S.E., and Partwardhan, V.N. (1973). *Am. J. Clin. Nutr.* 26:973
- Soni, V.K. (1971) Report on the Malaysian Association for the Blind Mobile Eye Clinic East Coast Project, May - Aug. 1971. Ministry of Health, Malaysia.
- Teoh Soon Teong (1973). *Med. J. Malaysia* 27:243
- U.S. Department of Health, Education and Welfare (1974). *Food Composition Tables for Use in East Asia*. Bethesda, Maryland U.S.A.
- Van Veen, A.G. and Van Veen, M.S. (1973). In *Vitamin A, Xerophthalmia and Blindness* p.52. vol. 2: Agency for International Development, U.S. Department of State, Washington, D.C.
- World Health Organisation (1967). *Requirements of vitamin A thiamine and niacin*. Technical Rep. Series No. 362. W.H.O. Geneva

The Management of Residual Bile Duct Calculi

by HUSSEIN BIN MOHAMED SALLEH

MB.BS. (Adelaide): F.R.C.S. (Edinburgh):

A.M. (Malaysia)

Consultant Surgeon and Head

Surgical Unit 3, General Hospital

Kuala Lumpur

After any operation on the gall bladder or bile passages, there is always the possibility of a residual stone, that is, a retained stone which had been overlooked or a recurrent stone which had formed later. It is a serious complication due to the potential development of ascending cholangitis with subsequent liver damage. In the hands of even the most experienced biliary-tract surgeons, the incidence of retained stones after choledocholithotomy varies from 8% to 9% (SMITH et alii 1957) up to 16% to 25% (PRIBRAM 1947) of choledocholithotomies.

PROPHYLAXIS

COMMON BILE DUCT EXPLORATION

HAVARD (1960) has shown that the more often the common bile duct is explored, the lower is the incidence of residual stones. However, routine exploration of the common bile duct has its hazards, there being increased morbidity and mortality. BARTLETT and WADDELL (1958) reported a mortality rate of 0.6% after cholecystectomy alone whilst combined cholecystectomy and choledochotomy produced a 1.8% mortality rate. COLCOCK (1958) stated that there was a 0.9% mortality rate following cholecystectomy only and this increased to 1.1% with the addition of choledochotomy. The length of hospital stay is one of the factors contributing to morbidity after biliary surgery (SALLEH and BALASEGARAM, 1974) and the addition of choledochotomy to cholecystectomy certainly increases the time that the patient spends in hospital (NIENHUIS 1961).

The indications for exploring the common bile duct are now well standardised (ADAMS and STRANAHAN 1947; COLCOCK and PEREY 1964), namely:—

- (1) A present or past history of obstructive jaundice or biochemical evidence of such

jaundice.

- (2) Frequent acute attacks of fever, chills or biliary colic.
- (3) Multiple stones in the gall bladder.
- (4) A dilated or thickened common bile duct.
- (5) "Dirty-looking or muddy" bile aspirated from the gall bladder or bile duct.
- (6) The patient has symptoms and signs of biliary tract pathology but the gall bladder appears and feels normal at operation.
- (7) The gall bladder is small and contracted.
- (8) Suspicious or unsatisfactory findings on palpation of the common bile duct.
- (9) Pancreatitis — acute or otherwise.

CHOLANGIOGRAPHY

Intravenous cholangiography has only limited use as the resulting picture of the bile ducts is often rather vague, the finer details of the ducts being lacking. The procedure is contra-indicated if the serum bilirubin is 3 milligrams per 100 millilitres or more, denoting inability of the liver to excrete the dye into the bile in significant amounts. Moreover even if the serum bilirubin is less than 3 milligrams per 100 millilitres, there is a high incidence of non-visualisation of the bile ducts after intravenous cholangiography and BEARGIE et alii (1962) reported insufficient opacification of the bile ducts in 39% of such cases.

Percutaneous transhepatic cholangiography is useful only in those instances where the intra-hepatic bile ducts are so dilated that they can be easily entered by a needle. A stone may be present in the common bile duct without producing dilatation of the intrahepatic ducts. Furthermore, there is the known danger of bile leakage resulting in biliary peritonitis with possible mortality after a successful percutaneous transhepatic cholangiogram in a patient with greatly increased intraductal biliary pressure.

Cholangiography is most useful when done pre-operatively before and after common bile duct exploration. Pre-exploratory operative cholangiography is more accurate than the accepted "clinical" indications for choledochotomy and should become a routine procedure in all biliary operations (LAWSON and GUNN 1970). Post-exploratory per-operative T-tube cholangiography is a less accurate procedure in visualising stones due to oedema and spasm following bouginage (GRIFFIN and WILD 1967) and the presence of intra-ductal air bubbles.

ASSOCIATED PROCEDURES

When there is much sludge and debris in the common bile duct and where there has been significant damage to the liver so that it is thought possible that matter will fall from the liver into the common bile duct, it is wise to consider some form of internal biliary drainage procedure. This will mean that residual stones are more likely to be discharged into the small intestine. The procedures available are sphincterotomy, choledochoduodenostomy and choledochojejunostomy.

SPHINCTEROTOMY

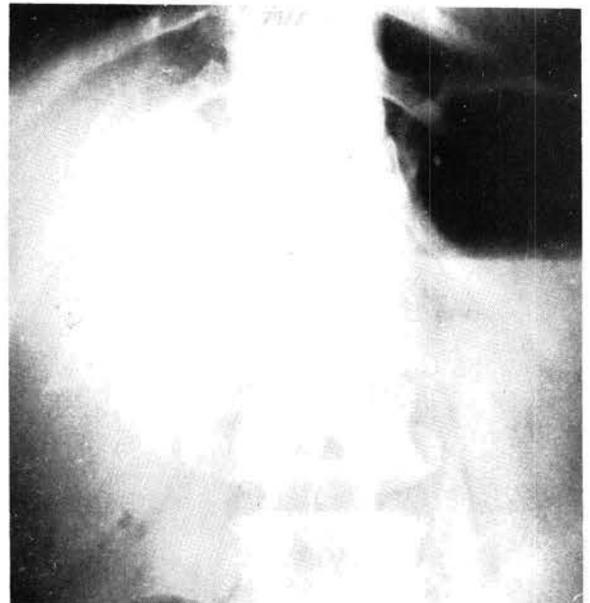
The advantages of this operation are that there is no anastomosis and bile passes along its normal route. However there is an increased possibility of ascending cholangitis since intra-duodenal pressures may be quite high (SMITH 1973). Further the pancreatic duct may be damaged during the operation. A potentially serious complication of sphincterotomy is acute pancreatitis (JOHNSON) and RAINS 1972). KEIGHLEY *et alii* (1969) reported that 56% of patients who underwent sphincterotomy or dilatation of the sphincter had significantly raised serum amylase levels post-operatively. When post-operative pancreatitis does occur, the mortality may go up to 77% (THOMPSON *et alii* 1957). In addition after a sphincterotomy, the patient may develop a leak from the duodenotomy incision.

CHOLEDOCHODUODENOSTOMY

In favour of this procedure is the resulting large stoma and the ease and speed of performance - particularly useful in poor risk patients. It has few immediate post-operative complications. A disadvantage of the operation is that there is an increased risk of ascending cholangitis since the intra-duodenal pressures may be quite high. Further, that part of the common bile duct between the stoma and the

ampulla of Vater may fill with food residue resulting in biliary calculi and ascending cholangitis (SMITH 1973).

CASE REPORT - Female, L.A.Y. Age 35 years. GIP No. 492/74. Admitted to General Hospital, Kuala Lumpur, on 10-4-74 with rapidly deepening jaundice and early liver failure. Emergency common bile duct decompression was performed on 11-4-74. At operation, there were multiple small liver abscesses and a huge common bile duct, 6 centimetres wide and containing about 100 millilitres of dirty looking bile under great pressure, was drained. 6 stones were quickly removed from the duct and 2 large branched stones removed from the left main hepatic bile duct by splitting the liver substance. Due to the extremely poor state of the patient no further time was lost in trying to remove other ductal stones which were present. A T-tube was inserted. On 16-5-74, when the patient's jaundice had disappeared and she was in a very good state of health, re-exploration of the bile ducts was performed to remove multiple stones which were shown on T-tube cholangiography after the first operation. Eight stones were removed and a choledochoduodenostomy was done (FIGURE 1).



CHOLEDOCHOJEJUNOSTOMY

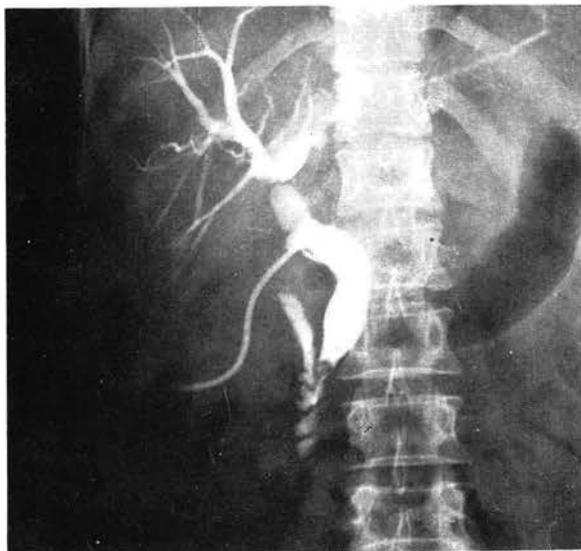
This may be performed either end-to-end ROUX-en-Y or end-to-side with entero-enteric anastomosis. The advantage of the operation is that the pressure within the lumen of the jejunal loop used for the anastomosis is minimal so that there is less risk of ascending cholangitis. The disadvantages of the procedure are that there are two anastomotic sites and it is a more difficult and slower operation so that it is usually not suitable for poor-risk patients. It is important to avoid excessive mobilisation of the common bile duct so that the blood supply of the duct near the anastomotic site is not compromised (ONG 1962).

TREATMENT

NON-OPERATIVE METHODS

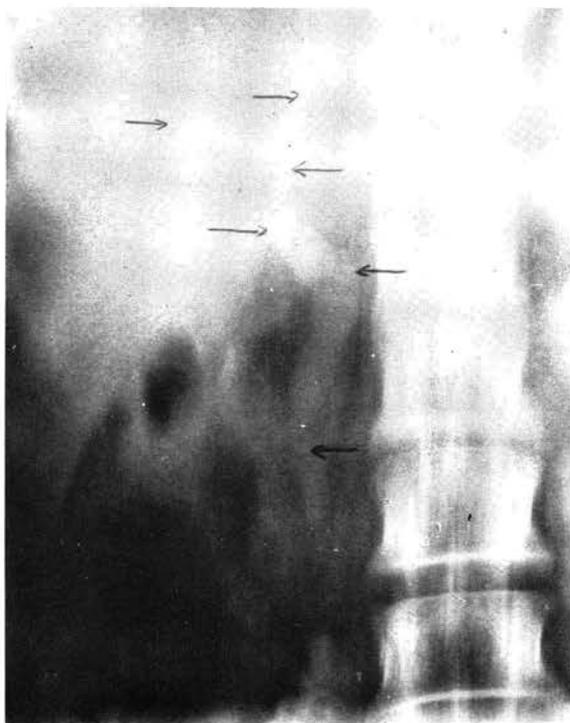
Since secondary choledocholithotomy is associated with an operative mortality of approximately 10% (THOMSON 1956), every other available non-operative procedure should be tried first in the management of residual stones. Early re-exploration to remove residual stones is fraught with danger (HUGHES 1955) and operative methods should not be tried for at least one month after the original operation (WAY et alii 1972). Four procedures are available, namely:—

- REMOVAL OF THE T-TUBE
- CHEMICAL DISSOLUTION
- FLUSHING
- INSTRUMENTAL MANIPULATION



REMOVAL OF T-TUBE—If the stone appears small on the T-tube cholangiogram and therefore seems likely to pass out on its own or if the patient is too ill to tolerate other procedures to remove it, including secondary lithotomy, then the T-tube is clamped for a week. If this does not lead to pain or jaundice or chills and rigors, then it is removed.

CASE REPORT — Female K.K. Age 34 years. GIP No. 1431/72. Admitted to General Hospital Kuala Lumpur on 22-11-72 with empyema gall bladder. She was operated upon on 23-11-72 when a large empyematous gall bladder together with three small common duct stones were removed. T-tube cholangiogram (FIGURE 2) done on the tenth day post-operatively showed a small stone in the lower end of common bile duct. Clamping the T-tube for seven days produced no complaints and it was then removed. She was re-admitted on 13-12-72 with chills, fever, rigors, jaundice and severe biliary colic which rapidly improved over the next 2 days. Intravenous cholangiogram (FIGURE 3) done on 27-3-74 was reported by the specialist radiologist as normal. Presumably the patient passed her biliary stone on the second admission to hospital.

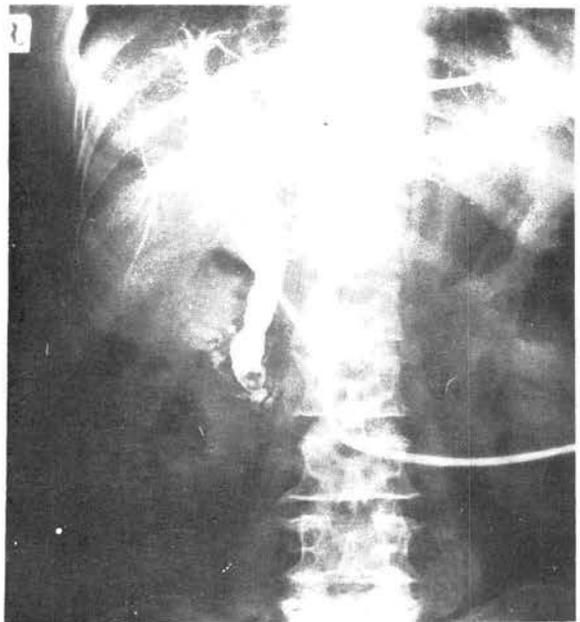


CASE REPORT - Very obese female ABHB. Age 48 years. Suffers severe diabetes and ischaemic heart disease. GIP No. 422/72. Admitted to the unit at General Hospital, Kuala Lumpur, on 28-3-74 with severe obstructive jaundice. The patient was operated upon on 4-4-74 as an emergency due to deepening jaundice and early liver failure. At operation, it was found that the liver was cirrhotic with multiple small abscesses and the gall bladder was inflamed. Cholecystectomy was done and a common bile duct stone removed. Due to the very poor general condition of the patient, very little time was spent in exploring the common bile duct. T-tube cholangiogram on the tenth day showed a large stone in the lower end of the common bile duct (FIGURE 4). Common bile duct flushing was attempted with no success and the patient complained of severe pain during the procedure. T-tube clamping produced no complaints, and it was removed. To-date she remains well.

CHEMICAL DISSOLUTION - WALKER (1891) was the first to do this successfully when he used ether topically through a cholecystostomy fistula to dissolve a stone. PRIBRAM (1947) achieved 100% success in 51 patients by injecting ether repeatedly through the T-tube and into the common bile duct to treat retained stones. BEST et alii (1953) found chloroform effective for dissolving cholesterol stones. GARDNER et alii (1971) instilled a heparin solution through the T-tube into the common bile duct and achieved some degree of success in removing retained calculi. They postulated that the suspension stability of particles in bile is increased by the addition of a highly negatively charged ion. Heparin supplies such an ion. COLE and HARRIDGE (1957) reported that in nine patients after bile salts were given orally daily for some weeks, retained stones disappeared. Possibly this was due to increased biliary flow or increased capacity of the bile to solubilise cholesterol. WAY et alii (1972) infused sodium cholates into the common bile duct via the T-tube and had some success in removing residual stones. It is theorised that one of the causes of cholesterol gall stone formation is an increase in the amount of cholesterol relative to bile salts and therefore cholesterol gall stones can be dissolved in micellar bile salt solutions.

FLUSHING - This was applied in a patient with retained common bile duct stones (FIGURES 8 and 9). The method used was that described by CATT et alii (1972). The flushing fluid consists of one litre of sterile normal saline containing 40 millilitres of 1% lignocaine and this is run through the T-tube into the common bile duct as rapidly as possible after the injection of 100 milligrams of buscopan (hyoscine N-butylbromide) intra-muscularly thirty minutes previously.

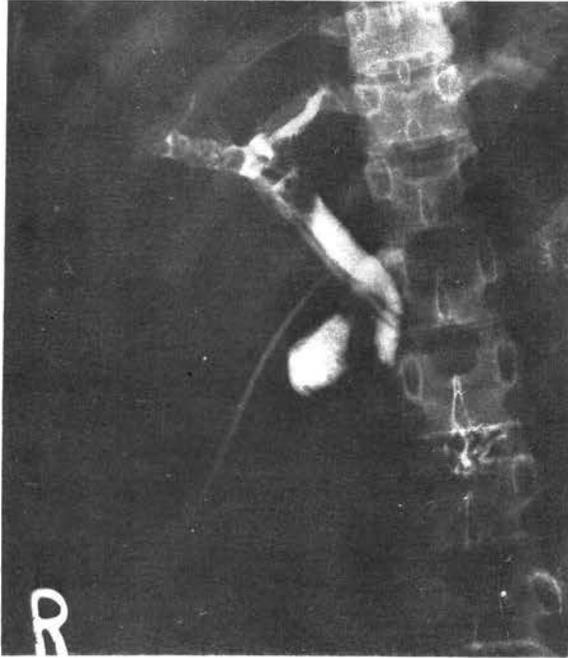
INSTRUMENTAL MANIPULATION - WAY et alii (1972) have successfully used the DORMIA ureteral stone basket under radiological control to extract retained common bile duct stones. This instrument was passed through the T-tube and into the common bile duct.



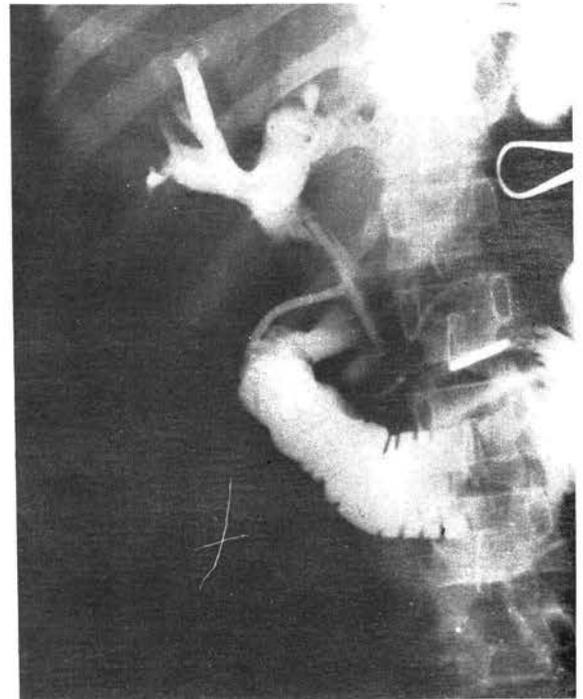
OPERATION

When all the above non-operative methods have been tried, and especially when in addition T-tube clamping produces complications due to the residual stone, secondary choledocholithotomy is required to remove the residual stone. It is essential that the T-tube be left in-situ so that it acts as a guide to the common bile duct at the second operation which is made difficult due to fibrous adhesions around the duct. In some cases where so many small and large stones have been

left behind at the original operation, it is pointless to try the non-operative methods and re-exploration of the common bile duct should be done one month later.



CASE REPORT - Female Y.A.E. Age 25 years. GIP No. 157/74 Admitted to General Hospital, Kuala Lumpur, on 2-2-74. Operated upon by another doctor on 6-2-74 when the gall bladder and three stones from the common bile duct were removed. Post-operative cholangiogram on the seventh day showed many residual stones in the common bile duct (FIGURE 5). On 13-3-74 that is just over one month after the first operation, secondary choledocholithoromy was performed yielding over a hundred small and large stones from the common bile duct (FIGURE 6). T-tube cholangiogram done per operatively was reported by the specialist radiologist as "normal - no stones seen", (FIGURE 7). Post-operative T-tube cholangiogram seven days later showed three stones in the right hepatic bile duct (FIGURE 8). These were flushed out by the method of CATT et alii (1973) using saline and lignocaine after a preliminary injection of buscopan (hyoscine N-butyl-bromide). The final T tube cholangiogram was normal (FIGURE 9). She remains well to-date.





SUMMARY

Residual stones in the extra-hepatic biliary ducts after bile duct exploration occur in a significant number of cases. The routine use of operative cholangiography in addition to the accepted "clinical indications" for exploring the common bile duct will reduce the incidence of residual stones. Secondary choledocholithotomy carries a definite mortality and usually should be performed only after all non-operative methods of removing residual stones have first been tried.

Illustrative cases operated upon by the author are reported

ACKNOWLEDGEMENTS

I thank the DIRECTOR GENERAL, Health Ministry, Malaysia, TAN SRI DATUK (DR.) A.M. ISMAIL, F.R.C.S.(E); M.CH. (ROTH); F.R.A.C.S., for his kind permission to publish this article. The assistance given by my radiologist colleagues at the General Hospital, Kuala Lumpur, is gratefully acknowledged. I thank Miss Ng Fei Fei for typing the manuscript.

I thank PROFESSOR G.B. ONG, Professor of Surgery at the Medical School of the University of Hong Kong and A.M. ISMAIL gold-medallist

(College of Surgeons of Malaysia) for kindly reviewing my article.

REFERENCES

1. ADAMS, R., and STRANAHAN, A. (1947) *Surg. Gynec. Obstet.* 85:776
2. BARTLETT M.K., and WADDELL, W.R. (1958) *New Eng. J. Med.* 258: 164
3. BEARGIE, R.J., HODGSON, J.R., HUIZENGA, K.A. and PRIESTLEY, J.T. (1962) *Surg. Gynec. Obstet.* 115:143
4. BEST, R.R., RASMUSSEN, J.A. and WILSON, C.E. (1953) *Ann. Surg.* 138:570
5. CATT, P.B., HOGG, D.F., HARDIE, I.R. and CLUNIE, J.A. (1973) *Asian Med.J.* 9:234
6. COLCOCK, B.P. (1958) *Surg. Clin. N. Amer.* 38:663
7. COLCOCK, B.P. and PEREY, B. (1964) *Surg. Gynec. Obstet.* 118:20
8. COLE, W.H. and HARRIDGE, W.H. (1957) *J.A.M.A.* 164:238
9. GARDNER, B., OSTROWITZ, A. and MASUR, R. (1971) *Surgery* 69:854

10. GRIFFIN T.F.R. and WILD, A.A. (1967) Br. J. Surg. 54:609
11. HAVARD, C. (1960) Ann. Roy. Coll. Surg. Eng. 26:88
12. HUGHES, E.S.R. (1955) Br. J. Surg. 43:198
13. JOHNSON, A.G. and RAINS, A.J.H. (1972); Br. J. Surg. 59:277
14. KEIGHLEY, M.R.B., JOHNSON, A.G. and STEVENS, A.E. (1969) Br. J. Surg. 56:424
15. LAWSON, R.A.M. and GUNN, A.A. (1970) J.I.R. Coll. Surg. Edin. 15:222
16. NIENHUIS, J.I. (1961) Ann. Surg. 154:192
17. ONG, G.B. (1962) Arch. Surg. 84:199
18. PRIBRAM B.O.C. (1947), Surgery 22:806
19. SALLEH, HUSSEIN BIN MOHAMED and BALASEGARAM, M. (1974) Br. J. Surg. 61 : 705
20. SMITH, R. (1973). Personal communication, LONDON.
21. SMITH, S.W., ENGEL, C., AVERBROOK, B. and LONGMIRE, W.P., Jr. (1957); J.A.M.A. 164:231
22. THOMPSON, J.A., HOWARD, J.M., and VOWLES, K.D.J. (1957) Surg. Gynec. Obstet. 105:706
23. THOMSON, F.B. (1956), Surg. Gynec. Obstet. 103:78
24. WALKER, J.W. (1891) Lancet 1:874
25. WAY, L.W., ADMIRAND, W.H. and DUNPHY, J.E. (1972) Ann. Surg. 176:347

LEGENDS

- FIGURE 1 - Patient L.A.Y. Choledochoduodenostomy done. Gas in biliary tree after drinking "Pepsi Cola"
- FIGURE 2 - Patient K.K. T-tube cholangiogram ten days after operation shows small stone in lower end common bile duct.
- FIGURE 3 - Patient K.K. Intravenous cholangiogram with tomography 16 months after operation shows no stone.
- FIGURE 4 - Patient A.B.H.B. T-tube cholangiogram 10 days post-operatively shows large stone in lower end common bile duct.
- FIGURE 5 - Patient Y.A.E. Cholangiogram seven days after first operation shows numerous stones in extrahepatic bile ducts.
- FIGURE 6 - Patient Y.A.E. More than 100 stones removed at the second operation.
- FIGURE 7 - Patient Y.A.E. Post-exploratory T-tube cholangiogram during second operation reported as "normal, no stones seen".
- FIGURE 8 - Patient Y.A.E. T-tube cholangiogram done seven days after second operation shows three stones in right hepatic duct.
- FIGURE 9 - Patient Y.A.E. T-tube cholangiogram after flushing is normal.

Problems In The Early Diagnosis Of Genital Tuberculosis

by

Dr. A. Puraviappan, MBBS, FRCS(Edin), MRCOG.

Dr. Ng Keng Hing, MBBS, FRCS(Edin) MRCOG.

Dr. Wong Wai Ping, MBBS, FRCS(Edin) MRCOG.

Genital tuberculosis is found in 3-4 per cent of necropsies in women and 7-8% of those who had pulmonary tuberculosis. Although the incidence of pulmonary tuberculosis is 154 per 100,000 population in Peninsular Malaysia (Global Epidemiology of Tuberculosis 1967), our experience of genital tuberculosis in Malaysia is infrequent. Between 1968 and 1973, out of a total of 8,644 gynaecological admissions there were only six cases of genital tuberculosis. Moreover out of a total of 493 infertility cases seen between 1968 and 1971 only in one case was genital tuberculosis confirmed. The reason for this infrequent occurrence of genital tuberculosis here may be because this is a peculiarity to this part of the world. But on the other hand it may be possible that we may be missing some cases here.

SYMPTOMATOLOGY:

AGE

This ranged from 22 years to 48 years as shown in Table 1.

SYMPTOMS

The patients presented with a variety of symptoms, namely infertility, pain, fever, menstrual disorders, or a mass in the abdomen. Table 1 shows the mode of presentation of these cases.

PAST HISTORY

None of these patients gave a history of previous pulmonary tuberculosis or even family history of tuberculosis.

CLINICAL FEATURES

The findings that were detected in these cases are given in Table II. Patient number 6 initially had a pelvic abscess but it was not until she developed sub-phrenic abscess six months later that a diagnosis of pelvic tuberculosis was made.

The time taken between the initial diagnosis and the final correct diagnosis varied from patient to patient. Table III illustrates the time taken in the diagnosis.

In none of these cases was an initial diagnosis of genital tuberculosis made. The initial and final diagnosis is given in Table IV.

The investigations that were done in each of the individual is given in Table V and Table VI.

DISCUSSION:

The presentation of these six cases of genital tuberculosis are varied in certain respects. Although one patient was investigated for infertility initially, three of the patients did not have any children although they were married. Abdominal pain was the main symptom in four patients and this corresponds with most of the series reported (Sutherland, 1943; Schaffer, 1965)

The mode of presentation had been difficult in each case so that each mimicked some other condition. As we can see from table IV, the initial diagnosis was never tuberculosis. The last two cases were only diagnosed at a later period for they both presented as acute salpingitis or pelvic abscess. Only when the tubes were sent for histology that a diagnosis of genital tuberculosis was made.

In all these cases there was no history of tuberculosis or even any evidence of tuberculosis in the chest. This suggests that genital tuberculosis is often a complication of mild forms of pleuropulmonary tuberculosis. (International Symposium on Female Genital TB 1964).

The correct diagnosis was arrived at histologically in five of these cases and this seems to be the best aid since there seems to be a relatively lower incidence of this condition in Malaysia. Again the fallopian tubes were affected in all the three cases that have been sent for histology. Except for the two cases where tuberculosis was confirmed by culture and Guinea Pig Innoculation, the rest were based on histological diagnosis.

CONCLUSIONS

The incidence of genital tuberculosis seems to be rare in Malaysia and the early diagnosis

is often difficult. Hence clinicians should be on the look out for it, in order to avoid delay in diagnosis. Histological diagnosis is more useful although additional information from culture, guinea pig inoculation would be most helpful.

REFERENCES

1. Fertility & Sterility, 14: 284-299, 1963
2. Schaefer G., Obstet. & Gynae. Survey, 8: 461 1953
3. Schaefer G., Sutherland, Arthur M., Am. J. Obstet. & Gynaecol., 91: 714, 1965
4. Stallworthy, J., J. of Obstet. & Gynae. Brit. Cwlth, 59: 729, 1952
5. Studdiford W., Am. J. of Obstet. & Gynaecol., 69: 379, 1955
6. International Symposium On Femal Genital TB., July 1964

TABLE I

AGE AND SYMPTOMS OF PATIENTS

Patients	Age	Infertility	Pain	Fever	Menstrual Disorders		Mass In The Abdomen
					Amenorrhoea	Oligomenorrhoea	
1	30	+	-	-	-	-	-
2	22	-	+	-	-	+I	+
3	48	-	+	-	-	-	+
4	31	-	-	-	+I	-	-
5	25	-	+	-	-	+L	-
6	25	-	+	+	+L	-	-
		1	4	1	2	2	2

+ Present
- Absent

I When Initially Seen
L Follow-up

TABLE II

CLINICAL FEATURES

Patients	Tenderness Over Abdomen	Mass In Abdomen	Tenderness Over Fornix	Pelvic Abscess
1	—	—	—	—
2	—	+	—	—
3	—	+	—	—
4	—	—	+	—
5	+	—	—	—
6	+	—	+	+
	2	2	2	1
	+ Present		— Absent	

TABLE III

PERIOD BETWEEN INITIAL AND FINAL DIAGNOSIS

Patients	Initial	Final	Time Lapse
1	19.8.68	15.11.68	3 months
2	3.2.71	26.3.71	1½ months
3	1.8.72	18.8.72	17 days
4	30.7.73	15.8.73	16 days
5	23.12.72	13.3.74	1 year 4 months
6	16.2.73	16.10.73	8 months

TABLE IV

INITIAL AND FINAL DIAGNOSIS

Patients	Initial	Final
1	1 ^o Infertility — ? Cause	Genital TB — TB Endometritis
2	(L) Ovarian Tumour — Tubo-Ovarian Mass	Genital TB
3	Ovarian Tumour	Genital & Peritoneal TB
4	Ovarian Tumour	Genital TB
5	Acute Salpingitis	Genital TB — TB Salpingitis
6	Pelvic Abscess & Subphrenic Abscess	Genital TB — TB Salpingitis

TABLE V
INVESTIGATIONS

Patients	X-Ray Chest	ESR mm/hr	Histology	Culture	Guinea Pig Innoculation
1	Negative	30	Material Insufficient	Positive	Positive
2	Negative	46	TB	Positive	Positive
3	Negative	68	TB	Negative	Negative
4	Negative	35	TB	Negative	Negative
5	Negative	27	Suggestive of TB	Negative	Negative
6	Negative	30	TB Salpingitis	Negative	Negative

TABLE VI
TYPES OF TISSUES SENT FOR HISTOLOGICAL DIAGNOSIS

Patients	Endometrium	Tubes	Ovarian	Modes & Others
1	Material Insufficient	Not Taken	Not Taken	Not Taken
2	Negative	Positive	Positive	Positive
3	Not Done	Not Taken	Not Taken	Positive
4	Negative	Not Taken	Biopsy Negative	Positive
5	Negative	Positive	Negative	Negative
6	Negative	Positive	Negative	Negative

Acute Myocardial Infarction In Systemic Lupus Erythematosus

K.L. KHOO and PILLAY, R.P.

Department of Medicine,
General Hospital,
Kuala Lumpur,
Malaysia.

The heart is commonly involved in systemic lupus erythematosus, the usual manifestations of this are Libman-Sacks endocarditis, pericarditis, myocarditis, and sometimes vasculitis effecting small coronary vessels. Acute myocardial infarction occurring without other predisposing factors is rare in systemic lupus erythematosus. We report such a case in this paper.

CASE REPORT

The patient was a 37 years old nurse who developed severe idiopathic thrombocytopenic purpura in April 1958. This could not be controlled with corticosteroids but she improved following splenectomy and after this required no other treatment. The blood was examined for L.E. cells and was negative on six occasions.

During the next five years her hair became scanty. She developed acute nephritis in November 1969. L.E. cells were detected then for the first time and a diagnosis of systemic lupus erythematosus was made. She was treated with prednisolone and improved. The blood pressure returned to normal though she still had occasional slight proteinuria. She was maintained on prednisolone 5 mg on alternate days. In October she was admitted to hospital for fever, rigors and generalised bodyache for 5 days. She had a left-sided chest pain, palpitation and shortness of breath the day prior to her admission and was said to have fainted once at home on the day of admission.

She was observed to have a generalised fit as she was wheeled to the ward. She looked pale and had a temperature of 100°F. There was no ankle oedema. The pulse was regular 44/min and

the blood pressure was 80/50 mmHg. The apex beat was not palpable. There was varying intensity of the first heart sound. No murmurs or pericardial friction rub was heard. The lungs were clear on auscultation. The rest of the physical examination did not reveal any further abnormality. The electrocardiogram was grossly abnormal. It showed complete heart block (Fig. 1) with atrial rate 125/min and ventricular rate 47/min. Peripheral blood picture showed leucocytosis and L.E. cells were found on three successive days. Urine did not contain protein. Serum lipids were normal: Cholesterol 164 mg%, triglycerides 72 mg%. Serum uric acid 3.7 mg%, serum proteins 7.7 g% albumin 3.7 g% globulin 3.8%. S.G.O.T. 690 Reitman-Frankel units/ml, E.S.R. 57 mm in 1 hour and blood urea 45 mg%. On the next day the S.G.O.T. was 520 units/ml and S.G.P.T. more than 400 units/ml.

She was given intravenous atropine, isoprenaline by infusion and hydrocortisone 200 mg four hourly. The patient reverted to sinus rhythm 14 hours later. The electrocardiogram (Fig. 2) confirmed this, and showed extreme left axis deviation, dominant R and ST elevation in the right praecordial leads, and ST depression and T wave inversion in the left praecordial leads. The tracing indicated severe myocardial ischaemia and possible infarction.

DISCUSSION

Myocardial infarction is not uncommon in other collagen diseases, for example polyarteritis nodosa (Holzniger et al 1962) and rheumatoid arthritis (Swezey 1967 and Sokoloff 1964), but it is rare in systemic lupus erythematosus.

Several authors who reviewed the cardiac manifestations of systemic lupus erythematosus have found no instance of occlusion of a major coronary artery (Shearn 1959, Brigden et al 1960, Hejtmancik et al 1964). On the other hand, there have been a few reports of myocardial infarction (Larson 1961, Anon 1962, Dubois 1966, Keat and Shore 1968, Bonfiglio 1972, E. Sande 1972).

In our case, the patient gave a history suggestive of myocardial infarction on the day before her admission to hospital and of two Adam-Stokes attacks, one at home and the other on admission. The diagnosis of infarction is supported by the electrocardiographic observations and the raised SGOT level. Complete heart block was present initially, but sinus rhythm returned within a short time. The widespread electrocardiographic changes suggest possible involvement of more than one major coronary artery.

Systemic lupus erythematosus is most probably the cause of myocardial infarction in this case as there was no recognized coronary risk factors. It is well known that age and hypertension are predisposing factors for myocardial infarction as in Ben-Asher's patient (1951) who had a blood pressure of 220/110 mmHg and sustained a heart attack at 62 years of age. The heart of his patient was enlarged and there was sclerosis of the vessels of the optic fundi. Our patient was only 37 years old. She was in her menstrual period of her life and was not on oral contraceptive. Her blood pressure was normal and there was no evidence of cardiomegaly.

In view of the absence of predisposing factors, S.L.E. must be considered as the direct cause of myocardial infarction in this case presumably due to vasculitis of the coronary artery in accordance with the experience of the pathological findings of others (Bonfiglio et al 1972, Hejtmancik et al 1964, Dubois 1966, Keat and Shore 1958).

The patient was thus treated with large doses of hydrocortisone 200 mg four hourly to reduce the inflammatory changes due to vasculitis. Isoprenaline infusion was given for her complete heart block to prevent further Adam-Stokes attack and correct her hypotension.

She made a rapid recovery and reverted to sinus rhythm within 14 hours of admission. Her renal function improved and the blood urea fell from 45 mg% to 33 mg% the next day as the urine output increased.

Systemic lupus erythematosus is a common disease with involvement of multiple system. Myocardial infarction has rarely been recorded till the last decade or so. The increasing number of cases being documented (Bonfiglio et al 1972, Sandoe 1972) could be due to setting up of new coronary units, aggressive approach to the management of cardiac arrhythmia, early admission of case with infarction, prolonged life span of cases with S.L.E. and better medical treatment.

SUMMARY

A 37 years old lady with systemic lupus erythematosus who developed acute myocardial infarction is described. There were no predisposing coronary risk factors apart from systemic lupus erythematosus. She developed complete heart block with Adam-Stokes attacks and was treated successfully with hydrocortisone and isoprenaline.

REFERENCES

- ANON (1962) Case Records of the Massachusetts General Hospital New England Medical Journal 266, 42
- BEN-ASHER'S (1951) Recurrent Acute Lupus Erythematosus Disseminatus: Report of a case which has survived 23 years after the onset of Systemic Manifestations Annals of Internal Medicine 34, 243
- BONFIGLIO, T.A., BUTTY, R.E., and HAGSTROM, J.W.C. (1972) Coronary Arteritis, Occlusion and Myocardial Infarction Due to Lupus Erythematosus American Heart Journal 83, 153
- BRIGDEN, W., BYWATERS, E.G., LESSOF, M.H., and ROSS, I.P. (1960) The Heart in Systemic Lupus Erythematosus, British Heart Journal 22, 1

DUBOIS, E.L. (Editor): Lupus Erythematosus, New York 1966, McGraw - Hill Book Company Inc

GERTLER, M.M., WHITE, H.H., and WELSH, J.J. (1967) Assessing the Coronary Profile. Geriatrics 22, 71

HEJTMANCIK, M.R., WEIGHT, J.C., QUINT, R., and JENNINGS, F.L. (1964) The Cardiovascular Manifestations of Systemic Lupus Erythematosus American Heart Journal 68, 119

HOLZINGER, D.R., OSMUNDSON, P.S., and EDMONDS, J. (1962) The Heart in Periarthritis Nodosa, Circulation 25, 610

KANNEL, W.B., CASTELLY, W.P., and McNAMARA, P.M. (1967) The Coronary Profile: 12-year follow-up the Framingham Study. Journal of Occupational Medicine 9, 611

KEAT, E.C., and SHORE, J.H. (1968) Gangrene of the Legs in Disseminated Lupus Erythematosus British Medical Journal 1, 25

SANDOE, E. (1972) Personal Communication

SHEARN, M.A., (1959) The Heart in Systemic Lupus Erythematosus American Heart Journal 58, 452

SOKOLOFF, L. (1964) Cardiac Involvement in Rheumatoid Arthritis and Allied Disorders: Current Concepts, Modern Concepts of Cardiovascular Disease 33, 847

STAMLER, J. Prevention of Atherosclerotic Coronary Heart Disease. Chapter 6 in Modern Trends in Cardiology. Edited by Morgan Jones. Butterworth London 1969

SWEZEY, R.L. (1967) Myocardial Infarction Due to Rheumatoid Arthritis, Journal of the American Medical Association 199, 855.

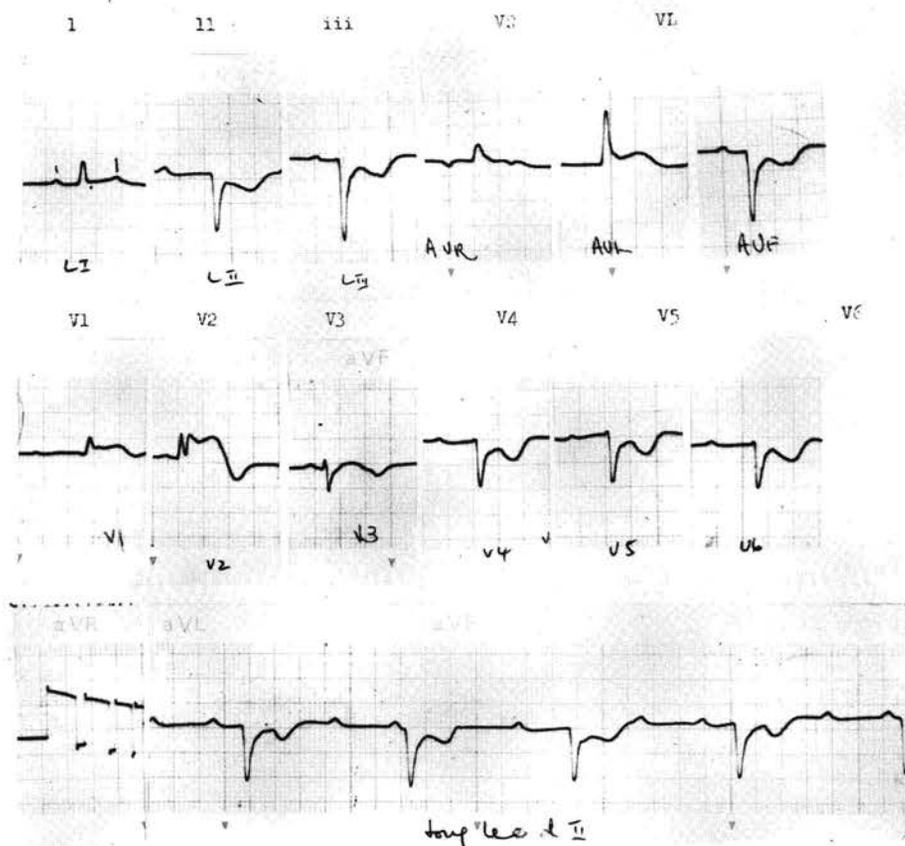


Figure 1. Electrocardiogram of patient on admission

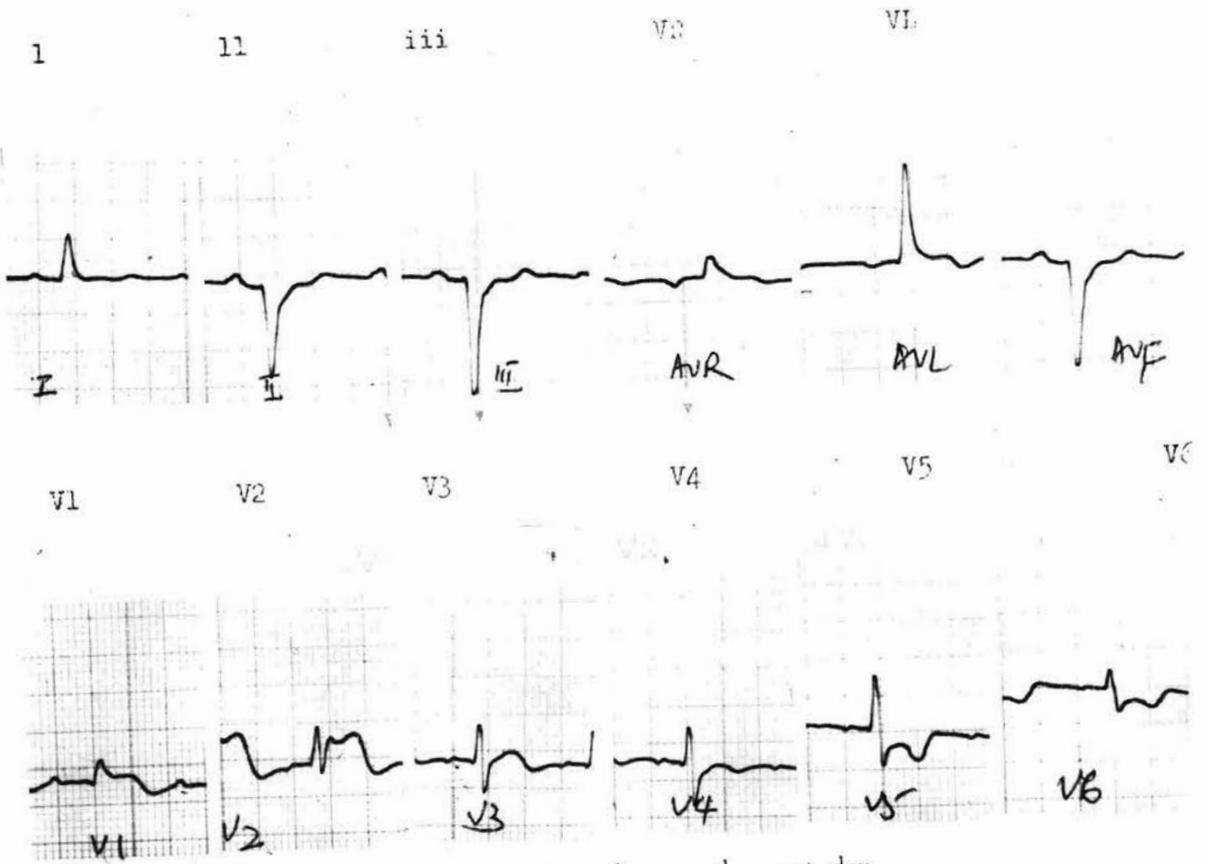


Figure 2. Electrocardiogram the next day

“Catapres In The Management Of Hypertension”

BY

NARINDERPAL SINGH, MBBS, MRACP,
PHYSICIAN, HOSPITAL BESAR, KANGAR,

AND

V. MENON, MBBS,
MEDICAL OFFICER, HOSPITAL BESAR,
KANGAR,
MALAYSIA.

Introduction:

The trend in hypertension to-day is to treat it early, even when the patient is free of symptoms. By this means one is able to avert deaths due to heart failure and cerebrovascular accidents. Deaths due to myocardial infarction are unaffected, while deaths from renal failure will commonly occur when treatment is started where renal insufficiency is already severe. (A. Ebringer et al). Many of the drugs currently used in hypertension have side effects that discourage patients, particularly the asymptomatic ones, from taking them. There is an urgent need, therefore, for a drug that will be effective over a wide range of blood pressures and yet be relatively free of side effects.

The aim of the trial was to test the efficacy of Catapres in hypertension and to note whether its use was attended by any serious side effects. Catapres is the proprietary name for Clonidine:— 2 (2,6 - dichlorophenylamino) imidazoline hydrochloride. It is an imidazoline derivative, closely related to tolazoline (Priscol) and phentolamine (Regitene). It has probably several mechanisms of actions. It may be centrally inhibiting sympathetic activity. It has central sedative and anticholinergic actions. It probably reduces venous return, produces a fall in cardiac output and therefore a fall in blood pressure as the peripheral resistance does not fall in response to the reduced cardiac output. Given acutely intravenously to control hypertension in labour produces a transient and slight rise in blood pressure. Catapres is available as 0.15 mgm tablets. We report here our experience with this drug for the mangement of all grades of hypertension.

Patients and Methods:

Altogether 38 patients were selected for the trial. The trial was commenced in early June 1973 and came to an end on 31st. March 1974 when the last patient in the trial had completed 6 months of continous therapy with Catapres. The patients were picked from the admissions to the medical unit of the Kangar General Hospital. Any new case of hypertension seen for the irrespective of age, sex or severity of hypertension; however in cases of hypertensive emergencies patients were sometimes left out and treated with routine drugs for ethical reasons. In addition patients who were known hypertensives but responding poorly to their current drugs were also admitted to the trial. In this manner patients were selected on a first come basis till the 38th patient had entered the trial. Thereafter no new cases were admitted to the trial.

As far as possible, all patients had a running-in period of one week before they were started on Catapres. During this time the blood pressure was watched several times to note its level. All patients were admitted to the ward to initiate treatment. The blood pressure was taken in the standing and lying positions. All doctors and staff-nurses concerned in taking blood pressures were specifically instructed to take lying blood pressure after 5 minutes of lying down and standing blood pressure after standing 1 minute. The level of the diastolic blood pressure was indicated in all cases by the disappearance of the sounds on auscultation.

The patients' blood pressure was classified into the following grades:-

Mild Diastolic blood pressure . . 90 - 110 mm
 Moderate -do- . . 110 - 120 mm
 Severe -do- . . 120 - and above.

A detailed clinical history was taken from each patient and the following investigations were done for all the patients: F'b, T.W.D.C., Platelet Count, Peripheral Blood Film, Urine FEME, Blood Urea, Blood Uric Acid, Serum Electrolytes, Blood Sugar, Serum Cholesterol, Liver function test. In addition every patient had an ECG and an X-ray chest. When indicated, plain X-ray of the abdomen and IVP were also done. By these means we tried to assess the patients' complications and to determine whether the hypertension was essential or secondary.

(1. TWDC: Total White and differential count.)

(2. Urine FEME: Urine for full and microscopical examination.)

At the end of about 3 months, all patients had the following investigations repeated:-

Hb., TWDC., Platelet Count, Peripheral Blood Film, Blood Urea, LFT., ECG., X-ray Chest. The aim of these tests was to see whether any deterioration occurred in them either as a result of the drug or of the disease itself.

The patients were initially started on Catapres ½ tablet tds. The dosage was then altered in either direction till the blood pressure was controlled. The maximum dose of Catapres given was 8 tablets a day. In those instances when control was unsatisfactory with Catapres alone, Aldomet or Chlorothiazide was added to the regime.

After the patients had been stabilised in the ward they were discharged and followed-up in the Medical Unit follow-up clinic. During this period the dosage of the drug was altered if needed.

All throughout the patients were closely watched for any side effects of the drug. Their incidence and persistence were noted down carefully. The patients were impressed upon to maintain a regular attendance at the clinic. Defaulters were immediately traced by post or messenger. However, those who defaulted for too long were dropped from the trial.

The response of the patients was graded as follow:-

Excellent response	Diastolic Blood Pressure—	80 — 95 mm
Good Response	-do-	96 — 99 mm
Fair Response	-do-	100 — 110 mm
Failed	-do-	110 —, though reduced: or no change in BP; or therapy stopped because of side-effects.

Results: No. of Patients Completing Trial.

Out of a total of 38 patients only 22 completed the trial. Out of the remaining, 10 patients defaulted treatment and were dropped from the trial. One patient had to be changed over to Inderal. He had very marked sedation after taking Catapres and therefore could not tolerate the drug. He also had mild postural hypotension when on Catapres (BP - 100/80 on standing). Another patient had drug fever with Catapres - with rashes, fever and an increase of his blood Eosinophils from 3% to 12%. This was relieved when Catapres was stopped and he was discharged on Aldomet alone. Another elderly Malay patient who was asthmatic as well died of myocardial infarction after 5 months of treatment with Catapres. His control of blood pressure had been excellent up to the time of death. The last patient who dropped out of the trial was a 53 year old lady. She had severe hypertension of several years' standing that had been poorly controlled in the past. She had had past episodes of CCF also; she was also a known case of Bronchial Asthma and used to have frequent attacks. She was admitted to the trial in June 1973 due to her poor control of hypertension. She was put on a combination of Aldomet and Catapres, but her BP control was very poor (110 mm). In January she was admitted for Bronchial Asthma; in the ward she also developed a left hemiplegia. Her condition was poor and she took a discharge at her own risk; we have not seen her since then.

Results: Age and Sex Distribution:

Out of the 22 patients who completed the trial, there were 15 male and 7 female patients, with the age distribution as shown in the table 1.

Age	Male	Female
20 – 29 years	1	0
30– 39 years	3	1
40 – 49 years	5	2
50 – 59 years	4	2
60 – 69 years	2	2
Total:	15	7

Severity of Hypertension:

The classification of the severity of hypertension in the 22 patients was as follows as Table 2:—

Mild (90 – 110 mm)	7 patients
Moderate (110 – 120 mm)	7 patients
Severe (120 and above)	8 patients

All patients in the study had essential hypertension.

Effectiveness of Therapy:

One of the aims of the trial was to see how effective Catapres was in reducing the diastolic blood pressure of patients with different severities of hypertension. We noted that Catapres was effective in lowering the blood pressure satisfactorily in all types of patients. Table No. 3 gives the responses of patients with mild, moderate and severe hypertension and demonstrates that the majority of patients could be satisfactorily controlled with Catapres.

Severity of Hypertension.	No. of Patients.	Types of Response			
		Excellent. (80-95mm)	Good. (96-99mm)	Fair. (100-110mm)	Failure. (—)
90 – 110 mm	7	6	—	1	—
110 – 120 mm	7	6	—	—	—
120— and above	8	5	1	2	—

For the purpose of assessing the response, the mean of these patients' lying and standing blood pressures was noted in each case.

ECG Changes During Therapy:

ECG's of the patients were done at the start of the trial and once again about 3 months later. 11 patients had normal ECG's at the start of the trial. Of these patients, 10 patients had normal repeat ECG's. The remaining one patient showed mild ischaemic changes in his repeat ECG.

The patients had ischaemic changes in their ECG at the start of the trial. Their repeat ECG's 3 months later were normal.

Two patients had evidence of left ventricular hypertrophy in their ECG at the start of their treatment; their repeat ECG's after 3 months showed the same pattern. Five patients had minor ischaemic changes at the start of therapy: their repeat ECG's did not show any significant changes. Two other patients had ischaemic changes in their ECG's at the start treatment; however, no repeat ECG's were available in their case.

Thus out of 20 patients who had repeat ECG's, only one patient showed a deterioration of his ECG. Two showed a marked improvement and 7 severe had initial changes of ventricular hypertrophy or ischaemia that persisted. The remaining 10 patients had normal ECG's that did not deteriorate.

Changes in the Chest X-ray During Therapy:

14 patients showed cardiomegaly on their chest x-ray at the start of therapy; 8 patients had hearts of normal size. A repeat x-ray was done for the patients after about 3 months. One patient showed a reduction in the heart size at this stage. No changes were noted in any of the other patients.

Effects on Renal, Hepatic and Haemopoietic Systems:

Laboratory investigations done at the start of the trial and about 3 months later did not reveal any deterioration in the kidney and liver functions or any adverse effects in the blood.

Incidence of Side-Effects:

The incidence of side-effects in the 22 patients during the trial was noted. None of these effects were permanent.

Side Effects:	No. of Patients:
Rashes	2
Sedation	4
Postural Hypotension	3
Paraesthesiae	2
Asthenia	5
Nausea	1
Anorexia	1
Dry mouth	1

In none of the 22 patients was it necessary to stop the drug because of side effects. In one patient, however, sedation was found to be troublesome and the dosage schedule had to be altered to obviate the effect during working hours. This list does not include the patients who were taken off Catapres because of drug fever and of marked sedation and postural hypertension (Vide Supra).

Adjuvant Drugs for Controlling Hypertention:

20 patients were controlled with Catapres alone. The other two patients were long standing severe hypertensives who had been poorly controlled in the past with other drugs. One of them was on Aldomet and Chlorothazide before the trial; the other was on Aldomet and Ismelin. Both were given Catapres in addition to their previous drugs and had fair control of their blood pressure.

Tolerance to Catapres:

7 patients developed early tolerance to Catapres and needed an increase in the dosage 1 – 2 weeks after initial stabilisation to attain proper control of the blood pressure. The other 15 patients remained well stabilised on the initial doses.

Complication of Hypertension During Therapy:

One patient had congestive cardiac failure. There was no incidence of angina pectoris; left ventricular failure or renal failure in participants during the period of the trial. One patient died of myocardial infarct after 5 months of good control with Catapres. Another patient had a stroke - but his blood pressure was well controlled.

Discussion:

The trial showed that Catapres is an effective and safe drug for the control of all grades of hypertension in all age groups. The majority of patients had an excellent response to Catapres. In 20 patients, Catapres was sufficient to control the blood pressure alone and in two other patients who had been poorly in controlled with other drugs in the past, Catapres was a useful adjuvant in controlling the blood pressure.

The incidence of side effects was not very high and mostly the side effects were transients. No patient complained very severely about the side

effects. Only two patients were taken off Catapres because of a side-effects. However, tolerance to the drug was noted in 7 (32%) of the patients after initial stabilisation; with further increases of dosage, the blood pressure could be well controlled.

It was significant that the ECG deteriorated in only one patient during the trial and definitely improved in another two. This is perhaps a good sign to indicate slowing down of complications though our findings differ from those of other workers (W.B. Jackson). No patient showed increased heart size after treatment, though in one patient the heart size was reduced. One case each of myocardial infarct, stroke and congestive cardiac failure occurred during the course of the treatment.

There were no adverse effects on the kidney, liver or blood due to the drug.

Summary:

Catapres is a safe and useful drug for the management for all grades of hypertension, either alone or as an adjuvant to other drugs. The incidence of side effects is low and does not prevent the patients from taking the drug.

Acknowledgements:

We would like to thank the following:—

- i) Boehringer Ingelheim Company for supply samples of Catapres for the initial part of the trial
- ii) The various doctors in the Kangar Hospital who helped to select cases for the trial and who clerked them.
- iii) Che Ah bt. Yahaya and Mr. Rao for typing the manuscript.

References:

1. A. Ebringer et al:
“The use of Clonidine (Catapres) in the treatment of Hypertension”. *Medical Journal of Australia*, 1970, 1 : 524.
2. W.B. Jackson:
“Tolerance and side effects during long term treatment of Hypertension with Debrisoquine”. *Australian and New Zealand Journal of Medicine*, Vol. 2, No. 4. November 1972.

3. C.J. Johnson et al:
"The control of high blood pressure during labour with Clonidine (Catapre)". Medical Journal of Australia. 1971, 2 : 132.
4. A.I. Mac Dougal et al;
"Treatment of Hypertension with Clonidine". British Medical Journal, 3, 440 - 442, 22nd. August 1970.
5. Prichard, BNC:
"HYPOTENSIVE AGENTS". British Journal of Hospital Medicine Vol. 10, No. 1, July 1973.
6. Raftos, John:
"The use of Catapres in the treatment of severe Hypertension". Medical Journal of Australia, 1969, 2 : 684.

Lorazepam In Patients With Mixed Psychic And Somatic Symptoms

K. Sundarm, M.B.B.S.
Kuala Lumpur, Malaysia

Introduction

Lorazepam, a new compound of the benzodiazepin class, is more potent on a weight for weight basis than its analog diazepam; a potency ratio at least as high as 1 to 5 has been demonstrated in studies comparing the anxiolytic effect of lorazepam with diazepam in hospital and general practitioner populations.¹⁻³ Lorazepam-treated patients have reported fewer sedative side effects than patients treated with diazepam.^{4,5} Such an agent is particularly desirable for use in ambulatory patients with anxiety since with it there should be less interference with the daily routine.

Method and Materials

During an open study, 65 outpatients (28 female and 37 male) with anxiety or tension were treated with 1 to 3 mg/day of lorazepam. Their ages ranged from 15 to 77 years (average, 44 years) with over half the patients between the ages of 30 and 50. Diagnoses (Table 1) were made on the basis of a detailed history and a careful psychiatric interview. No pregnant women or patients with serious physical illnesses were admitted to the study.

At the initial and each subsequent visit, patients' symptoms were rated using the Hamilton Anxiety Scale. Each symptom was evaluated as either 5, very severe; 4, severe; 3, moderate, 2, mild; or 1, absent. Frequency and initial severity of symptoms are given in Table II. The mean severity of each symptom was compared between the initial and first week (1 to 8 days) and the initial and third week (16 to 22 days). All patients were included in these evaluations. The number of patients with relief of each symptom at the end of treatment was determined. For this purpose, relief was regarded as a reduction of at least two

levels of symptom severity, i.e., moderate to absent, severe to mild or absent or very severe to at least moderate. Patients whose symptoms were mild initially were not included in this evaluation.

The overall response to treatment was also recorded for each patient. This evaluation was based on the percent reduction (actual reduction/possible reduction) of the total score on the Hamilton Anxiety Scale at the final visit as compared with the baseline total. A final score of 14 indicated the absence of all symptoms. A 70 to 100% reduction was marked improvement, 50 to 69% was moderate, 20 to 40% was slight, and 0 to 19% was nil. The latter two ratings were considered unsatisfactory.

Side effects were recorded only if volunteered by the patient.

The number of visits varied as each patient required; some patients came in several times during the first two weeks, whereas others had weekly or monthly appointments. Lorazepam was administered as 1 mg tablets in doses ranging from one-half tablet twice daily to one tablet three times daily.

According to the Hamilton Anxiety Scale ratings, the most substantial relief in the 14 symptom areas occurred within the first eight days of treatment; the mean severity of symptoms decreased by 48 to 75% (mean, 65%) during this period and decreased from 8 to 38% more (mean, 18% more) as the study continued (Table III).

Relief of symptoms (reduction by at least two levels of severity) occurred in over 75% of cases for each symptom category (Table IV). The number of patients showing improvement was statistically significant for every symptom category except "Fears," which had a sample size too small for analysis.

At the final visit, 55 patients (85%) showed marked improvement (Table V), a statistically significant number ($p < 0.01$). Thirty-six (55%) had complete remission of all symptoms.

Seven patients had an unsatisfactory overall response to treatment. Of these, two discontinued after only three days and were lost to follow-up. One woman was dropped from the study after 55 days because she was very unreliable in keeping appointments and taking medication. A 45-year-old man with anxiety neurosis improved initially on 1 mg/day lorazepam but regressed; after 26 days he was switched to diazepam and improved rapidly. Three others treated with 1 to 2 mg/day left the study between 9 and 22 days because of lack of improvement.

Duration of treatment ranged from 2 to 101 days (average, 20 days); 75% of the patients left the study by the end of the third week. All but six stopped treatment within 3 weeks because they felt well.

One woman reported giddiness on 2 mg/day. No other side effects were noted.

Discussion

During this study, depressed mood and somatic symptoms even of a severe degree were relieved rapidly and effectively—effects which also occur with other psychotropic agents of the benzodiazepine class.⁷

Although lorazepam has anxiolytic activity equivalent to that of diazepam, it has no muscle relaxant properties and produces few sedative side effects at doses that produce an anti-anxiety effect.⁸ The relief of insomnia that occurred in this study probably reflects the alleviation of anxiety, tension, depression, and disturbing physical symptoms.

Summary

During an open study, lorazepam (1-3 mg/day) was administered to 65 outpatients presenting with anxiety, tension, depression, and somatic symptoms. Substantial symptom relief of symptoms (48-75%) was evident by the end of the first week of treatment. Fifty-five patients showed marked overall improvement by the end of treatment; 36 were symptom free. One case of giddiness occurred after 14 days of treatment with 2mg.

References

1. Haider, I.: Lorazepam in the treatment of anxiety. *Curr. Med. Res. Opin.* 1(2): 70-73, 1972.
2. Gomez, G.: Double-blind trial of lorazepam for anxiety in general practice. *Brit. J. Clin. Pract.* 26: 11, 1972.
3. Coates, H.: Lorazepam and diazepam in severe neurotic illness. *Curr. Med. Res. Opin.* 1(2): 74-77, 1972.
4. Nanivadekar, A.S., Wig, N.N., Khorana, A.B., Master, R.S., and Kulkarni, S.S.: A multi-center investigation of lorazepam in anxiety neurosis. *Curr. Ther. Res.* 15: 500-507, 1973.
5. Khorana, A.B., Khorana, S., and Nanivadekar, A.S.: Comparison of lorazepam and diazepam in anxiety neurosis. *Curr. Med. Res. Opin.* 1(4): 192-198, 1973.
6. Hamilton, M.: The assessment of anxiety states by rating. *Brit. J. Med. Psychol.* 32: 50-55, 1959.
7. Blackwell, B.: Psychotropic drugs in use today. The role of diazepam in medical practice. *JAMA* 225: 1637-1641, 1973.
8. Meusert, W.: Prüfung von lorazepam (Wy 4036) in der nervenärztlichen Praxis. *Arzneim.-Forsch. (Drus Res.)* 21(7a): 1087-1090, 1971.

Table I

Psychiatric Diagnoses of Patients Participating in the Study

	Number of Patients
Anxiety - - - - -	31
Anxiety and depression - - - - -	12
Cardiac neurosis - - - - -	7
Senile depression - - - - -	4
Depression - - - - -	3
Reactive depression with anxiety - - - - -	2
Depressive psychosis - - - - -	1
Personality disorder with depression - - - - -	1
Functional dyspepsia with duodenal ulcer - - - - -	1
Alcoholism, paranoia - - - - -	1
Total - - - - -	65

Table II

Frequency and Severity of Symptoms at Baseline

Symptom	Number of patients	
	Moderate to very severe	Mild
Anxious mood	46	5
Tension	49	11
Fears	6	0
Insomnia	34	8
Intellectual (cognitive) difficulties	17	8
Depressed mood	29	11
Somatic (muscular) symptoms	37	9
Somatic (sensory) symptoms	21	8
Cardiovascular symptoms	39	7
Respiratory symptoms	29	8
Gastrointestinal symptoms	31	7
Genito-urinary symptoms	25	4
Autonomic symptoms	40	11
Behavioral symptoms	38	12

Table III

Effect of Treatment on the Fourteen Symptom Categories of the Hamilton Anxiety Scale

Symptom	No. of Patients	Severity (mean score)			Reduction (mean %)*	
		Initial	At 1-8 days	At 16-22 days	At 1-8 days	At 16-22 days
Anxious mood	51	3.6	2.1	1.5	58	81
Tension	60	3.4	1.8	1.5	67	79
Fears	6	3.8	2.0	1.0	66	100
Insomnia	42	3.3	1.8	1.6	65	78
Intellectual (cognitive) difficulties	25	4.1	1.9	1.2	72	94
Depressed mood	40	4.2	1.8	1.3	75	91
Somatic (muscular) symptoms	46	3.3	2.0	1.7	56	70
Somatic (sensory) symptoms	29	3.1	2.0	1.3	48	86
Cardiovascular symptoms	46	3.7	1.9	1.4	67	85
Respiratory symptoms	37	3.2	1.6	1.2	73	91
Gastrointestinal symptoms	38	3.3	1.7	1.6	70	78
Genito-urinary symptoms	29	3.2	1.8	1.4	64	82
Autonomic symptoms	51	3.1	1.8	1.6	62	71
Behavioral symptoms	50	3.2	1.8	1.5	64	77

* Actual reduction/possible reduction. Calculations were based on the fact that severity could not be reduced to a number lower than 1.0, which is equivalent to absence of a symptom, i.e., the possible reduction for anxious mood is 2.6

Table IV

Number of Patients with Moderate to Very Severe Symptoms Initially Who Showed Symptom Relief* at the End of Treatment

	Number of patients(%)	Level of significance ⁺
Anxious mood	37 (80.4)	0.01
Tension	44 (89.8)	0.01
Fears	5 (83.3)	N.S. ^{**}
Insomnia	30 (88.2)	0.01
Intellectual (cognitive) difficulties	14 (82.4)	0.05
Depressed mood	24 (82.8)	0.01
Somatic (muscular) symptoms	29 (78.4)	0.01
Somatic (sensory) symptoms	17 (81.0)	0.01
Cardiomascular symptoms	33 (89.7)	0.01
Gastrointestinal symptoms	24 (77.4)	0.01
Genitourinary symptoms	23 (92.0)	0.01
Autonomic symptoms	35 (87.5)	0.01
Behavioral symptoms	32 (84.2)	0.01

* Relief is defined as reduction of symptom score by at least two levels (moderate to absent, severe to mild or absent, or very severe to at least moderate).

⁺Sign test.

^{**} Sample size to small.

Table V

Overall Effect of Treatment with Lorazepam

Improvement	Number of Patients
Marked -----	55
Moderate -----	3
Slight -----	2
None -----	5
Total -----	65

Salmonella Typhi Meningitis

A Case Report And Family Investigations.

Gooi Hock Chye, M.B.B.S.
and
Sia Tuan Hong, M.B.B.S., M.R.C.P.
Kelang Hospital, Kelang, Selangor.

Present Address: Leprosy Research Unit,
National Leprosy Control Centre,
Sungei Buluh, Selangor.

Meningitis due to *Salmonella typhi* is a rare but serious complication of typhoid fever. Huckstep (1962) in his series of 240 cases of typhoid fever in Kenya recorded evidence of meningitis in only 3 patients, diagnosed on the basis of positive blood cultures, and raised cell and protein counts in the cerebrospinal fluid; the latter was sterile during life, although in one patient *S. typhi* was subsequently cultured from the CSF obtained at post-mortem. Experience and management is based on the infrequent individual case reports (Gordon-Smith and Marsden, 1951; Ripy, 1956, Wagenhals and Tannenberg, 1960) and not on any series. This article reports another case of typhoid meningitis and the results of the epidemiological investigations.

CASE REPORT

History: The patient, a 17 year old Malay boy, was brought to the hospital by his younger brother who gave a history of one week of fever and one day of delirium.

Physical Examination: The patient was delirious. The axillary temperature was 103.6°F, the blood pressure 120/80 mm Hg and the pulse 144/min. The heart and lungs were normal. The abdomen was tense but not tender with the liver palpable 6 cm below the costal margin and the spleen was just palpable. No rashes or joint swellings were found but there was marked neck stiffness and Kernig's sign was positive.

Laboratory Investigations: Haemoglobin 11 gm%, TWDC 5,900/mm, neutrophils 66%, lymphocytes 26%, monocytes 3%, eosinophils 5%. Blood film for malaria parasites - negative. Cerebrospinal fluid - clear yellow with 111 cells/mm, mainly neutrophils, no organisms on smears, sugar 11 mg%, proteins 96 mg%

Clinical Course: 200 mg of chloroquine and 2 ml of metamizol (Bonpyrin) were administered intramuscularly immediately. After lumbar puncture the treatment was continued with ampicillin 250 mg and sulphadiazine 1 gm, given every 6 hours intramuscularly. The patient was able to take fluids by mouth.

On the 2nd day the patient's abdomen was more tense and there was generalised and rebound tenderness. X-ray of the abdomen showed no free gas under the diaphragm. The patient was started on intravenous fluids, nasogastric suction, and a third chemotherapeutic agent, chloramphenicol 250 mg intramuscularly every 6 hours. He also developed acute urinary retention and an indwelling catheter was inserted. The urinary output was good and the blood area was 36 mg%.

By the 4th day *S. typhi* ('Vi' phage type E₂) was cultured from the cerebrospinal fluid; but no pathogenic organisms were isolated from the blood or faeces. The Widal tests were T(O) 1: 125, T(H) 1: 5,000, A(H) O, B(H) Chloramphenicol was increased to 500 mg every 6 hours and sulphadiazine was discontinued.

The delirium ceased on the 3rd day. There was no abdominal tenderness from the 7th day and nasogastric suction was stopped. The patient was able to micturate normally by the 2nd week and was afebrile from the 9th day. The subsequent course was uneventful. The dosage of chloramphenicol was halved at defervescence and was discontinued on the 21st day while ampicillin was stopped on the 25th day. Lumbar puncture was repeated on the 18th day (CSF clear, 72 cells/mm³, neutrophils 10%, lymphocytes 90% sugar 44 mg%, protein 30 mg%) and at 4 weeks (CSF clear, 7 cells/mm³, neutrophils 30%, lymphocytes 70%, sugar 51 mg%, proteins 24 mg%). No organisms were cultured from these CSF samples and the patient was discharged a week later.

FAMILY STUDIES

His 15 year old sister fell sick at about the same time as the patient. She, too, became delirious and died at home on the same day as the patient was admitted.

The other members of the family were investigated (Table 1). Blood was taken for Widal testing and stools for culture. *S.typhi* ('Vi' phage type E₂) was isolated from the faeces of E, G and L. E and L subsequently developed fever while G remained asymptomatic. The Widal T(O) and T(H) for these 3 siblings were: E, T(O) O and T(H) 1:50, rising to T(O) 1:50 and T(H) 1:5000 after 16 days; G, T(O) 1:125 and T(H) 1:5000; and L, T(O) O and T(H) O. All three were admitted to hospital and treated with a 2 week course of ampicillin and chloramphenicol. L developed fever 19 days after completing the first course of treatment. *S.typhi* ('Vi' phage type E₂) was again isolated from the faeces and his Widal T(O) and T(H) were O and 1:50 respectively. He was given another 2 weeks course of ampicillin and chloramphenicol. A month later L was febrile again but on this occasion *S.typhi* was not cultured from the blood or stools. The Widal T(O) and T(H) increased from 1:50 and O respectively to 1:125 and 1:500 over 30 days. Another 2 weeks course of ampicillin and chloramphenicol was instituted and no further relapse occurred.

D suffered from an unexplained fever a month before the patient fell ill. He had been treated by a general practitioner with chloramphenicol and on recovery he developed alopecia. His Widal T(O) and T(H) were 1:125 and 1:5000 respectively.

COMMENTS

It is most probable that D was the index case in this outbreak of typhoid fever: he was ill a month earlier, had alopecia on recovery and the Widal tests were consistent with recent *S.typhi* infection. E and L had typhoid fever and the latter suffered 2 relapses while G was an asymptomatic carrier. The sister who died was probably another case of typhoid fever though it was not possible to ascertain whether the delirium was due to high fever or meningitis.

Typhoid fever was not suspected until abdominal signs developed on the 2nd day. Our patient confirms the previous observation of Huckstep (1962) that typhoid fever can present as acute pyogenic meningitis without preceding intestinal manifestations. Therefore, *S.typhi* needs to be considered as a rarer cause of meningitis, especially in endemic areas.

There are a number of possible explanations for the peritonitis experienced by this patient. It could have been due to an intestinal perforation, but this was not confirmed radiologically. However, small leaks may occur through the intestinal wall and cause peritonitis without x-ray evidence of perforation. Spread from a deep though apparently intact ulcer or the rupture of a softened mesenteric lymph node will also result in peritonitis (Huckstep, 1962).

The patient also developed acute urinary retention, another complication of typhoid fever noted by Gadenholt and Madsen (1963), who reported 10 such instances.

There is little guidance in the literature regarding the treatment of typhoid meningitis. Recorded experience with *Salmonella* meningitis over the past 25 years has been limited to isolated case reports and the review of these cases (Henderson, 1948; Beene, *et al*, 1951; Rabinowitz, *et al*, 1972). No large series of *S.typhi* meningitis has been reported and text books make only passing reference

to it and its management. The 3 cases of typhoid meningitis reported by Huckstep (1962) were treated with high doses of chloramphenicol and there was one fatality. Wagenhals and Tannenber (1960) successfully treated a case with chloramphenicol and penicillin. Our patient was also treated successfully with a combination of ampicillin and chloramphenicol in high dosage.

REFERENCES

1. Beene, M.L., Hansen, A.E. and Fulton, M., American Journal of Diseases of Children, 1951, 82, 567-573.
2. Gadenholt, H. and Madsen, S.T., 1963, Acta Medica Scandinavica, (1963), 174, 753-760.
3. Gordon-Smith, S.E. and Marsden, A.T.H., 1951, Lancet, 2, 430-431.
4. Henderson, L.L., American Journal of Diseases of Children, 1948, 75, 351-375.
5. Huckstep, R.L., Typhoid Fever and other Salmonella Infections, 1st edn., pp., 102, 181-182, 187, Edinburgh and London, E & S Livingstone, 1962.
6. Rabinowits, S.G. and Macleod, N.R., American Journal of Diseases of Children, 1972, 123, 259-262.
6. Ripy, H.W., Journal of Pediatrics, 1950, 36, 376-380.
8. Wagenhals, C.O. and Tanneberg, J., Journal of the American Medical Association, 1960, 173, 355-359.

ACKNOWLEDGEMENT

We wish to express our thanks to the Director-General of Medical Services for his permission to publish this article, Dr. M. Jegathesan for the bacteriological examinations and Mrs. K. John for the secretarial assistance.

TABLE 1. RESULTS OF FAMILY INVESTIGATIONS

FAMILY MEMBER	SEX	ORGANISM	"Vi" PHAGE TYPE	ISOLATED FROM	WIDAL TEST			
					T(O)	T(H)	A(H)	B(H)
A0 44 yrs	M	-ve	—	—	0	0	0	0
B) 38 yrs	F	-ve	—	—	0	1/50	0	0
C) 22 yrs	M	-ve	—	—	0	0	1/50	0
D) 21 yrs	M	-ve	—	—	1/125	1/5000	0	0
E) 19 yrs	M	Salm. typhi	E ₂	Faeces	(i) 0 (ii) 1/50	1/50 1/5000	0 0	0 0
F) 17 yrs	M	Salm. typhi	E ₂	CSF	1/125	1/5000	0	0
G) 16 yrs	F	Salm. typhi	E ₂	Faeces	1/125	1/5000	0	0
H) 15 yrs	F	DECEASED						
I) 13 yrs	M	Salm. lexington	—	Faeces	0	0	0	0
J) 12 yrs	M	-ve	—	—	0	0	0	0
K) 10 yrs	M	-ve	—	—	0	0	0	0
L) 7yrs	M	1) Salm. typhi	E ₂	Faeces	(i) 0 (ii) 0	0 0	0 0	0 0
		2) Salm. typhi	E ₂	Faeces	(i) 0 (ii) 1/125	1/50 0	0 0	0 0
		3) -ve	—	—	(i) 1/50 (ii) 1/50 (iii) 1/125	0 1/500 1/500	0 0 0	0 0 0
M) 4yrs	F	-ve	—	—	0	0	0	0
N) 11 mths	F	-ve	—	—	No permission to take blood			

Family member L was admitted on 3 occasion as indicated in the table. Where there are two or more entries under the Widal Test, they indicate the values obtained on separate blood specimen.

ABLATON: Single Intramuscular Injection to suppress lactation

by

Dr. K. B. Kuah, M.B.B.S., M.R.C.O.G.A.M., F.I.C.S.
The Clinic for Women,
15, Jalan 14/20,
Petaling Jaya,
MALAYSIA.

Numerous good reasons have been advanced for the choice of breast feeding. The fact is, breast feeding is losing the battle. The main reason for this is that more and more mothers are going back to work and therefore find breast feeding a bother. Secondly, manufacturers are producing Infant milk which prove satisfactory in replacing breast milk.

The increasing popularity of bottle-feeding in the last two decades has led to the search for an effective means of lactation suppression. Methods reported include varying doses of stilboestrol, analgesics, injection of hexoestrol, plentiful of water to drink and various superstitions, practices here in Malaysia.

The modern trend in obstetrics is to discharge the post-partum mother from institutions early. Large doses of stilboestrol to be taken at home without supervision is unsatisfactory. However, stilboestrol is still the commonest oestrogen used in the suppression of lactation. This has to be given in large doses and over a long period to be really effective. Hodge & Carlise (1969) found that stilboestrol 15mgm four times daily for four days was only effective in 85 per cent of patients. Furthermore, rebound breast filling was a prominent problem. Stirrat et al (1968) also found that stilboestrol was effective but after the first five days engorgement was a problem.

On the other hand, there are also very favourable reports. Holand et al (1955) reported good results "with almost any oestrogen as long as therapy is started early and continued for long enough." Arbabanel and Goodfriend (1940) also reported good results (95 per cent) by giving stilboestrol for 24 days.

Kuku (1968) gave single oral dose of Quinestrol (Estrovis) to a group of patients and found that only 67 per cent had lactation successfully suppressed. He gave ethinyl oestradiol for five days and had 63 per cent success.

Loke and Lean (1970) gave a single injection of Ablaton and found it to be effective in 100 per cent of patients.

Material & Method

This is a study of 251 patients delivered in the Clinic for Women, Petaling Jaya in the years 1971, 1972, 1973. The patients are asked on admission whether they wished to have an injection to suppress lactation of milk. All those who wished to have injection are included in the trial. They are divided into two groups:-

Group A: Injection given immediately before delivery.

Group B: Injection given immediately after delivery.

The reason for this grouping is to see if Ablaton will work before the separation of the placenta. The Manufacturer advises: "One citole of Ablaton is injected intramuscularly, if possible before the exclusion of the placenta."

Ablaton is an oily solution containing the following short and long acting hormone esters:-

Oestrogen: Oestradiol benzoate 5mg,
Oestradiol valerate 8mg.

Progestogen: Norethisterone acetate 20mg.

Androgen: Testosterone cenantate 180mg.

The short-acting hormones produces a rapid onset of suppression of lactation and long-acting

hormones ensure the continuation of this action. This will avoid the rebound filling and irregular

bleeding per vaginam. Both these side-effects are common with oestrogen therapy.

Ablaton comes in a prepacked disposable citole ready for injection. Each patient in the two groups received one citole of injection in the gluteal muscle.

Results

The results are assessed according to the scheme used by Loke & Lean (1970):-

- I. Complete suppression.
- II. Incomplete suppression.
 - i) milk secretion.
 - ii) milk secretion & breast engorgement/tenderness.
 - iii) breast abscess.

Possible side effects eg. headache, giddiness, nausea, vomiting, hirsutism and voice changes are recorded.

Patients are discharged from the maternity home on the third postnatal day if suppression is complete. Others stay another two days before going home. Thereafter patients are seen at the end of six weeks and again at the end of eight months. At these visits, signs of virulisation and menstrual disturbances are looked for.

All the patients attended the six weeks visit and 75 per cent of patients attended the eight months visit.

Tables 1 & 2 shows that in group A, 84 patients (65.6 per cent) and in group B, 99 patients (81.3 per cent) had complete suppression of lactation following injection of ablaton.

Group A also had 44 patients with incomplete suppression - 11 patients had painless secretion of milk while 33 patients had engorgement and/or tenderness. The same figures for Group B are 18 patients and 6 patients. The engorgement and tenderness are usually mild. No case of breast abscess was recorded.

No side effect was recorded.

Table 1. Group A: Ablaton before Delivery

Day	1	2	3	4	5	TOTAL
I. Complete Suppression	84	—	—	—	—	84
II. Incomplete Suppression	—	—	8	3	—	11
Milk Secretion	—	—	10	19	4	33
Milk & Engorgement tenderness	—	—	—	—	—	0
Breast Abscess	—	—	—	—	—	0
TOTAL						128

Table 2. Group B: Ablaton gives After Delivery

Day	1	2	3	4	5	TOTAL
I. Complete Suppression	99	—	—	—	—	99
II. Incomplete Suppression	—	—	7	10	1	18
Milk Secretion	—	—	—	6	—	6
Milk & Engorgement tenderness	—	—	—	—	—	0
Breast Abscess	—	—	—	—	—	0
TOTAL						123

Follow-up before 6 weeks

Although patients are discharged satisfactory (the patients who showed signs of engorgement and/or tenderness stayed till the 7th day) some patients came back before the post-natal appointment at 6 weeks.

Group A	8 patients..
Group B	2 patients.

Those patients in group A came because of rebound filling. The two patients in group B are those who had engorgement and/tenderness prior to discharge.

Follow-up at 6 weeks

Apart from the 10 patients mentioned above, another 6 had mild congestion after discharge from the nursing home. All were not sufficiently uncomfortable for the patients to seek treatment. Three of these were in Group A and three in Group B.

None of the patients complained of menstrual problems however, only 149 patients have had one period each.

There was no sign or symptom of virilisation. All patients in the trial attended this follow-up clinic.

Follow-up at 8 months

A total of 188 patients (74.9 per cent) attended this clinic. No sign or symptom of virilisation was noted. No abnormality was noted in the breast.

As most of these patients have started on oral contraceptives it would not be fair to comment on their menstrual patterns.

Discussion

Lean and Loke (1970) reported that Ablaton given to 20 patients for primary suppression was effective in 100 per cent of the patients, if given within 5 hours of birth of the infant. The present study shows that Ablaton given immediately following the delivery of the infant was effective in suppressing lactation in 81.3 per cent of the patients. The manufacturer also claims that in

a trial all but one patient had satisfactory primary suppression.

The study indicates that Ablaton is superior to oestrogens to the suppression of lactation viz Hodge and Carlisle (1969) who reported 68 per cent success. Furthermore, there are some objections to the use of oestrogens. The side effects of stilboestrol e.g. abnormal bleeding from the genital tract outweighed the benefits (Winter & Robinson 1964). Daniel et al (1967) believe that stilboestrol predispose to thromboembolism in the puerperium, although this may not be such a serious objection in Malaysia and Singapore. Finally, MacDonald and O'Driscoll (1966) stated that the use of stilboestrol is not justified since a placebo is almost as effective.

Single injection of Ablaton is also superior to Quinestrol in suppressing lactation. Kuku (1968) reported 67 per cent success using a single oral dose of Quinestrol (Estrovis).

The efficacy of Ablaton is less when given immediately prior to the delivery of the presenting part. The reason for this is obscure since the time difference between this and an injection given immediately after the delivery of the infant is not long.

Although rebound filling is noted in 8 patients it is not a big problem. No other side effect was noted.

Since androgen is one of the components of Ablaton virilisation is a concern. However, in the follow-up to 8 months in some of the patients, no virilisation is noted.

Summary

ABLATON is given to 250 patients in a clinical trial to assess its efficacy for the primary suppressing of lactation. In the group whose injections were given immediately after the delivery of the infant a 81.3 per cent success was recorded. When the injection is given before the delivery there is only 65.6 per cent.

No major side-effect was noted.

Reference

1. ARBARBANEL, A.R., and Goodfriend, M.J., (1940). The Effects of Stilboestrol upon Lactation. *Am. J. Obst. & Gynaec.*, 40, 1037.

2. DANIEL, D.C., CAMPBELL, H. and TURNBULL, A.G. (1967). Puerperal Thromboembolism and Suppression of Lactation. *Lancet*, 2, 287-189.
3. HODGE, C. and CARLISLE, J.S. (1969). Relief of Pain During Suppression of Lactation. *J. Obst. Gynaec. Brit Cwlth.*, 76, 66-68.
4. Kuku, S.B. (1968). Inhibition of Lactation with Quinestrol. *J. Obst. Gynaec. Brit Cwlth.*, 75, 103-104.
5. LOKE, Y.N. and LEAN, T.H. (1970). Suppression of Lactation with a Single Intramuscular Injection - Ablaton. *Proc. Obst. Gynaec. Soc., Singapore*, 1, 38-42.
6. MACDONALD, D. and O'DRISCOLL, K. (1966). *Lancet*, 2, 623.
7. ROLAND, M., VEPROVSKY, E., and LINHART, M. (1955). The use of various endocrine preparations in the suppression of Lactation. A comparative study in 800 cases. *Am. J. Obst. Gynaec.*, 70, 1004-1011.
8. STIRRAT, G.M., ANDERSON, G.E., GRANT, C. (1968). The Effectiveness of Stilboestrol in the Suppression of Postpartum Lactation. *J. Obst. Gynaec. Brit Cwlth.*, 75, 313-315.
9. WINTER, R. W. and ROBINSON, S.C. (1964). Prevention of Lactation. *Obst. Gynaec.*, 23, 906-909.

Accidental Vaccinia Infection - A Case Report

K.L. Lam,[†] V.J.L. How,^{*} & S.K. Lam^{*}

[†]Department of Paediatrics

^{*}Department of Medical Microbiology
University of Malaya

It is often forgotten that smallpox vaccine is a live virus and that due care has to be taken in its handling and administration by medical personnel. The recipient or, in the case of a child, those responsible for its care, should be warned of the nature of the vaccine and its infectivity to himself and to others. The risk of accidental vaccinia is greatest when there is free lymph at the vaccination site soon after inoculation or after rupture of the pustule but the risk is always present until the scab separates.

Accidental vaccinia infection can occur when a susceptible person comes in close contact with a recently vaccinated member of the same household. It can also be the result of autoinfection of other areas of the body through scratching or, as occasionally happens, the doctor or nurse giving the vaccine may be infected through finger abrasions. It is also possible that the virus can penetrate apparently intact skin³ and mucous membranes.¹

Practically any part of the body may be affected,^{1,2,3,4,5} the sites reported include satellite lesions around the original vesicle, the eyes and eyelids, more rarely the neck, face, lips, tongue, nostrils, skin wounds, and even the anus and genitalia.⁴ These often appear as isolated lesions with little constitutional disturbance but could be serious if they occurred, for example, in a person with eczema.

We report a case of accidental vaccinia infection on the tongue and gum margin.

NSM is a 9-month old Chinese female, who was first seen in Polyclinic, University Hospital, on 5.10.72 with the complaint of an ulcer on the tongue. This was first noticed 4 days ago when the child was irritable and not feeding well. Two days later, another ulcer was seen on the upper

gum margin adjacent to the first ulcer. There was no fever but the child had a little loose stool.

Three weeks earlier, an elder sibling aged 1½ years had had a successful primary smallpox vaccination.

On physical examination the child was afebrile, the only abnormality being a superficial ulcer 1 cm in diameter with a whitish base on the right side of the tongue (Fig. 1). There was no bleeding or tenderness. A smaller almost healed ulcer 2 mm in diameter was seen in the adjacent upper gum margin. There was slight enlargement of the sub-mandibular glands.

A swab taken from the ulceration on the tongue grew normal bacterial flora but cultures on chorio-allantoic membranes of 11-day old eggs showed lesions resembling vaccinia pocks (Fig. 2). Electron micrograph of the virus particle supported this finding (Fig. 3). The identity of the virus was confirmed as vaccinia virus by haemagglutination-inhibition using immune serum.

The child was treated topically with gentian violet 1% and the ulcers healed completely in 12 days without any visible scarring.

Comment

It is not difficult to see how this child caught the infection from her elder sibling.

There is very little information in the literature of the incidence of accidental vaccinia. It has been estimated at about 13.6 per million by Neff et al. in the U.S.A.⁵ The incidence is unknown in this country.

Recognition of suspected vaccinia infection is by virus isolation from the vascular fluid or by rise in specific antibody titre.² In this child,

we were able to culture the virus and identify it. Serology was not attempted as we were not able to obtain the second blood specimen.

In administering smallpox vaccine, the responsibility of the doctor or nurse does not end at determining the usual contraindications on the patient to be vaccinated.⁶ He or she should also enquire into whether the household contacts have any form of dermatitis, are on steroid or immunosuppressive therapy or are suffering from any debilitating disease. Should there be any such person or persons whose immunisation status is also in doubt, the procedure should be postponed. Should this not be possible (e.g. vaccination for travelling abroad), such contacts at risk should be protected with specific gammaglobulin or the person vaccinated should be separated from them until the scab has dropped off.

In summary, we report a child with accidental vaccinia infection on the tongue and gum margin. Her contact was a recently vaccinated elder sibling.

References

1. Baernstein, H.D. et al. (1967): Accidental secondary vaccinia on the tongue. *Clin. Ped.*, 6: 435.
2. *Epidemiology: Vaccinia infection.* (1971) *B.M.J.*, 1: 121.
3. Horwitz, M.S. et al. (1966): A family outbreak of vaccinia. *J. Ped.*, 68: 308.
4. Hutfield, D.C. (1968): Accidental vaccinia. *B.M.J.*, 2:828.
5. Neff, J.M. et al. (1967): Complications of smallpox vaccination, *New Eng. J. Med.* 276:125.
6. Coriel, L.L. (1966): Smallpox vaccination - when and whom to vaccinate. *Pediatrics*, 37: 493.

Acknowledgements

We would like to thank the Department of Medical Illustration for the photographs and Mrs. M.T. Ng of the Department of Paediatrics for the secretarial work.

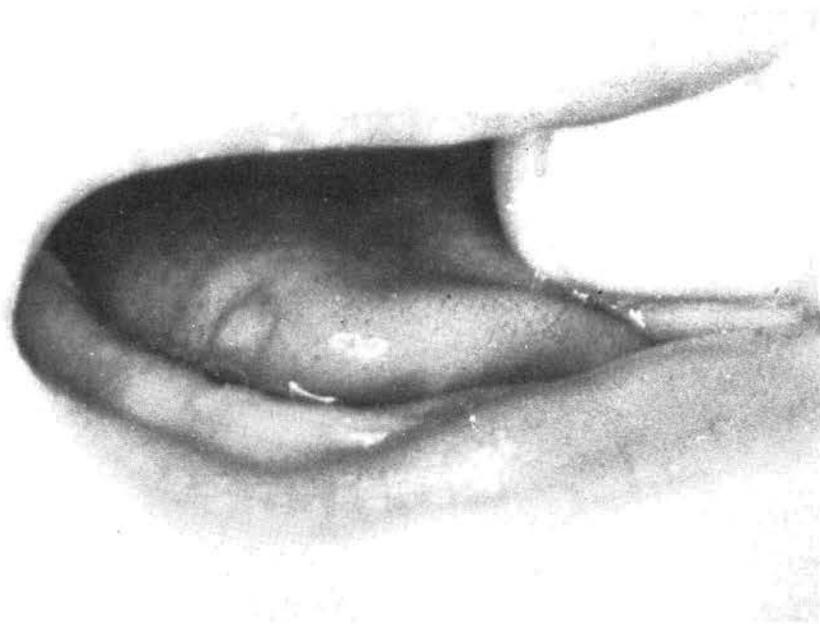


Fig. 1. Note the healing ulcer on the right side of the tongue. The photograph was taken on the 8th day by which time the ulcer on the upper gum margin had healed.

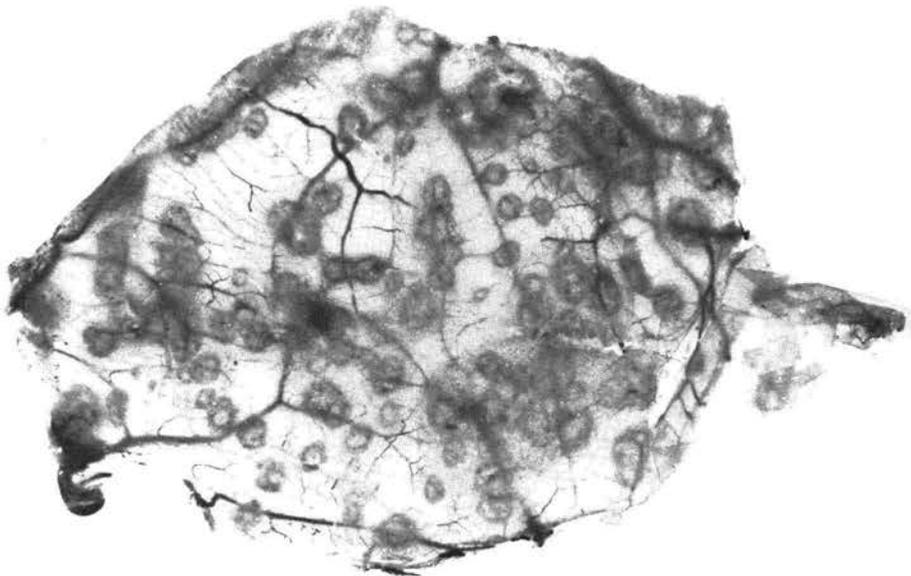


Fig. 2. Chorion Allantoic Membrane of 11-day old chick harvested after 72 hours showing numerous pocks with necrotic bases typical of those produced by vaccinia virus.

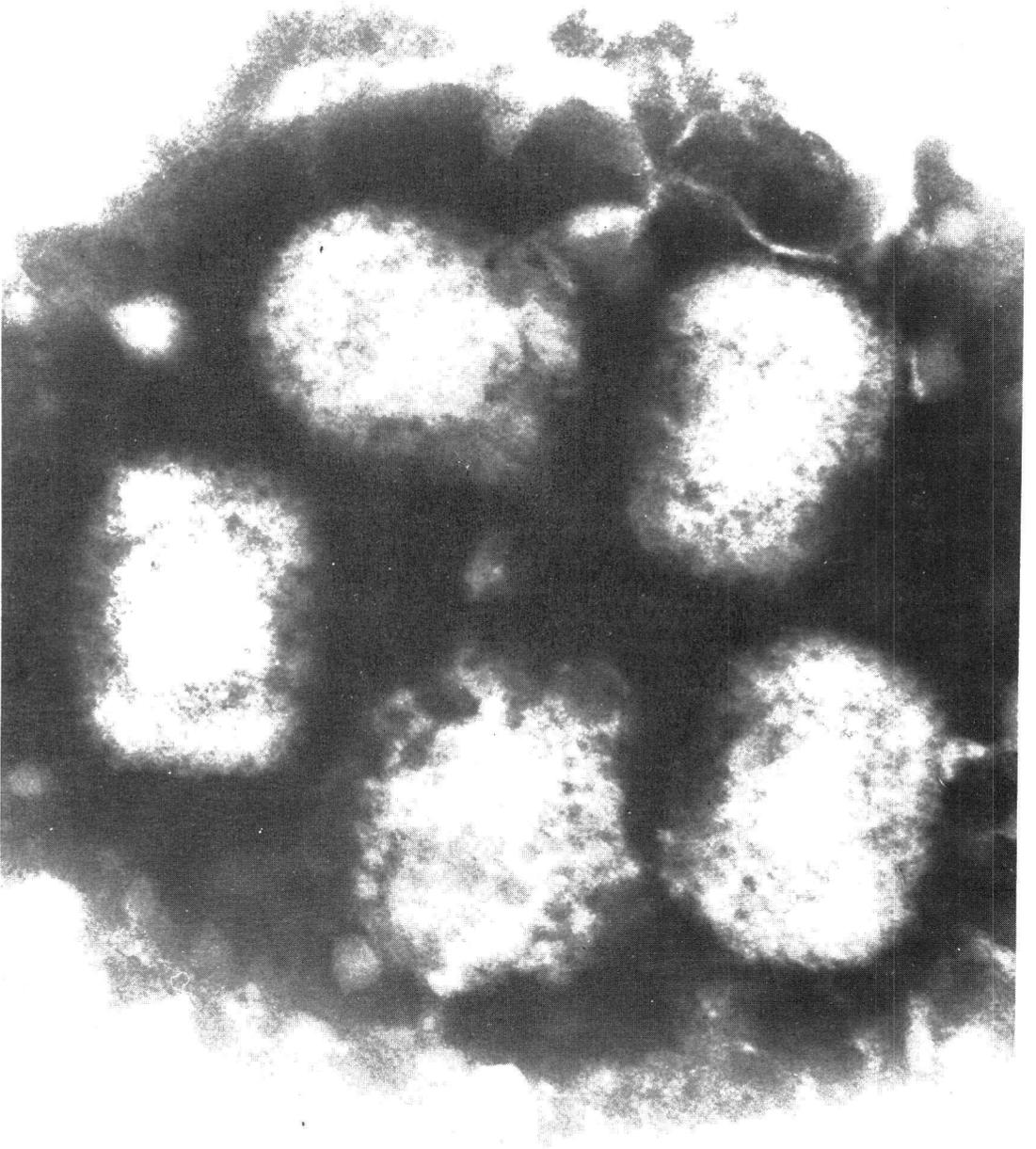


Fig. 3. Electron photomicrograph showing 5 typical brick shaped vaccinia virions. (Magnification 3.6 x 54,000)

Lipoma: An Unusual Case With A Brief Review Of The Literature

Yan Kor LEE, M. B. (Syd.), F.R.A.C.S.
Surgeon, Kluang District Hospital, Johore.

INTRODUCTION

An unusual case of lipoma was seen in Kluang District Hospital, Johore in February, 1974. It arises in the intermuscular plane between the pectoralis major and minor.

The purpose of this paper is to i) report this unusual case from the point of view of the site of occurrence, the problem in diagnosis and its pathological behaviour, ii) to review briefly the literature in lipoma which is a very common benign tumour.

CLINICAL RECORD

The patient - J. bin S. R.N. 1477/74 - is a 68 years old Malay man who first noted a swelling over his right breast 28 years ago. This swelling, he remembered, was initially small, but progressed in size over a period of one year. There was no pain. He had it excised in Johore Bahru General Hospital. There was no record of the pathology.

He was asymptomatic until 2 years prior to the present admission to hospital, when he again noted a swelling over the right pectoral region. This grew progressively towards the right axilla. There was no pain.

On examination there was a multinodular soft mass deep to the right breast and axilla. It was fixed to the underlying pectoral muscle. It was not tender. There were no lymphadenopathy in the axilla or neck. The left breast was normal.

Chest X-rays were normal. There was no rib involvement. The lung fields were clear.

Preoperative diagnosis of lipoma was made with a suspicion of malignant change.

On the 4th March, 1974 the lipoma was excised under general anaesthesia. An inframammary incision was made extending into the axilla. The multilobulated lipoma was found to lie in the plane between the pectoralis major and minor. The pectoralis major muscle was retracted and the lipoma dissected free from the pectoralis minor muscle to which it was attached at places. The wound was closed with a tube drain and compression bandage was applied.

Immediately post operative in the ward there was a lot of blood oozing from the drain. The patient went into shock which responded to 500 mls of whole blood transfusion. The compression bandage was reapplied and the oozing stopped. The rest of the post operative course was uneventful. On the 10th post operative day he was discharged in a satisfactory condition after the sutures were removed.

He was last seen two months post operative without any evidence of further recurrence of the lipoma. He is still being followed up.

The histopathology report:-

The specimen consists of three well circumscribed lumps attached together by fibrous strands. The largest measures 8.0 cms. in diameter. Out surface is uniformly yellowish.

Microscopically they are composed of lobules of fat separated by thin fibrous septae.

The features are those of a simple Lipoma.

Part of the underlying muscle has also been excised and this does not show any pathological change.

REVIEW OF THE LITERATURE

Lipoma is a very common benign tumour. It can arise from almost anywhere in the body. Commonly it is found subcutaneously in the neck, back, shoulders, and abdomen. These are usually solitary, sometimes they are multiple. Adair et al. reported 6.7% of patients with lipomas have multiple lesions. Four fifth of patients with multiple lipomas are males according to a study by Muller. Other rare sites are face, scalp, hands, feet and sternal region. Lipomas arising in intermuscular planes especially the thighs and calf region, intrathoracic, retroperitoneal and the gastrointestinal tract have been described. Some occasionally arise from fascia and articular capsular of larger joints.

Lipoma can occur at any age, but according to Anderson 40 to 50% appear in the 4th and 5th decades. Similarly in a collective review published in the Journal of Surgery, Gynaecology and Obstetrics in July 1968 under the title of Cutaneous Lipoma and Lipomatosis, the average age of the patient is 41 years. From the same article, is a review of 134 patients seeking medical attention 73% were female. However, Muller noted that it is commoner in males but gave no figures.

Certain pathological features of lipoma are of interest. Wells in 1910 showed that the lipoma has no deficiency in lipase. He concluded that there were no reasons to believe it is beyond reach of body use. It is also known that lipoma grows while the body becomes emaciated. Deep seated lipomas for example in the thorax, abdomen, cranium, retroperitoneus, kidneys, tendons of hands and feet cause pressure symptoms. Angiolipoma is frequently painful, tender and red as compared to simple lipoma.

The etiology of lipoma is unknown. However several possible factors are implicated. They are:-

1. Genetic. Multiple lipomatosis is thought to be transmitted by Mendelian dominant gene.
2. Associated defects and conditions like multiple telangiectasia, neurofibrous, Gardener's Syndrome, and rheumatoid arthritis.
3. Local trauma. However Ewing showed that there was poor evidence for trauma as a cause.

4. Other etiologies like endocrine disease. Ballard et al. 1964 found lipoma in 11 of 85 patients under study for multiple endocrine adenomatosis. Syphilis and hypercholesterolemia have been shown to be associated with lipoma.

DISCUSSION

The case presented here has several interesting features.

1. The lipoma recurred about 25 years after initial excision. This is an uncommon feature and was a factor which led us to suspect malignant change. One hundred and thirty four patients with lipoma were reported in a review in Surgery, Gynaecology and Obstetrics in July 1968 in which four lesions were recurrent, one recurring as a liposarcoma.
2. The site of the lipoma is unusual. However lipomas arising from intermuscular planes especially in the limbs have been described. To the author's knowledge, lipoma arising in the pectoralis muscle plane has not been reported.
3. The problem of diagnosis in this case is apparent. It appears like a breast lump and especially in a female it can be mistaken for a breast cancer or a retromammary tumour. The latter is rare. Leggett 1973 reported in detail 4 patients from his large personal series. None of the four was a lipoma.

SUMMARY

An unusual case of lipoma is described here. Its unusual features are highlighted. A brief review of the literature on lipoma is presented.

ACKNOWLEDGEMENT

The author thanks Dr. Tan Sri Dato (Dr.) A. M. Ismail, FRCS(E), M. Ch. (Orth.), FRACS., Director-General of Medical and Health Services, Malaysia, for permission to publish this article. Thanks also to Dr. C. H. Teoh for reading the manuscript.

REFERENCE

1. Anderson - Pathology; Publisher Mosby; 5th edition 1966, Vol. 1, p438.
2. Cutaneous lipomas and lipomatosis, Surgery, Gynaecology and Obstetrics, 127: 122-32, July 1968.

3. Adair F. E., Pack, G. T., and Farrior J. H., Lipomas, *American Journal Cancer* 1932, 16: 1104.
4. Ewing, J., *Neoplastic Disease* 4th ed. P. 190, Philadelphia and London W.B. Saunders 1940.
5. Ballard H. S., Frame B, and Hartsol R. J., Familial multiple endocrine adenoma - peptic ulcer complex. *Medicine*, 1964, 43: 481.
6. Leggett C. A. C. Retromammary Tumours of the Pectoralis Major Muscle. *The Aust. and N. Z. Journal of Surgery*, 431 July 1973, P. 37.

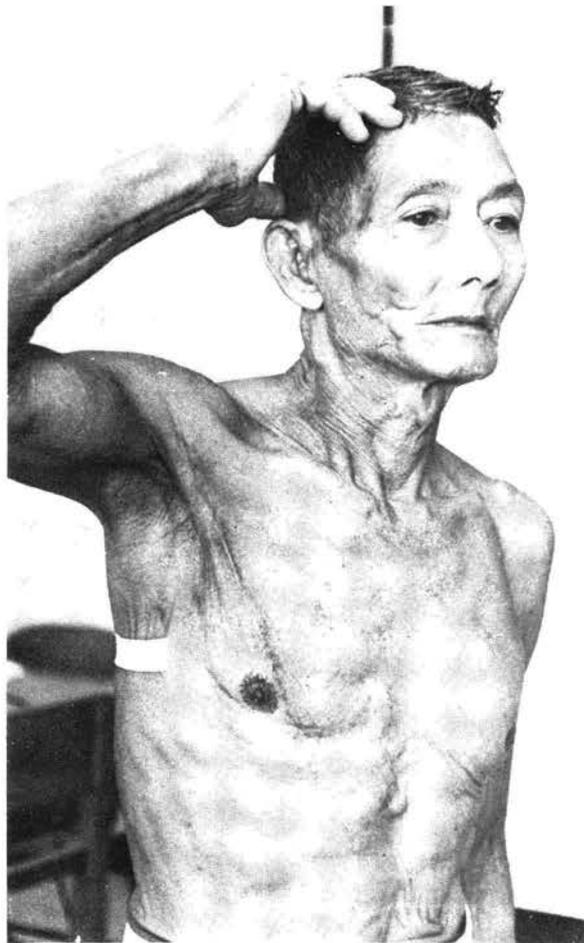


Figure 1. Two months post operatively, showing the inframammary scar of present surgery and a vertical scar due to surgery 25 years ago.

AN INFANT OESOPHAGEAL STETHOSCOPE

Authors: Dr. Rober P.C. Liew
Dr. Yeo Keat Him
Dr. Cheah Ui Jin

Address: Department of Anaesthesiology.
University of Malaya.
Kuala Lumpur, MALAYSIA.

The diaphragm of an oesophageal stethoscope is a 10 - 11 cm length of infant size (3/4 cm diameter) Pauls rubber tubing. This tubing is commonly used with the colostomy glass rod for colostomy in children.

The tubing is smooth, and relatively taut. For neatness, one end is tied twice with a piece of 1/0 silk and the tubing turned inside out.

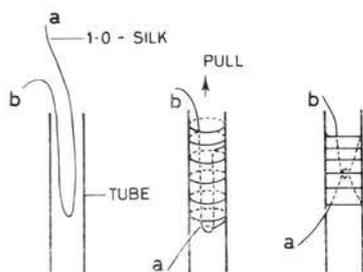
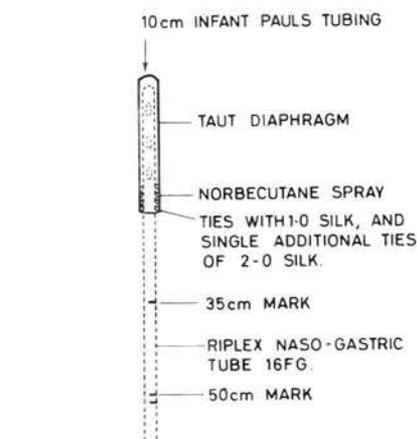
The tubing is tied onto a size 16FG Riplex naso-gastric tube which has 5 lateral eyes and markings on the tube at 35 cm, and 50 cm.

The Riplex tube is stiff enough for oral insertion and easy negotiation at the crico-pharyngeus. Its small size does not interfere with the subsequent passage of another naso-gastric tube into the stomach or an oesophageal temperature probe.

It is suitable for use in the newborn, children and adults. It is easier to pass and is more sensitive than the commercially available soft bulbous red rubber oesophageal stethoscope.

A method of fixation with nobecutane and of tying the Pauls tubing is shown below.

AN INFANT OESOPHAGEAL STETHOSCOPE



A METHOD OF TYING

BOOK REVIEW

HUMAN RIGHTS IN HEALTH: Ciba Foundation Symposium 23 (New series) 1974. pp. Viii & 304. Elsevier. Excerpta Medica, North Holland. Edited by Katherine Elliott and Julie Knight. U.S. \$15.00

Twenty eight contributors from twelve countries attempt to explore the practical implications – in terms of funding, human and materials resources, and management needs – of adopting four determinants of health as universal human rights. The determinants are safer water to drink, sufficient food, protection against communicable disease and access to the means of controlling fertility. All are interlinked, and they lead to a fifth – the right to have within reach some form of health care covering all the others.

The contributors attempt to estimate the necessary costs, the social changes involved and the likely effects on the pattern of world development of converting these rights into realities. Ways in which limited financial resources for health can be supplemented by tapping new resources within developing countries and by extending and rethinking the aid policies of outside countries, are stressed. A recurring theme is the need to use existing local resources, both material and human, and to integrate traditional technology and practice with newer methods.

The symposium should interest those working in the fields of tropical medicine, epidemiology, hygiene and nutrition and all thinking people.

THE POISONED PATIENT: THE ROLE OF THE LABORATORY

Ciba Foundation Symposium 26 (new series) pp. Viii & 325. Elsevier. Excerpta Medica. North Holland. Edited by Ruth Porter and Maeve O' Connor. US \$21.20.

In this symposium an international group of clinicians, laboratory workers and pathologists discuss the role of the laboratory in the treatment of patients and the control of addicts who have abused barbiturates, tranquilizers, amphetamines, cannabis, LSD (lysergide), heroin and others.

The care of acutely poisoned patients and of narcotics is surveyed. Different laboratory techniques are evaluated, including immunological methods for detecting drugs. Drug analysis in overdosed patients – alive or dead – and the likelihood of iatrogenic disease being noticed are discussed. The limitations of haemodialysis and forced diuresis are debated and the share clinical pharmacology and toxicology should have in medical education is examined.

These papers and discussions should interest all clinicians, laboratory workers and pathologists.

SYMPOSIUM: PUBERTY AND ADOLESCENCE.

Royal College of Physicians of Edinburgh. Publication No. 45. Edited by A. T. Proudfoot, paper cover, pp. 95. £1.50

In this symposium, the following aspects are dealt with authoritatively: physical changes at puberty; adreno-cortical function in normal, delayed and precocious puberty; gonadal problems at puberty, clinical disorders of puberty; emotional changes of puberty and adolescence; medical services for adolescents and social services for the adolescent.

RESEARCH IN MEDICAL CARE, edited by W.W. Holland. Brit. Med. Bulletin Vol. 30 No. 3. Sept. 1974. Published by the British Council, 65 Davies street, London W1Y 2AA. £2.50

In the 26 years since the foundation of the National Health Service in the United Kingdom various problems have emerged. After much discussion plans for reorganising the health services were drawn up and agreed, and these were put into effect on 1st April, 1974.

This number of the British Medical Bulletin is a timely one and contains papers from some of the researchers involved representing the broad spectrum of medical care activities. It should be of value to all those involved in health care planning in other parts of the world.

PROGRESS IN QUALITY CONTROL IN CLINICAL CHEMISTRY

Editors: G.Anido, E.J.Van Kampen, S.B.Rosalki,
Publishers: Hans Huber, Berne 9. *Transactions of the Vth International Symposium: Geneva April 10-11 1973.* p.401, 104 illustrations, 120 tables, Price US. \$20.00.

This is an impressive presentation by 15 nations on the problems of Quality Control, Six working groups dealt on selected topics in depth,

The American group concentrated on protein fractions and lipoprotein studies. Synthesized protein mixtures as protein controls were found to be suitable. Changes in lipoprotein during storage were also noted and discussed.

The presentation by the British Group touched on the problems of accuracy from absolute methods and from using patient data. The accuracy assessment in enzyme determination was most interesting with two-point and kinetic assay systems being discussed. Problem associated with optimum con-

centration and purity of both substrate and cofactor was also dealt with. More presentation on problems of enzyme measurement and quality control was given by the Swiss - German - Austrian group.

The Dutch - Belgium group and the Latin group covered general aspects of Quality Control. Drug interference in Clinical Chemistry was a topic discussed along with two other papers on the effects of drug interference on Estrogen and Calcium determinations.

The section on Free Communication was well presented covering topics which will interest most. Some topics discussed were: Precise temperature control, optimizing analytical methods, Radioisotopic procedures in Clinical Laboratory and various aspects of automation.

I should have liked to see more uniformity in enzyme nomenclature and abbreviation and perhaps this could be a topic for the next Symposium. Besides this, the book on the whole is excellent and should be in every library of Institutions or departments associated with medicine or biology.

J. E. Buttery.