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GUEST EDITORIAL

HYBRIDOMAS – MEDICAL DIAGNOSIS OF THE FUTURE

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INTRODUCTION

ANTISERA prepared in animals or obtained from human sources and containing specific antibodies against a particular antigen are widely used in medical diagnosis. For example, these preparations are used in:

1. diagnosis of various microbial infections e.g. detection of hepatitis B surface antigen (HBsAg) and final identification of bacterial organisms isolated from clinical specimens.
2. quantitation and determination of plasma proteins e.g. immunoglobulins and complement.
3. detection of cell surface antigens e.g. blood grouping (ABO and Rh antigens), HLA typing, enumeration of B lymphocytes.
4. immunoflurorescence tests e.g. detection of *auto*antibodies using tissue sections; rapid diagnosis of viral infections on clinical specimens.
5. radioimmunoassay procedures to measure levels of various hormones (e.g. insulin, T3, T4, TSH), IgE, alpha-foetoprotein (AFP) etc.
6. pregnancy testing ie. the use of anti-HCG antisera.

Several problems, however, are associated with the production and use of these antisera preparations. Immunization of an animal with an antigen produces *many different antibody molecules to the same antigen.* Hence, antisera from these animals invariably represent a complex mixture of antibodies of *polyclonal* origin which are also heterogenous with respect to affinity and specificity towards the immunizing antigen. Additionally, two or more different animals never produce both quantitatively and qualitatively the same immune response (ie. the same antisera) hence giving rise to problems of continuous reproducibility and standardization.

Ideally, antibodies used in medical diagnosis should be monospecific and homogenuous ie. *monoclonal* in origin. This goal, as mentioned above, is very difficult to achieve by immunizing animals and obtaining their sera. However, a recent development in cellular immunology has provided an elegant solution for the *in vitro* production of monoclonal antibodies of a desired specificity for unlimited time and theoretically, at least, in unlimited amounts. The technique was developed by Kohler and Milstein (Kohler and Milstein, 1975, 1976; Kohler *et al.*, 1976) who fused normal antibody-producing cells (B lymphocytes/plasma cells) with an appropriate B cell tumour *in vitro.* These tumour cells (myeloma cells) are 'immortal' and can be grown indefinitely in *in vitro* culture. The fusion results in a *hybridoma* ie. a hybrid cell line originating from a single antibody-producing cell which is immortal and which is also producing antibodies to a specific antigen. Cloning of these cells gives rise to a uniform line of cells producing absolutely identical (ie. monoclonal) antibodies. With these type of antibodies all problems of standardization of medical diagnostic reagents disappear and the antibodies produced are of unprecedented specificity thus also eliminating the problem of cross-reactions with other antigens (New Scientist, 1977; Staehelin, 1978).

THE HYBRIDOMA TECHNOLOGY

The *in vitro* fusion between myeloma cells and

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antibody-producing cells (normally spleen cells from an immunized animal) is achieved by treating the cell mixture with inactivated Sendai virus (Kohler and Milstein, 1976) or, more commonly, with polyethylene glycol (Pontecorvo, 1975). The stimulated spleen cells (plasma cells) produce antibodies against the desired antigen but are themselves unable to survive and proliferate in tissue culture medium. The immortality *in vitro* is provided by the fused myeloma cell. However, in order to select out the myeloma cell which has fused to spleen cells from the many unfused myeloma cells, one has to use a *mutant* myeloma which cannot survive in a special selection medium unless it is fused with a normal cell (ie. the spleen cell) which cures the genetic defect. This defect is usually in the form of a missing enzyme now supplied by the spleen cell. Thus, only the hybrids will be able to survive and proliferate in the growth medium (unfused spleen cells eventually die because they cannot divide *in vitro*] (Kohler and Milstein, 1975, 1976). Following fusion, the cells are *cloned* and after further growth, the antibody product of these hybrids can be detected in the culture supernatant by a variety of methods including radioimmunoassay, ELISA (enzyme-linked immunosorbent assay) and indirect immunofluorescence. A summary of the procedure is given in Fig. 1.

Following the establishment of these hybrid cell lines the antibody product could be subjected to further biochemical analysis and purification, 'large scale' production of antibodies carried out by injecting the cells into histocompatible mice (where they grow in ascites form and where the ascitic fluid may contain up to 1 mg/ml of specific antibody when harvested) or the hybrid cell lines frozen until further use.

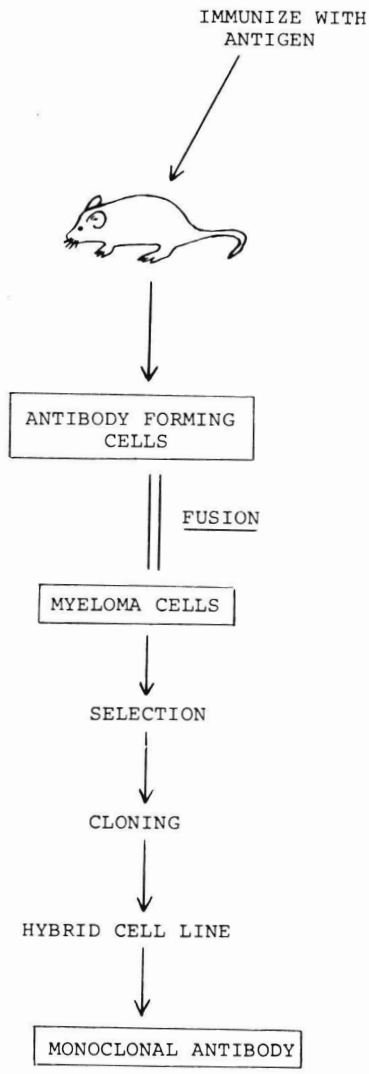

Fig. 1. Production of hybridomas

IMPORTANT FACTORS IN HYBRIDOMA PRODUCTION

Several factors need to be taken into consideration for the successful production of hybridomas:

1. **Cell properties**

a. *ontogenetic* restriction - in order to 'rescue' B cell function (ie. antibody production) it appears to be necessary to carry out the fusion with a B cell tumour (ie. myeloma cells). Conversely, preservation of T cell function in the hybrid requires that the T cells be fused with a T cell tumour (Goldsby *et al.*, 1977).

b. *phylogenetic* restriction-fusion between the same or between closely related species are preferred e.g. fusion between mouse myeloma cells and mouse or rat spleen cells produces many more successful, specific hybrids than fusions between mouse myeloma cells and human or frog cells (Kohler and Schulman, 1978).

c. *stage of cell cycle* - large, dividing lymphocytes (B cells) from the spleen are preferred to 'resting' cells for fusion with myeloma cells.

2. **Immunization protocol**

The type of antigen preparation, dose, frequency of administration and time elapsed between immunization and collection of spleen cells are important factors which subsequently influences the success of fusion procedures.

3. **Fusion conditions**

Optimal conditions for fusion (e.g. concentration of polyethylene glycol) need to be carefully determined.

4. **Screening methods**

Rapid and reliable methods to detect the antibody product of the hybrids are necessary.

RELEVANCE OF HYBRIDOMAS TO MEDICAL DIAGNOSIS AND PRACTICE

There are many aspects of medical diagnosis and practice in which hybridomas are of immediate relevance. The chief attraction lies in the resolving power of the hybridoma product: its *monoclonal* nature, its *homogeneity,* its *high affinity* and *absolute specificity.* These features together with the technique's simplicity and thus economical production costs for such antibodies will eventually benefit everyone from the general practitioner doing simple laboratory diagnostic procedures, the transplant surgeon interested in tissue typing and matching, and the research scientist involved, for example, in identification of parasite antigens. More specifically, the areas in which the hybridoma technology has been used or will be of specific value include the following:

1. **Parasitic diseases**

In parts of the world where parasitic diseases are endemic, the detection of antibodies in patients is of little diagnostic value. In relation to this problem, monoclonal antibodies would be invaluable for the detection of parasite *antigens* in infected hosts. Additionally they represent ideal reagents for identification of parasite *variants* e.g. in trypanosomes (Vickerman, 1978), *purification* of antigens from parasite extracts and identification of antigenic determinants on parasite membranes which are involved in the development of immunity to the parasite. These analyses may in turn lead to better *vaccines* against various parasites. Studies using hybridomas have already been initiated with malaria, trypanosomiasis and schistosomiasis (W.H.O., 1979).

2. **Transplantation**

Tissue typing (HLA typing) is still a cumbersome process and monospecific anti-HLA antisera are scarce and difficult to produce. To this purpose, mice could be injected with human lymphocytes or purified human HLA antigens and monoclonal anti-HLA antibodies produced by the hybridoma method as has been done with rodents (Galfre *et al.,* 1977). Truly identical antibodies produced in this way would enable a finer distinction between tissue antigens thus resulting in better matching of tissues prior to transplantation (see New Scientist, 1977; Staehelin, 1978). Additionally, these monoclonal antibodies would be of immense value to researchers attempting to unravel the nature of the association between histocompatibility antigens and human disease e.g. HLA-B27 and ankylosing spondylitis (Staehelin, 1978).

3. **Endocrinology**

Research in several institutes and (significantly) the laboratories of Hoffmann-La Roche in Switzerland has also led to the production, by the hybridoma technique, of high affinity, highly specific antibodies to HCG (human chorionic gonadotrophin), HLH (human luteinizing hormone) and HFSH (human follicle-stimulating hormone) (see New Scientist, 1977; W.H.O., 1979). The commercial availability of these reagents may result in cheaper, more reliable pregnancy testing and may also aid in the diagnosis of choriocarcinoma.

4. **Immunogenetics and Virology**

Hybridoma antibodies have been used to actually map the location of the immunoglobulin heavy chain gene in the mouse (W.H.O., 1979). It has also been used to map the surface of the influenza virus haemagglutinin with obvious implications for serotyping of the various influenza viruses (Cancro *et al.,* 1978).

Looking into the future, the application of

the hybridoma technique appear to be limitless. It could, for example be used to provide better identification of *tumour-specific* antigens and those tissue antigens associated with *autoimmune* diseases. Such reagents may also prove as most important tools for the development of *immunoprophylaxis* against a variety of human diseases.

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HELMINTHIASES IN PENINSULAR MALAYSIA — PREVALENCE AND DENSITY OF INFESTATION OF HOOKWORM, *ASCARIS* AND *TRICHURIS* IN RURAL SCHOOL CHILDREN

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INTRODUCTION

WORM infestations are common in Malaysia, especially in the rural population. Over the past 50 years or so prevalence studies resulted in a few published papers on worm infestations, the prevalence for which tended to variy from study to study and from place to place, and in most instances worm burdens in terms either of actual worm counts or eggloads were left out. Only a few papers on mass treatment of worms of significant sample size are available locally. Consequently a number of practical questions concerning mass treatment from the viewpoint of the National Worm Control Programme could not be answered. The treatment of intestinal helminthic infestations were reviewed by Sandosham (1934). However, in recent years several anthelmintics have been introduced, thus reviving again the question of mass treatment of worm infestations, especially with the use of single dose regimens, as an integral effective measure in worm control.

Consequently this field study on helminthiases in Peninsular Malaysia was designed and implemented over a period of 12 months to determine and compare under field conditions the acceptability and side effects of single doses of 4 currently available anthelmintics and their efficacies against hookworms, roundworms and whipworms in terms of egg reduction; the effects of single doses of anthelmintics on haemoglobin levels, weights and egg-loads at intervals of one, six and twelve months after treatment; and lastly, to note any problems due to mass treatment primary school children in a school environment.

The four anthelmintics included in the study were:

Pyrantel pamoate ('Combantrin'), Phenylene di-iso-thiocyanate 1,4 ('Jonit'), L-Tetramisole ('Decaris'), and Bephenium hydroxynaphthoate ('Bephenate'). The placebo for the control group was vitamin C.

The study was carried out in 3 phases. For publication purpose it has to be presented in a number of papers. This paper deals with the prevalence and density of worm infestations, that is Phase I of the study which began on 24.4.72 and was completed in 4 days.

MATERIALS AND METHODS

Three primary schools in 3 rural kampongs in Teluk Datuk area some 45 miles from Kuala Lumpur City were selected after personal visit by the senior author to the kampongs, taking into account the toilet-house ratios (Kampong Bukit Changgang, 76%; Kampong Labohan Dagan, 25%; Kampong Olak Lempit, 59%), the number of school children in each school (Kampong Bukit Changgang, 296; Kampong Labohan Dagan, 358; Kampong Olak Lempit, 339), and the distances of the kampongs from the temporary field laboratory which was set up for the study in Teluk Datuk.

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Permission and co-operation were obtained from the teachers and parents for the study. Each child was given a numbered plastic sample bottle with a wooden spatula and a pictorial guide as to how to take a stool sample. It was then explained to them by one of us how and when to take the stool sample, warning them not to exchange the bottles amongst themselves, not to mix stool with urine, water or soil, and to bring their own stool samples to school the next morning. Stool samples were collected back the following morning from each child in the classroom: the child's name was called and the sample bottle returned by the child was checked to see if the index number on the bottle coincided with that for the child in the class list. A few who failed to open their bowels were given the chance to try and bring their stool samples the next day.

The stool samples were examined by Stoll's (1923) volumetric dilution method. The ova of hookworms, roundworms and whipworms were counted with tally counters. The consistency of the stool was noted as normal (N), mushy (M) or watery (W), and a correction factor of 1x, 2x and 4x was applied respectively to the calculation of eggloads which were recorded as "Eggs Per Millilitre" of stool (EPM). A small number of samples were insufficient in amount and were examined by direct smear method, but the children were excluded from the study.

Hookworm culture was done on all positive stool samples, using the method of Harada & Mori (1951) and Hsieh H.C. (1971).

Statistical significance tests used included significance test of difference between two proportions, chi square of 2 x 2 and 2 x k contingency tables with the use of tukey's t, and critical ratio, z.

RESULTS

Prevalence and Density of Worm Infestations:

Of 967 stool samples collected from school children aged 6 to 12 years, 834 samples were examined by Stoll's method and the rest by direct smears. Only the results obtained by Stoll counts were included in this study.

Table I shows the crude hookworm, roundworm and whipworm prevalence rates, as well as the percentages of single, double and triple infestations. The species prevalence rates for hookworm, roundworm and whipworm varied from 33 - 51%, 84 - 89% and 79 - 88%, respectively. Analyses of the data showed that there was no statistical significance at 95% proability level between the various rates by sex, age and by school.

Double worm infestation was the most common occurrence, accounting for 45.1% of all infestations: roundworm + whipworm (39.6%), hookworm + whipworm (3.5%) and hookworm + roundworm (2%).

Table II shows the densities of helminthic infestations in term of Eggs Per Millilitre (EPM), by sex of host. The average eggloads for hookworm, roundworm and whipworm were 1964, 59 700, and 6 233 EPM, respectively.

DISCUSSION

The results of this study confirmed that worm infestations were common, particularly in the rural population like the one studied. The hookworm, roundworm and whipworm infestation rates were 43.2%, 86.7%, and 84.5%, respectively. The prevalence of *Enterobius vermicularis* remained unknown, since stool examination is not suitable for its detection. The densities of infestations in term of eggloads could be considered light to moderate for hookworm, and moderate to heavy for roundworm and whipworm. The range of eggloads varied widely, reflecting the variability of the helminths' egg-laying capacities, especially that for roundworms, which were similarly observed by Lie *et al.* (1971).

The subject of worm infestations in Malaysia was reviewed by Lie (1964). Russel (1934) found in the Straits Settlements (1925-1928) a prevalence rate of 5% in 0 - 5 years old, 74% in 6 - 12 years, 51% in 13 - 18 years, 74% in 19 - 40 years, and 78% in 41 - 70 years old, for hookworm infestation, the combined prevalence rate being 70.7%. It is interesting to note that the hookworm infestation rate for pre-school children then was very low, while that for primary school children aged 6 - 12 years old was much higher than rates obtained in this and other studies. Perhaps the findings of Russel for

Table I

PREVALENCE OF WORM INFESTATIONS IN RURAL MALAY SCHOOL CHILDREN AGED 6 — 12 YEARS

SEX	TOTAL NO. OF SAMPLES EXAMINED	TOTAL NO. POSITIVE FOR ONE OR MORE WORMS	PREVALENCE RATE [%]				INFESTATION [%]			
			CRUDE	HOOK-WORMS	ROUND-WORMS	WHIP-WORMS	NONE	SINGLE	DOUBLE	TRIPLE
MALE	435	414	95.2	48.1	86.4	84.1	4.8	13.3	40.2	41.6
FEMALE	399	378	94.7	37.8	87.0	85.0	5.3	12.0	50.4	32.3
BOTH	834	792	95.0	43.2	86.7	84.5	5.0	12.7	45.1	37.2

$$\text{CRUDE WORM PREVALENCE RATE} = \frac{\text{TOTAL NO. OF POSITIVE SAMPLES X 100}}{\text{TOTAL NO. OF SAMPLES EXAMINED}}$$

$$\text{HOOKWORM PREVALENCE RATE} = \frac{\text{TOTAL NO. OF H.W. POSITIVES x 100}}{\text{TOTAL NO. OF SAMPLES EXAMINED}}$$

Table II

INTENSITIES OF HELMINTHIC INFESTATIONS IN RURAL MALAY SCHOOL CHILDREN AGED 6 — 12 YEARS

SEX	TOTAL NO. OF SAMPLES EXAMINED	TOTAL NO. POSITIVE FOR ONE OR MORE WORMS	EGGS PER ML. OF STOOL [STOLL'S METHOD]								
			HOOKWORM			ROUNDWORM			WHIPWORM		
			NO. OF CHILDREN	AVERAGE	RANGE	NO. OF CHILDREN	AVERAGE	RANGE	NO. OF	AVERAGE	RANGE
M	435	414	209	2111	100-20000	376	62252	100-447552	366	7052	100-182000
F	399	378	151	1761	200-9612	347	56934	276-756000	339	5348	182-224000
B	834	792	360	1964	100-20000	723	59700	100-756000	705	6233	100-224000

M=MALE F=FEMALE B=BOTH

hookworm infestation could be attributed to poorer environmental sanitation and socioeconomic standard at that time. Sandosham (1955) found a hookworm prevalence rate of 30.6% for 46 208 stool samples from the Straits Settlements. Lie *et al.* (1971) found that in rural infants and children near Kuala Lumpur, the hookworm infestation rate ranged from 24 - 33%, while 33 - 82% and 31 - 84% in two rural areas were infested with roundworms and whipworms, respectively. The worm burdens were generally low, ranging from less than 2 000 to 4 200 EPG for hookworm, less than 50 000 to 274 000 EPG for roundworm and less than 2 000 to 63 000 EPG for whipworm. These results were comparable with this study.

According to the worm infestation surveys in the Environmental Sanitation Pilot Project (ESPP) areas in eleven states of Peninsular Malaysia conducted at Public Health Institute in 1968 (Low, D.O. unpublished), out of 8 131 samples examined 84.4% were positive for one or more species of worms with a range of 67.1% to 95.5%. The hookworm, roundworm and whipworm infestation rates were 35.6%, 68% and 55.8% respectively, with no significant difference by sex. Prevalence by ethnic groups, namely, Malays, Indians, and Chinese was 87.3%, 72.0%, and 71.6% respectively. The infestation rate for children 6 to 12 years old ranged from 79.2% to 89.0%, with a mean of 85.1%. Some of these results were comparable with those obtained in the present study, while some tended to be slightly lower. No significant difference was found between the crude prevalence rates for ages 6 to 12 years in the ESPP survey, nor in the present study.

One important point to note as shown by the ESPP survey was that the crude infestation rates tended to fall with increasing age, e.g., for 85.1% for ages 6 to 12 years, down to 11.8% for adults. Another point of interest, perhaps worthy of further study, was the relationship between latrines and worm infestations. No significant differences were found in prevalence and worm burden amongst the schools in the three kampongs, although there were important differences in the means of human excreta disposal. For example, Kampong A had a latrine/house ratio of 76% (98% pit, 2% pour-flush latrines), compared with Kampong C and Kampong B which had latrine/house ratios of 59% (67% pit, 33% pour-flush latrine) and 25% (94% pit and 6% pour-flush latrines) respectively. There were probably many reasons for this anomaly such as the insufficient number and/or unsuitable types of latrines, the distance of the latrine from the house, and the KAP of the people leading to the under-utilisation of the available latrines, especially by the young children, who are the main reservoir of infestation.

Environmental sanitation in the control of worm infestations is a slow process and changes in the attitude and practice of the people is even slower. There is also evidence to suggest that environmental sanitation alone cannot control worm infestations such as ascariasis (WHO Expert Committee on Control of Ascariasis 1967). A combination of methods, including mass treatment for worms and the improvement of the nutritional status of the community, supported with effective health education, is more likely to succeed.

SUMMARY

The reasons for this field study were stated. This paper presented and discussed the prevalence and density of worm infestation of hookworm, *Ascaris* and *Trichuris* in 834 rural school children aged 6 to 12 years. The crude worm prevalence rate was 95.0%, and the mean species prevalence rate for Hookworm, roundworm and whipworm was 43.2%, 86.7% and 84.5% respectively. Mixed infestations were most common, 45.1%, 37.2% and 12.7% being double, triple and single infestations respectively. The average eggloads for hookworm, roundworm and whipworm were 1964, 59 700, and 6 233 EPM respectively.

The relation of environmental sanitation in term of latrine/house ratios and the degree of infestation was highlighted, and the need for a combination of methods for worm control was stressed.

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FOOD BELIEFS OF RURAL MALAY WOMEN OF TRENGGANU

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INTRODUCTION

MALNUTRITION is the product of a wide variety of dietary as well as non-dietary factors. In the developing world, defective dietary intake is perhaps the principal cause of malnutrition. Defective intake itself may be due to a series of factors of which poverty and traditional food habits are the most important.

In this paper, the authors report a study carried out in several rural Malay communities in Trengganu before the Applied Food and Nutrition Programme was launched in these communities and examine their observations regarding the traditional food beliefs of this sample of 216 rural Malay women.

METHOD

216 women from villages in the Applied Food and Nutrition Programme area in Trengganu were asked in mid-1975 for their responses to a list of different foods. These were classified according to whether they were perceived to be (A) highly beneficial (B) beneficial (C) neutral or of uncertain value (D) taboo (food to be avoided), for (1) toddlers, 1-4 years old (2) expectant mothers (3) postnatal mothers. The findings are discussed in this paper.

STUDY POPULATION

General Socioeconomic Characteristics

Out of the 216 households surveyed, 44% were engaged in agriculture for a living. 54% of the study population were self-employed, 38% were employed by others, 5.6% by the government, 0.5% were employers and 1.9% were unemployed. 45% of the study population did not own land, 71.8% owned their own houses, 50.9% had radios while 8.3% had television sets. 195 or 40.3% earned less than $300 per month, while the average monthly income per household was $144. This is very much lower than the national average monthly income in 1970 of $275. More than ¾ of the population had 6 years of education or less, however a third had had no education at all.

General Characteristics of the Respondents

31 out of the 216 women were pregnant at the time the study was made, 84 had children below 1 year of age and nearly 90% (88.4%) had 1 or 2 children below the age of 5. This area is well served by government services as the majority of the women make use of the *bidan kerajaan* (government midwife) or a *bidan kampung terlatih* (a trained traditional midwife).

The attitude towards breastfeeding is positive on the whole. Of those who are pregnant, all except two, prefer to breastfeed, most of them for 11-12 months or more. Furthermore, 77 or 91.7% of the women with infants less than a year old breastfed them; 14 (16.7%) for less than a month, 29 (34.5%) for 11-12 months, and 21 (25%) for more than a year.

OBSERVATIONS

It is obvious from this study that different food values were assigned to different foods by this rural community in Trengganu. These varied according to whether the group were toddlers, pregnant women, or postnatal women. Thus it was noted that, what was thought to be good for a pregnant woman might be considered taboo for a woman after delivery.

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Toddlers

From Tables I-III, it will be seen that more than 5% of those questioned would have toddlers avoid rabbit, catfish, eel, dogfish and *petai*. Fermented rice, fish fry, sting ray, tuna, cockle, salted fish, fish paste, prawn paste, cucumber, fresh buffalo's milk, cashew nut shoots, bamboo shoots, bitter gourds, brinjal and guava were all considered taboo for toddlers by 1% to 4.9% of the respondents. All the other foods were generally considered to be highly beneficial or beneficial for toddlers. In fact, rice, the cultural superfood, was considered by 88.9% to be highly beneficial and the remaining 11% to be beneficial for toddlers.

Table I

Per cent distribution of responses of 216 Malay women according to their perceived value of carbohydrate foods in relation to toddlers.

Food Item	Per cent responses according to perceived value of food [A-D] in relation to toddlers [1-4 years]				
Carbohydrate Foods	A	B	C	D	Total
Rice	88.9	11.0	0.0	0.0	100
Glutinous rice	5.6	87.5	6.5	0.5	100
Fermented rice	3.2	70.8	21.8	4.2	100
Bread	37.0	61.1	1.4	0.5	100
Noodles	32.9	66.7	0.5	0.0	100
Corn	12.0	76.9	0.8	0.9	100

A - perceived to be highly beneficial

B - perceived to be beneficial

C - perceived to be neutral or uncertain

D - perceived to be taboo and to be avoided

Expectant Women

Most of the foods considered taboo for toddlers were also considered to be taboo for expectant women (Tables IV to VI). Thus, between 1% to 4.9% of the respondents considered fermented rice, fish fry, sting ray, tuna, cockle, salted fish, fish paste, prawn paste and cucumber to be harmful for the expectant woman and more than 5% of them considered rabbit, catfish, eel and dogfish to be taboo for the expectant woman.

Table II

Per cent distribution of responses of 216 Malay women according to their perceived value of protein foods in relation to toddlers.

Food Item	Per cent responses according to perceived value of food [A-D] in relation to toddlers [1-4 years]				
Protein Foods	A	B	C	D	Total
Milk powder	48.6	45.4	6.0	0.0	100
Fresh cow's milk	35.2	56.5	8.3	0.0	100
Sweetened condensed milk	18.5	78.2	3.2	0.0	100
Fesh buffalo's milk	19.4	69.4	9.7	1.4	100
Beef	43.5	56.5	0.0	0.0	100
Mutton	38.4	61.1	0.5	0.0	100
Poultry	40.3	59.3	0.5	0.0	100
Rabbit	6.9	39.4	38.9	14.8	100
Eggs	35.2	63.0	0.9	0.9	100
Turtle's eggs	8.8	89.8	0.9	0.5	100
Fish roe	5.1	94.0	0.9	0.0	100
Fish fry	8.3	85.6	3.2	2.8	100
Anchovy	39.8	60.2	0.0	0.0	100
One-finlet scad	34.3	65.3	0.5	0.0	100
Chubb mackerel	33.8	65.7	0.5	0.0	100
Round scad	34.7	62.0	3.2	0.0	100
Stingray	3.7	58.8	30.6	6.9	100
Catfish, eel	0.0	53.2	38.4	8.3	100
Tuna	4.2	88.0	5.6	2.3	100
Dogfish	1.9	50.5	30.6	17.1	100
Prawn	21.8	78.2	0.0	0.0	100
Squid	21.8	76.9	1.4	0.0	100
Cockle	16.2	71.3	9.3	3.2	100
Salted fish	2.8	78.7	9.7	8.8	100
Fish paste	1.4	75.5	15.3	9.9	100
Prawn paste	1.9	77.8	13.4	6.9	100

A - perceived to be highly beneficial

B - perceived to be beneficial

C - perceived to be neutral or uncertain

D - perceived to be taboo or to be avoided

However, expectant women would not have to avoid fresh buffalo's milk, cashew nut shoots, bamboo shoots, bitter gourds, brinjal, guava and *petai* - food items that are avoided by toddlers. In other words, expectant women had fewer taboos than toddlers and most of the taboo foods were the relatively "exotic" foods.

Postnatal Women

Postnatal women were expected to be much

Table III

Per cent distribution of responses of 216 Malay women according to their perceived value of vitamin foods in relation to toddlers

Food Item	Per cent responses according to perceived value of food [A-D] in relation to toddlers [1-4 years]				
Foods which provide vitamins and minerals	**A**	**B**	**C**	**D**	**Total**
Spinach	41.7	57.9	0.0	0.5	100
Cekor manis	35.2	63.4	1.4	0.0	100
Kangkong	32.4	67.6	0	0.0	100
Cabbage	24.1	72.2	3.2	0.5	100
Daun turi	6.0	68.1	25.0	0.9	100
Tapioca shoots	10.2	83.3	6.5	0.0	100
Sweet potato tops	11.1	84.7	4.2	0.0	100
Fern shoots	10.2	86.1	3.7	0.0	100
Pucuk/daun peraga	1.4	75.5	22.7	0.5	100
Cashew nut shoots	1.4	72.7	22.7	3.2	100
Bamboo shoots	1.4	87.5	8.8	2.3	100
Sawi	28.7	70.8	0.5	0.0	100
Ladies fingers	25.9	70.4	3.7	0.0	100
Gourds	14.4	83.8	1.4	0.5	100
Soya beans	23.1	59.7	17.1	0.0	100
French beans	24.5	69.9	5.6	0.0	100
Long beans	28.7	71.3	0.0	0.0	100
Bitter gourds	6.9	72.7	18.1	2.3	100
Petai/jering	2.8	74.1	17.1	6.0	100
Bean sprouts	16.7	82.4	0.5	0.5	100
Cucumber	10.2	87.0	0.0	2.8	100
Brinjal	7.4	89.4	1.9	1.4	100
Pineapple	13.0	85.2	1.4	0.5	100
Banana	24.5	75.0	0.5	0.0	100
Papaya	22.7	76.9	0.5	0.0	100
Lime	18.1	81.5	0.5	0.0	100
Ciku	12.0	87.0	0.5	0.5	100
Jackfruit	8.3	90.7	0.5	0.5	100
Guava	5.6	92.6	0.5	1.4	100
Belimbing	1.9	93.5	3.7	0.9	100
Watermelon	8.3	91.2	0.5	0.0	100

A - perceived to be highly beneficial

B - perceived to be beneficial

C - perceived to be neutral or uncertain

D - perceived to be taboo or to be avoided

Table IV

Per cent distribution of responses of 216 Malay women according to their perceived value of carbohydrate foods in relation to expectant mothers

Food Item	Per cent responses according to perceived value of food [A-D] in relation to expectant mothers				
Carbohydrate foods	**A**	**B**	**C**	**D**	**Total**
Rice	92.6	7.4	0.0	0.0	100
Glutinous rice	6.5	86.6	6.5	0.5	100
Fermented rice	5.6	78.7	12.5	3.2	100
Bread	35.2	63.0	1.4	0.5	100
Noodles	77.8	68.1	0.5	0.0	100
Corn	8.8	80.1	10.6	0.5	100

A - perceived to be highly beneficial

B - perceived to be beneficial

C - perceived to be neutral or uncertain

D - perceived to be taboo or to be avoided

more restricted in their food intake than either expectant women or toddlers (Tables VII to IX). Between 1% to 4.9% of the respondents believed that women after delivery should avoid all leafy vegetables, vegetables and fruits that are listed. All meat, eggs and fish on the list, except for ordinary hen's eggs, anchovy, one-finlet scad, chubb mackerel and round scad were also taboo foods for postnatal women. In addition, they were also expected to avoid glutinous rice, fermented rice, corn and fresh buffalo's milk.

In addition, more than 5% of the respondents believed that postnatal women should avoid all the foods that toddlers and expectant women were expected to avoid. Furthermore they were expected to avoid squid and most vegetables and fruits. In fact, more than 20% of those questioned believe that gourds, pineapple and *belimbing* should be avoided by postnatal women, indicating that "cold" foods particularly fruits and vegetables were considered to be very much taboo.

Table V

Per cent distribution of responses of 216 Malay women according to their perceived value of protein foods in relation to expectant mothers

Food Item	Per cent responses according to perceived value of food [A-D] in relation to expectant mothers				
Protein foods	**A**	**B**	**C**	**D**	**Total**
Milk powder	48.1	44.9	6.9	0.0	100
Fresh cow's milk	34.7	56.5	8.3	0.5	100
Sweetened cond. milk	19.0	78.7	2.3	0.0	100
Fresh buffalo's milk	18.5	70.8	9.7	0.9	100
Beef	44.0	56.0	0.0	0.0	100
Mutton	38.9	60.6	0.5	0.0	100
Poultry	41.2	58.8	0.0	0.0	100
Rabbit	6.5	40.7	38.0	14.8	100
Eggs	33.8	64.4	0.9	0.9	100
Turtle's eggs	10.6	88.4	0.5	0.5	100
Fish roe	7.4	92.1	0.5	0.0	100
Fish fry	8.8	88.9	0.9	1.4	100
Anchovy	39.8	60.2	0.0	0.0	100
One-finlet scad	34.3	65.7	0.0	0.0	100
Chubb mackerel	34.7	64.8	0.5	0.0	100
Round scad	33.8	63.9	2.3	0.0	100
Stingray	2.8	65.3	27.8	4.2	100
Catfish, eel	0.5	57.4	35.6	6.5	100
Tuna	4.2	91.7	2.3	1.9	100
Dogfish	1.4	49.5	32.9	16.2	100
Prawn	21.3	78.7	0.0	0.0	100
Squid	22.7	76.9	0.5	0.0	100
Cockle	17.6	71.3	9.3	1.9	100
Salted fish	3.7	88.9	2.8	4.6	100
Fish paste	3.7	92.1	1.9	2.3	100
Prawn paste	3.7	92.6	1.4	2.3	100

A - perceived to be highly beneficial

B - perceived to be beneficial

C - perceived to be neutral or uncertain

D - perceived to be taboo or to be avoided

Table V I

Per cent distribution of responses of 216 Malay women according to their perceived value of vitamin and mineral rich foods in relation to expectant mothers

Food Item	Per cent responses according to perceived value of food [A-D] in relation to expectant mothers				
	A	**B**	**C**	**D**	**Total**
Spinach	40.7	59.3	0.0	0.0	100
Cekor manis	32.4	66.7	0.9	0.0	100
Kangkong	30.1	69.9	0.0	0.0	100
Cabbage	24.1	73.1	2.3	0.5	100
Daun turi	6.5	71.3	21.3	0.9	100
Tapioca shoots	11.1	87.5	0.9	0.5	100
Sweet potato tops	11.6	88.4	0.0	0.0	100
Fern shoots	11.6	87.5	0.9	0.0	100
Pucuk/daun peraga	4.6	87.0	7.9	0.0	100
Cashew nut shoots	3.7	88.9	7.4	0.0	100
Bamboo shoots	3.7	9.2	1.9	0.0	100
Mustard leaves	29.2	70.8	0.0	0.0	100
Ladies fingers	26.4	70.8	2.8	0.0	100
Gourds	13.4	85.2	1.4	0.0	100
Soya beans	24.5	58.8	16.7	0.0	100
French beans	24.5	69.9	5.6	0.0	100
Long beans	31.9	68.1	0.0	0.0	100
Bitter gourds	9.7	79.2	10.6	0.5	100
Petai/jering	7.4	88.4	3.7	0.5	100
Bean sprouts	16.2	82.4	0.9	0.5	100
Cucumber	11.6	83.3	0.9	4.2	100
Brinjal	10.2	88.0	1.9	0.0	100
Pineapple	14.4	84.7	0.9	0.0	100
Banana	24.1	75.0	0.9	0.0	100
papaya	22.7	76.9	0.5	0.0	100
Lime	18.5	81.0	0.5	0.0	100
Ciku	12.5	87.0	0.5	0.0	100
Jackfruit	8.3	91.2	0.5	0.0	100
Guava	6.0	92.6	0.5	0.9	100
Belimbing	3.2	94.9	1.9	0.0	100
Watermelon	8.3	90.7	0.9	0.0	100

A - perceived to be highly beneficial

B - perceived to be beneficial

C - perceived to be neutral or uncertain

D - perceived to be taboo or to be avoided

Table VII

Per cent distribution of responses of 216 Malay women according to their perceived value of carbohydrate foods in relation to postnatal mothers

Food Item	Per cent responses according to perceived value of food [A-D] in relation to postnatal mother				
	A	B	C	D	Total
Rice	88.0	12.0	0.0	0.0	100
Glutinous rice	5.6	74.5	15.7	4.2	100
Fermented rice	6.9	67.6	22.2	3.2	100
Bread	34.3	63.0	1.9	0.5	100
Noodles	31.5	68.1	8.8	0.9	100
Corn	9.3	80.1	10.6	1.9	100

A - perceived to be highly beneficial

B - perceived to be beneficial

C - perceived to be neutral or uncertain

D - perceived to be taboo or to be avoided

Table VIII

Percent distribution of responses of 216 Malay women according to their perceived value of protein foods in relation to postnatal mothers

Food Item	Per cent responses according to perceived value of food [A-D] in relation to postnatal mothers				
	A	B	C	D	Total
Milk powder	47.2	46.3	6.5	0.0	100
Fresh cow's milk	35.2	54.6	9.7	0.5	100
Sweetened cond. milk	17.6	77.8	4.6	0.0	100
Fresh buffalo's milk	19.0	69.0	10.6	1.4	100
Beef	42.6	51.4	4.6	1.4	100
Mutton	38.0	56.5	4.2	1.4	100
Poultry	40.7	53.7	4.2	1.4	100
Rabbit	6.0	38.4	40.7	14.8	100
Eggs	33.8	61.6	4.2	0.5	100
Turtle's eggs	9.3	81.0	7.4	2.3	100
Fish roe	6.9	87.0	4.6	1.4	100
Fish fry	7.9	88.0	2.3	1.9	100
Anchovy	39.4	57.4	2.3	0.9	100
One-finlet scad	33.8	65.3	0.9	0.0	100
Chubb mackerel	33.8	66.2	0.0	0.0	100
Round scad	31.9	63.9	3.2	0.9	100
Stingray	2.3	48.1	41.7	7.9	100
Catfish, eel	0.0	45.8	48.1	6.0	100
Tuna	3.2	70.8	20.4	5.6	100
Dogfish	0.0	34.3	47.2	18.5	100
Prawn	17.6	58.3	17.6	6.5	100
Squid	17.6	58.8	16.7	6.9	100
Cockle	15.3	53.7	24.1	6.9	100
Salted fish	3.2	80.1	5.6	11.1	100
Fish paste	2.3	31.0	47.7	19.0	100
Prawn paste	1.9	33.8	45.4	19.0	100

A - perceived to be highly beneficial

B - perceived to be beneficial

C - perceived to be neutral or uncertain

D - perceived to be taboo or to be avoided

DISCUSSION

General Attitudes towards Foods

In general, there is less avoidance of food among pregnant women compared with postnatal women. Out of the 31 pregnant women, only 4 (12.9%) avoided one or more foods, whereas 49 out of 84 (58.3%) women avoided various foods after delivery. There is some avoidance of food among young children, especially toddlers of 1-4 years old. For this group, there is a greater avoidance of some kind of vegetables or fruits as well as hot foods [*makanan pedas*] rather than bread or cereal type of food.

A large proportion of the infants who were weaned (65.3%) started on "nestum" a pre-cooked cereal food that is a relatively expensive food product. Undoubtedly, nutrition education can play a constructive role in promoting the use of cheap and fresh local substitutes. Among the study population of 216 households, fresh milk is consumed in only 30 (13.9%) households. The attitude towards growing their own food is positive: most of them (69%) when asked said that they would grow soya beans for home consumption and every household responded favourably to growing vegetables. However, only 17.1% of the respondents said that they would rear rabbits for food whereas 30.1% would rear pigeons for a similar purpose. This is due to the cultural belief that a rabbit is a pet similar to a cat and should not be eaten, while pigeons are akin to the small birds that are ocassionally hunted as a food supplement.

Table IX

Per cent distribution of responses of 216 Malay women according to their perceived value of vitamin and mineral rich foods in relation to postnatal mothers

Food Item	Per cent responses according to perceived value of food [A-D] in relation to postnatal mothers				
	A	B	C	D	Total
Spinach	28.2	36.6	29.6	5.6	100
Cekor manis	24.1	51.4	20.8	3.7	100
Kangkong	23.6	47.2	25.0	4.2	100
Cabbage	19.9	58.8	18.5	2.8	100
Daun turi	4.2	55.1	37.5	3.2	100
Tapioca shoots	7.9	62.0	26.4	3.7	100
Sweet potato tops	7.4	61.6	26.4	4.6	100
Fern shoots	8.3	52.8	32.4	6.5	100
Pucuk/daun peraga	3.7	67.6	24.1	4.6	100
Cashew nut shoots	2.3	66.2	26.9	4.6	100
Bamboo shoots	2.3	53.2	31.5	13.0	100
Sawi	27.8	48.1	17.6	6.5	100
Ladies fingers	23.1	4.5	25.9	4.6	100
Gourds	4.6	19.9	54.6	20.8	100
Soya beans	19.4	45.4	33.3	1.9	100
French beans	22.7	54.2	19.0	4.2	100
Long beans	29.6	53.7	13.9	2.8	100
Bitter gourds	8.8	63.0	25.5	2.8	100
Petai	6.5	48.1	38.0	7.4	100
Bean sprouts	14.8	53.2	24.1	7.9	100
Cucumber	9.3	33.3	40.7	16.7	100
Brinjal	7.9	32.4	47.2	12.5	100
Pineapple	6.5	13.4	58.3	21.8	100
Banana	21.3	64.4	10.2	4.2	100
Papaya	16.7	39.4	30.6	13.4	100
Lime	15.7	46.3	24.5	13.4	100
Ciku	8.8	46.8	29.2	15.3	100
Jackfruit	6.0	32.4	44.4	17.1	100
Guava	4.6	39.8	39.4	16.2	100
Belimbing	0.9	20.8	57.4	20.8	100
Watermelon	4.6	28.2	47.2	19.9	100

A - perceived to be highly beneficial

B - perceived to be beneficial

C - perceived to be neutral or uncertain

D - perceived to be taboo or to be avoided

Taboo Foods

There are probably many varied reasons for avoiding different foods. Thus, some foods are avoided because they are believed to be cooling while some are believed to be heaty (Chen, 1977) and perhaps some are avoided because of practical problems associated with it (for instance, guava - the only fruit that are believed by more than 1% of the respondents to be harmful to toddlers - may be avoided because it is too hard for the child). Catfish, eel and dogfish resembles snakes and are culturally avoided as snakes are considered evil.

In general, it can be concluded from this study that the foods avoided by toddlers are also avoided by expectant women. However, more foods are taboo for toddlers than for expectant women. Nevertheless postnatal women, on the whole, appear to be the most constrained among the three groups in terms of food taboos. Thus, it appears that postnatal women are recognised to be the most vulnerable of all three. Ironically, it is precisely because they are more vulnerable that food avoidance would do them the most harm. Since most of the taboo foods for this group of women are fruits, vegetables, fish, meat and eggs, they would be deprived of vital sources of vitamins, minerals and proteins. This has been noted to be associated with low serum levels for folic-acid, carotene and iron (Wilson *et al.*, 1970).

How does the practice of avoiding foods affect the nutrition of the people concerned? For toddlers and expectant women, food avoidance is relatively limited in extent and probably not the main cause of malnutrition with the exception of very poor families who are avoiding an extremely cheap and rich source of protein or vitamins. In many instances alternatives can usually be found. Thus, salted fish, fish paste and prawn paste are good sources of protein and minerals. However, not much can be taken at any one sitting and hence they are not good sources for protein and would not be missed as a protein source even if avoided. In fact rice, the cultural superfood is the principal source of protein in most rural diets even though rice only contains 7.1% of protein. Cucumber, the only vegetable that is avoided by all 3 groups, is also not that important as it can be replaced by other and often better, sources of vitamins. Stingray, catfish, eel, dogfish, tuna and

fish fry can also be replaced by alternate sources of protein. However the need for health education to ensure the replacement by non-taboo foods must receive proper attention if malnutrition is to be avoided. Fermented rice is probably not too great a loss either, especially since rice itself is considered a cultural superfood. On the other hand, deliberate avoidance of fresh buffalo's milk would be a loss if the family possesses a buffalo.

The foregoing is only true for the relatively uncommon exotic foods avoided by toddlers and expectant women. However, the large number of taboos of postnatal women, and the fact that they are in a particularly vulnerable condition means that food avoidance among postnatal women usually have more serious consequences and greater care must be exercised.

Beneficial Foods

Rice ranks high above all other foods as the so-called cultural superfood, considered by nearly 90% of the respondents to be highly beneficial for all the 3 groups - toddlers, expectant and postnatal women. Interestingly enough, milk powder is considered more beneficial by a larger percentage of the respondents than fresh cow's milk whilst buffalo's milk is taboo for toddlers and postnatal women and most consider sweetened condensed milk to be beneficial but not highly so. The high standing of powdered milk is probably due to the associated high status value given to the milk by commercial advertisements.

Beef, mutton, poultry and anchovy, all excellent protein sources, are rightly considered highly beneficial by well over a third of the respondents. Spinach, a good source of iron, is also considered highly for toddlers and expectant women by more than 40% of those questioned although it is generally an avoided food item for postnatal women. The one-finlet scad and chubb mackerel are two fishes considered beneficial for postnatal women by nearly all the respondents which is good since these are relatively small and cheaper fishes. Bread and eggs are also considered beneficial foods.

All the foods considered beneficial are also good nutrient sources. Of special significance is rice, which is considered by more than 85% of the respondents to be highly beneficial for all 3 groups. This is important because rice is the staple food in Malaysia and is the principal source of protein in most rural diets. Beef and poultry are generally considered beneficial even for postnatal women although 1.4% of the respondents would still believe that it should be avoided by them. Thus, most of the foods classified as beneficial are nutritious foods although not all nutritious foods are classified as beneficial.

CONCLUSION

Findings from studies such as this have implications for the socio-economic development of Malaysia. Programmes such as the Applied Food and Nutrition Programme will have to take local customs and taboo practices into consideration in order to achieve its targets. Thus, if it is part of a programme to introduce a new food into the community, then one has to first assess the community's attitudes towards that new food. Harmful practices such as avoidance of some crucial foods by a highly vulnerable population group will be the concern of nutrition educators. A widespread belief in this country is that foreign or manufactured products are superior to local ones. In some poor families, this may lead to parents spending their limited income on these products while cheaper substitutes will do just as well or may even be better. For example, many families in this study area wean their children on "nestum". The nutritional qualities of "nestum" notwithstanding, nevertheless it is still an expensive food item which can be satisfactorily substituted for by a rice and fish broth (Chen, 1974; Chen 1978).

However, it should be borne in mind that food taboos *per se* are not the sole cause of malnutrition, but that malnutrition is caused by a complex series of multiple factors including socio-economic, educational, agricultural and other factors. It should also be noted that even with postnatal women, for any of the foods listed, only up to 21% felt that it was taboo. Nevertheless the study indicates that the need for nutrition education is present and should be pursued along with concerted efforts in all other related areas.

SUMMARY

216 women from rural villages in the Applied Food and Nutrition Programme area in Trengganu were asked to classify various foods accord-

ing to whether these were perceived to be highly beneficial, beneficial, neutral or uncertain and taboo, for toddlers aged 1-4 years of age, expectant mothers and postnatal mothers. It was found that several foods were perceived to be taboo. However more foods were perceived to be taboo for toddlers than for expectant women but that the most constrained among the three groups were the postnatal women. Since most of the foods were fruits, vegetables, fish, meat and eggs it was noted that this was associated with low serum levels for folic-acid, carotene and iron among the postnatal women.

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ATTITUDES ON HEALTH CARE OF VILLAGERS ATTENDING A RURAL CLINIC IN MALAYSIA

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INTRODUCTION

RURAL Malaysians use different health care resources to cure an ailment (Chen, forthcoming; Heggenhougen: forthcoming). The resources include traditional healers and cosmopolitan practitioners. It is questioned whether or not the practice of such medical pluralism calls for increased contact, if not collaboration, between practitioners of the different existing health care systems.

To get an idea of such pluralistic practices we interviewed one hundred persons attending a rural clinic in northwest peninsular Malaysia. The results of interviews with 100 people visiting a traditional, folk, healer has been recorded elsewhere (Heggenhougen; forthcoming B). The clinic is in a small town of about 3000 people. A hard surface road connects the town with a number of villages from which people come by bus, taxi, motorcycle or bicycle. Dirt paths connect nearer villages with the town. In addition to obtaining demographic data we asked the patients about the complaints for which they visit the clinic and about their views on the rural clinic in general. We were interested in their perceptions about etiology, whether or not other treatment methods had been attempted, and their reaction to, or use of, traditional healers or bomohs.

PROCEDURES

We interviewed persons waiting to be attended to at the clinic by asking demographic and open-ended questions during a two month period in 1978. We randomly interviewed recently arrived people so that they would not be delayed in being admitted to the clinic staff. Persons interviewed were assured confidentiality. They were told their participation would be voluntary and whether or not they agreed to be interviewed would not influence how they would be received or treated by the clinic staff. The interviews were conducted in Malay by two Malay men in their mid-twenties. Most of those interviewed were men. This no doubt makes for distortion as women might have refused to be interviewed by male interviewers (because of shyness or of being preoccupied with their children), but, unlike the situations reported for clinics elsewhere, the majority of persons attending this clinic (except for days set aside for maternal and child health) are men.

We felt some questions might be awkward for the respondents if asked of them directly, and thus in a number of instances we employed an indirect approach, assuming respondents would be more open when speaking about the attitudes and opinions of their neighbors (in general) whereas these might also reflect their own.

RESULTS AND DISCUSSION

The majority of patients came from the town where the clinic is located but a number came from as far away as ten miles. Of the 85 men and 15 women interviewed, ninety-three were Malays, three were Chinese, three were Indians and one "other." Twelve had no formal education, 25 had gone to school one to three years, 37 had gone four to six years, 7 had gone seven to nine years and nine had gone ten to twelve years. Among the respondents were seven students, 10 businessmen, four fishermen, five government clerks and four factory workers; the rest was either farmers, wives of farmers or people with odd jobs.

Eighty-two respondents were patients themselves. The other 18 were people (usually a

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parent) accompanying children who were the patients. Most complaints for which people had come to the clinic were minor (see Table I.).

Table I

Complaints as described by respondents

Complaints	Adult	Child
Fever	15	3
Cuts/sores/boils	13	4
Cough/sore throat	8	5
"Influenza" (cold)	8	—
"Twisted" bones	5	—
T.B.	5	—
Skin problems	5	1
Stomach ache	5	4
Toothache	4	—
General pain (and "nerves")	4	—
Asthma	4	—
Headache	3	—
Renal problems	2	—
Drug addiction	1	—
Mumps	—	1
Total	82	18

Sixty-six respondents said they had already tried another type of treatment for the ailment they presented at the clinic (see Table II). Seventy-seven percent of those with seven or more years of schooling had tried another health care resource before coming to the clinic with their present problem whereas only 64% of those with less, or no, schooling did so. However, more than twice as many of the least schooled (26%) had sought help from their neighbors than had the more schooled (10%). None of the more schooled denied that villagers sometimes went to both the clinic and the bomoh when sick, whereas 20% of the less schooled denied the dual use (possibly this reflects an attempt to seem "progressive" rather than the respondents' actual opinion).

Forty-one respondents had had their health problem three days or less and 68 had had it for less than a week. Twenty three had had the problem for at least a month; some indicated "several years." Contrary to other studies (Heggenhougen: forthcoming B), we found the length of illness could not be significantly correlated with whether or not another treatment method had been used before coming to the clinic.

Table II

Other health resources already used for current problem

Medicine from drug store[1]	23
Self treatment[2]	14
Chinese traditional medicine	10
Bomoh treatment	8
Help from neighbor or older person	2
Medicine from Malay medicine seller	1
Other	8

[1]The use of "medicine from drug stores" implies that people obtained the medicines specifically for their present problem.

[2]"Self-treatment" includes both the use of medicines obtained in provision shops or drug stores (often obtained at an earlier date for another but similar ailment) and a number of folk remedies still known to villagers (Heggenhougen: 1978A).

Fifty percent of our respondents felt some neighbors would not come to the clinic even if they were very sick because they were afraid of getting an injection. Others indicated that people would not come because they did not want to waste their time or because they had more important concerns than their health, an attitude which has been recorded in other societies (Messing, 1973).

When questioned how the people who do not come to the clinic cure their ailments, most respondents (41) indicated that the bomoh would be used; 34 said such people would first use medicines bought at the drug store. Twelve felt people would try home (folk) remedies; seven said that some people would go directly to a physician rather than to the clinic.

Only fifteen respondents said people will never go to both the clinic and the bomoh when sick. Twenty-seven said people will definitely avail themselves of both traditional and cosmopolitan health care resources, and 58 said people would do so sometimes. However, the overwhelming

majority (90%) indicated that this multiple resource use was only for certain, not for all, illnesses. Table III shows the complaints most frequently mentioned as those for which *both* the bomoh and the clinic would be used. The order of dual use for these problems was not indicated and is not easily established as there are other factors besides this type of complaint that influence resource use. It is generally agreed, however, that fractures are much more frequently presented to a bomoh than to cosmopolitan practitioners and certain other complaints are felt by many to be most appropriately dealt with by a bomoh (see Table III).

Table III

Complaints for which both bomohs and clinic are used by frequency of mention [some respondents mentioned more than one complaint]

Complain	Frequency of mention
Fracture	43
Fever	30
"Kayap" — abcess/sores	22
Measles	13
Cancer (?)	11
Snake bite	8
Skin problems	6
Stomach ache	5
Mental illness	2
Mumps	2
General body pain	2
Headache	2
"Sawan" — convulsions	1
Diabetes	1
Sore throat	1
Hypertension	1
Worms	1
Eye problems	1

When asked what action they would take if the clinic treatment did not seem to improve a patient's condition, 58 stated they would return to the clinic, 25 would go to the hospital, ten would to the bomoh, one would try home remedies and another Chinese traditional medicine. Of the more schooled, 65% would return to the clinic for a second treatment; 57% of the less schooled would do so. However, 26% of the less schooled would choose to go to the hospital as the second choice but only 19% of the more schooled would do so. Levels of schooling seems not to be a factor in choosing to go to a bomoh if the clinic treatment was found unsuccessful as this was the subsequent choice of 11% of the less schooled and 8% of the others.

When asked why or how they got the present ailment the following causes were given (see Table IV)-- as most of the complaints were minor, we felt it superfluous in this table to link causes with specific complaints. Table IV also records the respondents' perceptions (by frequency of mention) of why, in general, people become sick.

Table IV

Reasons given for having present problems and for becoming sick [in general] by frequency of response [some gave more than one reason]

	For present illness	In general
Improper food	9	33
Due to weather condition	33	2
Over-work	9	26
Ignores attention to own health	—	25
"Contagion"/germs	8	13
Accident	16	—
Don't know	12	—
Unhealthy environment ("swampy")	—	9
God's will	—	4
Poverty	—	4
No proper bath	—	3
"Fever" (?)	3	1
Natural cause of pregnancy	2	—
Hypertension	1	—
Worried by personal problem	1	—

Forty-three respondents felt that people could get sick by telling lies, by doing something bad to others, or by black magic. These respondents may be seen as having a more "traditional" etiologic perception than the 54 respondents who

felt that such activities could not cause illness. A much higher percentage (48%) of less schooled respondents thought people could get ill from telling lies, doing something bad to others, or from black magic than did the more schooled (31%). Both the "traditional" and non-traditional respondents reacted equally to questions about whether or not people make use of more than one health care resource for the same ailments. It is significant that only 43% of those believing in a more traditional etiology would return to the clinic for a second treatment if the first did not seem to work whereas 69% of the not so traditional respondent would return. As might be expected 19% of the first but only 4% of the second group, would next go to the bomoh. (For a further discussion of etiologic perceptions according to "predisposing conditions," "supernatural causes" and/or "physical causes" see Chen: 1970A and B).

Although 65 respondents felt that some people get sick more often than others (27 stated that all people become sick at the same rate) only one of those who thought the rate was unevenly distributed felt this was due to charms, the other reasons mentioned were that some people "don't take care of their health," some are often caught in "bad weather," some "eat improper food," some "overwork," some have "allergies," and other simply get sick more often because of "old age."

Ninety respondents felt there were certain types of illnesses which were best treated by the bomoh rather than by a clinic; only four felt this was not so (see Table V).

Sixty-one respondents knew of a neighbor who had gone to a bomoh; fifty-two felt the bomoh was able to help these neighbors and seven felt that he was not. Thirty-six respondents stated that they themselves had at one time or another gone to a bomoh but 64 claimed never to have seen a bomoh. Thirty-one stated they were helped by the bomoh and five that they were not helped. It is probable that the use of bomohs by the respondents was under-reported as they may have felt this method of treatment was not "modern" and might not be approved of by the interviewer (though the interviewers were trained to be neutral and to probe further when detecting responses which seemed to be for the purpose of pleasing the interviewer). In any case, most respondents were able to name a number of bomohs--a total of forty different bomohs were identified by the 100 respondents, twenty-eight of whom live in the immediate area and twelve live further away but were visited by the respondents or their neighbors.

Table V

Ailments felt to be best treated by a bomoh rather than by clinic, by frequency of mention [some mentioned more than one ailment]

Fracture	44	Fainting spells	3
"Kayap" (skin rashes)	36	"Karang" (V.D.)	2
Evil spirit	32	Convulsion	2
"Barah" -(cancer, tumor)	14	Diarrhoea	1
Measles	6	Exhaustion	1
"Resdong" (nose itch-ulcer)	4	Mumps	1
Snake bite	5	Poison	1
Stomach ache	5	"Semugut" (menstration problems	1
Fevers	4		

Whether or not a respondent knew of a neighbor who had gone to a bomoh, level of schooling was found not to be a factor, now was it a factor in distinguishing respondents who themselves had gone to a bomoh (since 34% of the more schooled and 35% of the less schooled indicated they had visited a bomoh). But it is significant that 74% believing in a more "traditional" etiology and only 49% of the not so traditional respondents said they knew a neighbor who had gone to a bomoh, and 45% of the traditional but only 27% of the not so traditional said they themselves had ever gone to a bomoh.

Fifty-four percent of the respondents knowing neighbours who had gone to a bomoh but only 28% of those without such neighbours thought the people who did not come to the clinic had their problems treated by a bomoh. Forty-seven percent of those claiming to have neighbours who had visited bomohs, but only 21% of those who did not think their neighbours visited bomohs said they had ever visited a bomoh. Of the respondents who had gone to a bomoh at one time or another 79% had first tried an

alternative method to cure the current problem before coming to the clinic whereas 60% of those claimed never to have gone to a bomoh had first tried another treatment method.

When asked what resource they would normally first use for most ailments, 67 respondents mentioned the clinic, and 15 the hospital, as their first choice. Eight stated they would first try medicine bought at the local store, seven would first go to a bomoh, two would try a traditional home remedy and one would first go to a private physician. This order changed when the respondents were asked to name the second resource choice, in case the first should not effect a cure, and it was found that 37 would then go to the hospital, 33 to the clinic, 15 to a bomoh, 12 to a private physician and three would "hope for Allah's blessings." Should this second choice of treatment also not produce a satisfactory result then 34 would go to the hospital as a third choice, 22 would "hope for Allah's blessings," 17 would go to a bomoh, nine would go to the clinic and one would go to a "specialist" (four did not answer). Level of schooling seem related to first choice of health care resource as indicated by Table VI.

Table VI

First health care resource choice by level of respondents' schooling

Type of health care resource	More schooled	Less schooled
Clinic	84%	61%
Hospital	8%	18%
Medicine from store	8%	7%
Bomoh	—	10%
Traditional home remedies	—	3%
Private Physician	—	1%

Twenty-one percent of respondents who themselves had never been to a bomoh would go to the hospital as a first means of treatment whereas only 6% of those having gone to a bomoh stated this as a first choice.

Of those who said the clinic was their first choice of treatment only 31% said that if the first treatment did not work they would return to the clinic, 36% would next try the hospital, 18% would go to a private clinic (physician), 12% would try a bomoh, and 3% would simply hope for Allah's blessing. Of those stating the first choice of treatment to be the hospital, 53% would return to the hospital if the first hospital treatment failed whereas 40% would next try a bomoh and 7% would hope for Allah's blessings. Of those who would use the bomoh as a first choice, 57% would next go to the clinic and 43% would go to the hospital if the bomoh treatment proved ineffective (however, the numbers are too small to be considered significant).

Though the numbers are small, it is still interesting that of the 15 respondents who would normally first use the hospital for an ailment, six (or 40%) would next go to a bomoh if the hospital treatment did not seem to work. One explanation for this might be that the hospital is seen as the highest order of cosmopolitan medicine and if this does not work, a different type of treatment (non-cosmopolitan) would then be appropriate. Often greater attention will be placed on the possibility of supernatural causation should cosmopolitan medicine be ineffective in treating the ailment.

On their preference of being treated by a physician or by a Hospital Assistant (H.A.), fifty-nine respondents stated they definitely felt that a physician could treat the ailment, for which the patient had come to the clinic, better than could the HA; another 33 felt this "might" be true. Only four did not feel a physician could treat the illness in question any better than could an HA (it should be remembered that most ailments were "minor"). Interestingly, a much higher percentage (68%) of the less schooled, than the more schooled (44%), definitely felt that a physician could treat the respondents' current problem better than an HA.

Sixty respondents stated that a physician is "better" in that he/she has more experience and knowledge. However, twenty-four felt that both HAs and physicians could treat the current ailment "more or less the same." Two stated that HAs could do it better (and another five made no comments). Forty-three respondents felt a physician could treat a "skin infection or minor cut" better than could an HA, 39 fel

that this might be the case and only eleven stated an HA could treat such cases as well as, if not better than, a physician. Thirty-five respondents commented additionally that both HAs and physicians could treat minor cases well.

When asked what might inhibit villagers from going to the clinic, 24 felt this might be due to the pressure of their work, 19 to the cost of travel, 17 to length of time, 12 to uncertainty about the effectiveness of clinic treatment, 11 to the lack of care for children while they were away and the rest gave a variety of other reasons. Forty-six respondents stated that what they liked most about the clinic was the "free treatment," 25 liked the "effective treatment best," eleven appreciated the proximity of the clinic to their home. When asked why some people would not go to the hospital, even though they were referred there by the clinic, 49 thought this was because "they are scared," 26 because of financial considerations, and ten because "they don't want to be admitted." Eighty-one respondents said they would go to the hospital immediately if referred by the clinic, 17 stated they would wait a few days, and two would not go at all.

The great majority (85%) felt that most people are "satisfied" (63) or "very satisfied" (21) with the attitude of the clinic staff and with the treatment and care received. Ten percent felt they were "not always satisfied" and only 5% stated they were "not satisfied."

A number of reasons why people might feel they are not treated properly were not receiving an injection (though others fear injections), not being listened to with a stethoscope, relapsing after discontinuing prescribed medications once some improvement has occured, and not achieving immediate recovery (cosmopolitan medicine is reputed to cause prompt and miraculous cures; if it does not, it is believed to have been improperly administered). Those who had at one time gone to a bomoh were more reserved in their statements of being satisfied with the clinic, in fact 20% of this group said they were "not always" satisfied whereas only 6% of those who do not go to bomohs felt they were "not always" satisfied with the clinic.

The villagers make frequent use of the clinic; 29 stated that this was their second visit in six months, 33 had been to the clinic from three to ten times, nine had visited the clinic more than ten times and only 29 stated that the current visit was the only one within the past six months. Most earlier visits had been for fever (19) or cough (18) but eleven other problems (mainly minor) were specifically indicated, such as cuts (6), stomach ache (6), asthma (5), chest pain (4), toothache, measles, worms, etc. Only one respondent indicated that he did not get better from an earlier clinic treatment; 85 said they did and 4 were not certain. The respondents with less schooling use the clinic more often than those with more schooling.

When asked how the villagers could have better health care services, 24 suggested additional midwife clinics should be built, 21 felt there should be a physician at the clinic, and 16 felt a mobile clinic was needed; others felt that health education campaigns should be held in the villages and seven felt that miniclinics should be set up on the village level.

Eighty-five respondents felt it would be a good idea if someone from their village were trained to work in the village as a part-time health worker (possibly in a miniclinic) and an additional five felt this "might be a good idea," but nine were opposed to this. Fifty-five respondents said such a village worker would be the first health resource they would consult with a health problem, 32 said they would first go to the clinic, and another 11 that use would depend on the illness. Thirty-six commented, additionally, that they would go to the village health worker first, not necessarily to be treated but to obtain advice as to what to do and where to go, and another 14 felt it would save money and time to go to such a village health worker. Years of schooling was not a factor in differentiating reaction to the training, or the use, of a village health worker.

The role of the bomohs should not be overemphasized as a result of this documentation nor do I wish to extol their healing capabilities. It is difficult to speak of the bomohs as a unified group; they are folk healers who despite similarities differ from one another, and have learned through individualiz-

ed training. It is somewhat futile, without adequate criteria, to compare their capabilities to those of cosmopolitan practitioners.

What we have learned, however, is that villagers know a great many such traditional folk healers and sometimes use their services for the same (or different problems) as those they present at the rural clinic. This is evident even in areas where there are few complaints about the clinic and where the clinic is within easy reach of most villagers (no villager lives more than three miles from a clinic).

An explanation of the villagers' persistence in using bomohs might be that bomohs deal with the supernatural etiologic aspects--the "why"--of an illness whereas cosmopolitan practitioners limit their concerns to the natural aspects--the "how." Villagers concern themselves with both the "how" and the "why;" etiological explanations are often stated in *both* natural and supernatural terms. Visiting a bomoh is also more convenient and comfortable, because the setting is familiar and he pays greater attention to the feeling of the patient (Taib Osman, 1976; Heggenhougen, 1979). Many have argued that the very process of healing is important to the outcome of certain treatments and that the system of meaning in which the process occurs affects healing itself (some even argue that creating symbols of healing constitutes healing). It may well be that the very character of bomoh treatment makes it effective and attractive to villagers (Kleinman, 1973; Moerman, 1979).

As was the case with the one hundred patients of a well-known bomoh interviewed in Kedah who would also use cosmopolitan health care resources (Heggenhougen, forthcoming B), our interviews with the respondents at the clinic confirmed that the various health care systems are not seen as antagonistic alternatives but that multiple use of health care resources is practiced without a sense of conflict (Chen, 1975B).

It is important for cosmopolitan health practitioners to acknowledge that widespread multiple health care resource use exists because not only can such practice be beneficial or harmless, but at times (if duplication of medication is involved) such practices are harmful indeed. It would therefore seem beneficial that practitioners not only should be aware of other resources used by their patients but that they might consider having some contact with these resources (Jelliffee & Jelliffee, 1977).

Concordant with current deliberations by the Ministry of Health to establish mini-clinics at the village level and to staff them with specially trained villagers to provide health care services and information on a part time basis, it can be seen that the villagers in this survey overwhelmingly would support such an idea and would avail themselves of such services. Other surveys, conducted elsewhere in the state of Kedah, also confirm these findings (Heggenhougen, 1978).

Whether or not the villagers to be trained for this role should include some of the bomohs is a matter for consideration but not something to be unilaterally supported here; as in certain circumstances, no doubt, this would be beneficial whereas in others it might not be so--it becomes a matter of individual case consideration. Training and incorporation of such healers, of course, has been instituted in other countries and was also practiced for a while in Malaysia, particularly for the Orang Asli Health Service (Bolton, 1968). Many of the traditional village midwives (bidan) have been trained by the Malaysian government and function in cooperation with the government midwives (Chen, 1975A). Some have argued that for people to fully use and reap the benefits of cosmopolitan medicine greater contact and cooperation should be established between the traditional and cosmopolitan systems (Aho & Minott, 1977; Mahler, 1977; W.H.O., 1975). But whether or not folk healers are to be included in a new team approach to rural health care, such a team must, in any case, be aware of their existence and of the villagers' reasons for their continued use.

It is of interest that the more educated villagers seemingly place greater value on the capabilities of the HAs, stating that HAs are able to treat minor ailments as well as physicians. The fact that most ailments presented at the clinic are minor does not necessarily negate the need for physicians in rural areas; there are problems only physicians can treat; but villagers must also be educated to realize that, for certain ailments, treatment by an HA is as good as by a physician. Otherwise, physicians will have to

spend much of their time treating cases that others with less training could treat equally well, thus consuming valuable health care resources by limiting the time physicians can spend on cases that require their highly developed skills and the time they need for teaching and for conferring with other members of the health team.

It is indeed encouraging that the president of the Malaysian Medical Association has emphasized the importance of primary health care and encouraged physicians "to make it their forte"; and that physicians are encouraged to practise in rural areas, and that rural postings are to be made more challenging and exciting (Kaur, 1979). However, public education is needed so that people seek treatment from health care personnel at the appropriate levels according to the seriousness of the ailment, rather than always look toward the physician no matter what the illness simply because the physician is at the clinic and is universally considered to be able to provide the best services no matter what the problem is.

SUMMARY

During interviews with 100 persons attending a rural clinic in northwest peninsular Malaysia, we found most people use the clinic for minor ailments and present their more serious health problems directly to a private physician, a hospital or a traditional healer (or a combination of these health care resources). Most of those attending the clinic had already tried one other form of treatment.

Certain ailments were said to be best presented to a traditional healer (bomoh). People with low or high levels of schooling will use multiple health care resources for the same ailment but those with less schooling rely more often on their neighbours in times of illness. The less educated tend to make greater use of the hospital and the bomoh as a first choice of health care resource.

Most respondents feel a physician can treat an ailment better than can a Hospital Assistant. Public education efforts are needed to inform villagers of the capabilities of the various cosmopolitan health care practitioners.

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STUDIES ON THE BIOLOGY OF ANOPHELES CAMPESTRIS REID (DIPTERA, CULICIDAE) AND ITS RESPONSE TO RESIDUAL SPRAYING WITH DDT, CARRIED OUT IN EXPERIMENTAL HUTS IN PENANG, MALAYSIA

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INTRODUCTION

ANOPHELES campestris Reid is an important vector of malaria along the coastal plains of Peninsular Malaysia, and of filariasis caused by the periodic form of *Brugia malayi*. It is a member of the *A. barbirostris* group and was formerly known as the 'dark winged form' of *A. barbirostris*, later raised to specific rank by Reid (1962).

In earlier studies in experimental huts, Reid and Wharton (1956) reported that residual spraying with DDT at 2 gm/m^2 did not have the required effect on this species after the first two months. Later however, Moorhouse and Chooi (1964) reported that *A. campestris* disappeared after two cycles of DDT spraying at 2 gm/m^2 in a Malaria Eradiction Pilot Project (MEPP) carried out in a 500 sq. mile area in Selangor state of Peninsular Malaysia from 1960 to 1964.

A Malaria Eradication Programme (MEP) was inaugurated in Peninsular Malaysia in 1967 starting from the north western part of the country and proceeding south and east in the following years. The island of Penang received its first cycle of spraying with DDT water dispersible powder (wdp) at 2 gm/m^2 in the second semester of 1968, followed thereafter by two cycles a year. After two years of spraying, *A. campestris*, the main vector of malaria in the south western part of the Island, not only did not disappear as was expected after the MEPP experience, but continued to transmit malaria at a low level in the area.

From the very inception of MEP spraying on the island, there were objections from the house-holders to the whitish deposit of the DDT wdp, resulting in high refusal rates, as high as 10-15%. Even in houses that accepted spraying, many areas like the roof and parts of the house were not allowed to be sprayed. Spraying, therefore, was mostly partial and added to this, many house-holders systematically washed or wiped off the DDT soon after spraying which was evident in as many as 80% of the houses in one village. Therefore, neither the coverage nor the DDT residue left on the walls was in any way near the very good coverage achieved by the MEPP with the emulsion formulation. The failure to interrupt transmission appeared to be mainly due to the inadequacy or the absence of DDT residue in the houses. But there were suggestions that continued transmission was due either to the development or resistance to DDT in *A. campestris* and/or to some behaviour changes in the vector by which it avoided coming into sprayed houses but maintained outdoor transmission. The reasons for these suggestions were (a) the area had been sprayed with DDT as an anti-malaria measure sporadically for about ten years before the beginning of the programme. DDT had also been used in agriculture against rice pests, and rice fields are common breeding places for this species. Both uses might have contributed to the development of resistance, if any, even before the advent of MEP. (b) most of the *A. campestris* collected in the area after spraying were from man-biting collections outdoors and very few from indoor collections, which some thought was due to the avoidance of the DDT by the vector or to a

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change in behaviour from indoor to outdoor biting, thereby maintaining an outdoor transmission.

The present study was therefore undertaken to see if there was a change of behaviour in *A campestris* and if it avoided coming into sprayed houses and if transmission could be interrupted in the area by DDT residual spraying. At the same time, susceptibility of the vector to DDT and other aspects of its biology which would add to the knowledge of the species, were also studied.

MATERIALS AND METHODS

Study area

The study was undertaken in the South West District of the Island of Penang which lies off the west coast of the mainland on the northern extremity of the Straits of Melaka. The Island has a total area of 108 sq. miles (300 sq. km) with a central range of hills. The study kampong (village), Jalan Baru is situated in the south west part of the island in the district of Balek Pulau, a narrow strip of flat land cultivated with rice and coconut, ideal for *A. campestris* breeding. The inhabitants were mostly malay living in wooden houses usually arranged on either side of the main road. Most of the houses were of a better quality with wooden walls and galvanised iron or attap (woven nipah palm leaves) roof with a wooden floor raised about O.6m (2 ft) to 1.2m (4 ft) above ground level. The houses usually had many windows and other openings for ventilation and would be bright inside during daytime. The walls were often painted with wood preservative and sometimes even with paint and generally the houses were well kept.

Jalan Baru is a typical kampong in the area with about 315 houses and 1,450 population. It was selected for the study as malaria cases were being regularly reported from the kampong and it was therefore considered a problem. Entomological investigations had also shown a reasonable density of *A. campestris* in the kampong.

Experimental huts

To study the entry and exit behaviour of vectors, window traps fitted to kampong houses would be ideal. But the types of houses in this country with such a large number of openings, do not lend themselves to window trap study, as most of the mosquitoes would escape by other routes. The next best would be to make the observations in experimental huts, built to simumate local houses as far as possible, where entry and exit of mosquitoes could be controlled. In spite of the report by Moorhouse and Wharton (1965) that most species in this country were reluctant to enter trap huts, it was decided to give it a try at Jalan Baru with *A. campestris.*

Two huts of the type shown in Figure 1 were built in 1971 among kampong houses in Jalan Baru. Each hut was 3.5m (11.5 ft) long, 2.6m (8.5 ft) wide, had 2.4m (8 ft) high walls with a roof 3m (10 ft) high at the highest point. The wooden floor was raised O.76m (2.5 ft) above the ground. The walls were of wooden plank and roof of attap. Each hut had a door 2m (6.5 ft) x 1m (3.3 ft) and five entry louvres each 1.8m (6 ft) x O.6m (2 ft) with louvres at an angle of 30° to the vertical and 3.8cm (1.5 in) apart. Four exit traps of the cone type each 38cm (15 in) cube were fitted one to each side of the hut.

Methods of collection

For indoor and outdoor biting collections, two collectors sitting down with their trousers rolled up to the knee, collected mosquitoes biting them, working 40 mins each hour and resting 20 minutes. To study the numbers entering the huts, local boys were hired to sleep in the hut for a small fee, the doors closed at 7 pm and hourly collections were made from window traps as well as the dead mosquitoes on the floor in the sprayed hut. For the study of the resting position and resting duration, the walls and roof were marked out into 1.2m x 1.2m (2 ft x 2 ft) numbered squares. Each hut was examined for resting mosquitoes by two collectors at 30 minute intervals and each mosquito seen was noted by the number of the square in which it rested and followed half-hourly till it left that position. This was done throughout the night and separate records were kept for fed and unfed mosquitoes.

All *A. campestris* collected were dissected for parous rates and all parous mosquitoes were dissected for gut and gland infections. Susceptibility tests on adults were carried out by the standard WHO test kit.

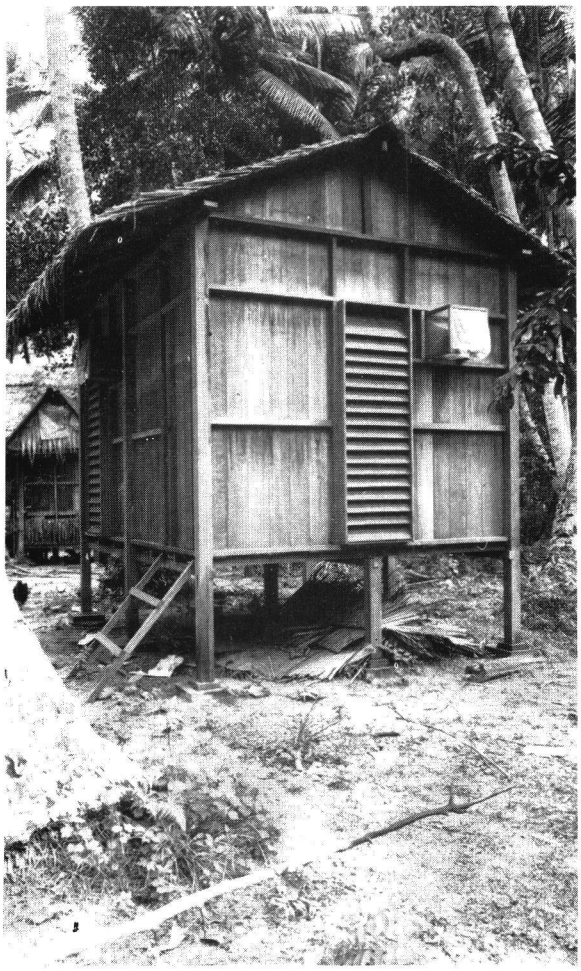

Fig. 1. Experimental hut in Jalan Baru, Penang.

BIOLOGY OF *A. CAMPESTRIS*

Most of the observations on the biology of *A. campestris* reported here were made in experimental huts which present an artificial situation to the vector and would not entirely represent conditions obtaining in nature. As this was the best possible that could be done the results are of value in understanding the behaviour of the vector. Unlike the observations made by Moorhouse and Wharton (1965), *A. campestris* readily entered the huts and during the study period of nearly two years, over two thousand mosquitoes were captured inside the experimental huts, this species forming nearly 95% of all the anophelines captured in the area.

Seasonal prevalence

Two years' results available from Jalan Baru on seasonal fluctuations of *A. campestris* are presented in Figure 2. In spite of the fact that the kampong was routinely sprayed at six monthly intervals as shown in the figure, fluctuation in density seen was not associated with the timing of spraying but rather to the rainfall. Rainfall figures from the Bayan Lepas airport which is a few kilometers away from Jalan Baru are also presented in Figure 2. May to August were the high density months for *A. campestris*, with peaks in June and July when 29.5 and 28.5 mosquitoes were collected per man-night, respectively, in 1972 and 10.5 and 14.5 for the same months in 1973. Another smaller peak was seen during December/January. It could be observed that the peak density of *A. campestris* follows one to two months after the heavy rainfall months of April/May and September to December. The heavier rainfall of September to December produces a smaller peak in mosquito density and the shorter rainfall during April/May produces higher densities of vector.

The main breeding place in the area is a swamp skirting the kampong and a sluggish waterlogged drain running through it. Density fluctuations could be correlated to the state of water in the swamp and drain. During the very dry months there is little or no water at all for breeding and during the very wet months, with flooding and continuous flow of water, breeding is again considerably reduced. When there is just enough water with little movement as happens immediately after the rainy months, breeding increased as was confirmed by larval surveys, resulting in high densities of vector.

Malaria figures from the South West District (C2) of Penang in which Jalan Baru is situated and the figures for the kampong itself for the years 1971 to 1973 are given in Table I. The table shows an increase in cases from May up to about September which corresponds to the increase in vector density during the same period.

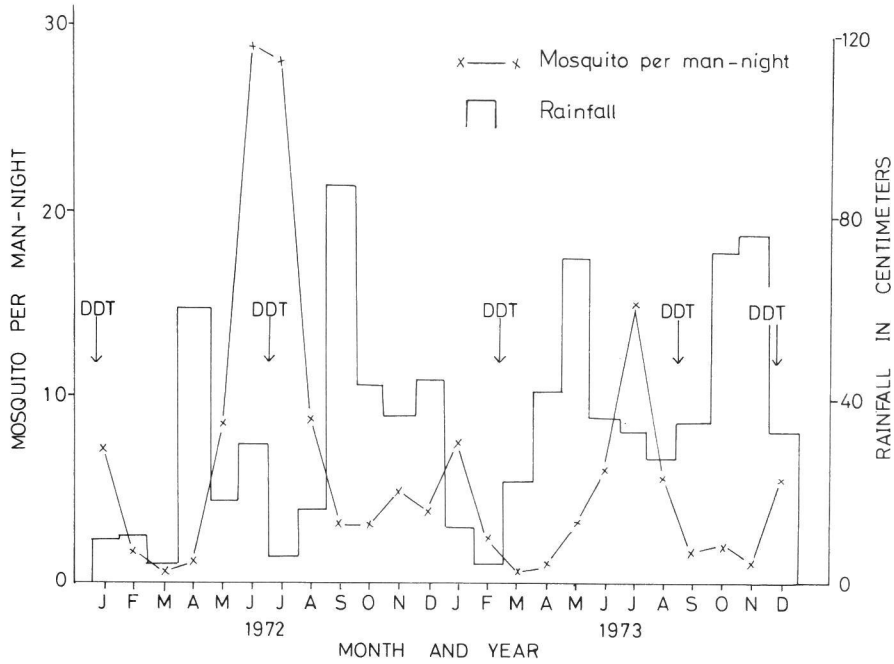

Fig. 2. Rainfall figures from Bayan Lepas and seasonal density of *A. campestris* obtained from Jalan Baru, Penang during 1972 and 1973.

Table I. Showing the number of malaria cases from Southwest District of Penang and Kpg. Jalan Baru for the years 1971, 1972 and 1973.

Year	Month	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total
	Area													
1971	South West Dt. Penang	17	7	11	11	42	51	56	118	54	17	16	20	420
	Jalan Baru	0	0	0	1	11	10	15	16	5	2	0	0	60
1972	South West Dt. Penang	13	18	11	8	22	36	21	16	11	11	7	3	177
	Jalan Baru	2	0	0	0	5	3	3	0	0	1	0	0	14
1973	South West Dt. Penang	2	12	8	9	18	16	38	40	35	8	21	4	211
	Jalan Baru	1	0	0	0	3	2	2	1	3	0	0	1	13

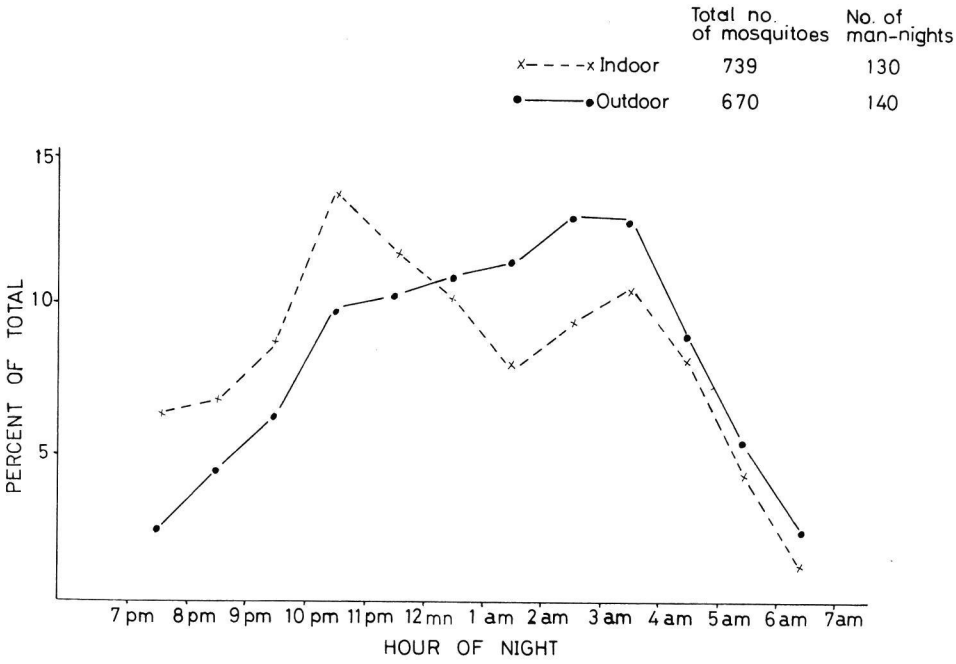

Fig. 3. Indoor [in experimental hut] and outdoor man-biting rhythm of *A. campestris* obtained by hourly catches at Kpg. Jalan Baru, Penang during 1972 and 1973.

Indoor and outdoor biting

Studies were carried out during 1972 and 1973 in about 140 man-nights in experimental huts and the results are presented in Figure 3. During this period, indoor biting collection of *A. campestris* was 739 (5.7 per man-night) and outdoor collection was 640 (4.8 per man-night). The indoor: outdoor biting ratio was 1.2 : 1 with a total of nearly 1,400 mosquitoes, showing a slight preference to indoor biting. Moorhouse and Chooi (1964) with about 100 mosquitoes collected in three nights had a ratio of 4.3 : 1 which shows a high degree of preference to indoor biting, where indoor biting was carried out in kampong houses. At the beginning of the present study, there was usually more outdoor biting than indoor biting in experimental hut, after which indoor biting increased considerably. This was probably due to the huts being new at the beginning gradually becoming more attractive after being slept in for several nights. It is probable that indoor biting : outdoor biting would be higher in kampong houses, than the present results indicate.

Biting rhythm

All night man-biting studies were carried out to see the biting rhythm of *A. campestris.* The results also seen in Figure 3 indicates that it bites right through the night, indoor biting gradually increasing to reach a peak between 2 am and 4 am. Outdoor biting starts off at a higher level from 7 pm and shows a fairly sharp peak between 10 pm and midnight and then again a smaller peak between 2 am and 4 am. These results are the average of about 140 man-nights' collections and a total of about 1,400 *A. campestris.* Moorhouse and Wharton (1964) also reported a peak biting between 8 pm and 2 am.

Egg laying

Over 80 wild caught fed females were kept for egg laying, out of which 49 laid a total of 7,997 eggs for an average of 162 eggs per female (range - 15 to 302). Thirty out of the 49 (about 60%) laid between 150 and 250 eggs.

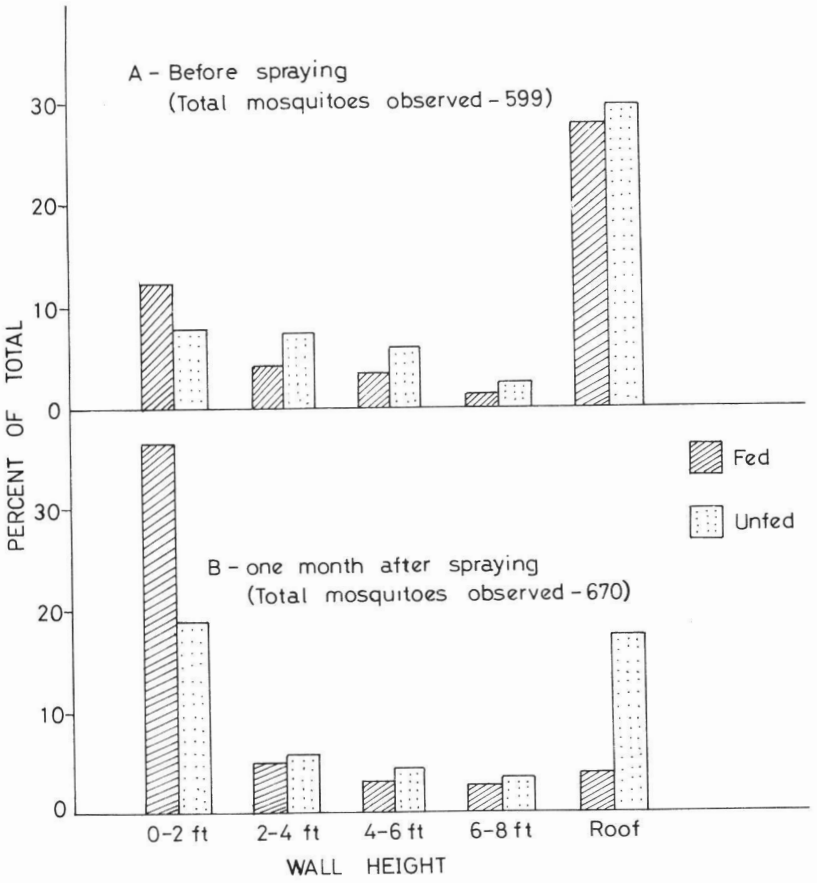

Fig. 4. Percentage of *A. campestris* resting at various heights of wall and roof of experimental huts at Kpg. Jalan Baru, Penang.

Gonotrophic cycle

The same 49 mosquitoes that laid eggs were also observed for the time taken from feeding to egg-laying, which is the gonotrophic cycle. The fed mosquitoes were collected from the experimental huts at three hourly intervals and egg-laying observed at 6 hourly intervals. It was therefore only possible to establish the time interval with a possible 9 hour error. Of the 49 mosquitoes, 37 (75%) laid eggs within 60 hours, 6 took 60 to 72 hours and the other 6 over 72 hours. As mosquitoes normally lay eggs in the early evening hours, it is reasonable to presume that the gonotrophic cycle for *A. campestris* is closer to two days than three.

Resting position

Experimental huts provide an artificial situation for this type of study where mosquitoes had to rest on walls or roof or sometimes on the floor, compared to the innumerable articles inside ordinary houses on which they could rest. The observations were made by noting the exact position of resting mosquitoes at half-hourly intervals. The results are presented in Figure 4 for observations made before and after spraying. Before spraying, 599 observations were made of which 56% were seen to rest on the roof, and 44% on the wall, the numbers on the wall decreasing progressively with height. This was repeated one month after spraying the hut, when

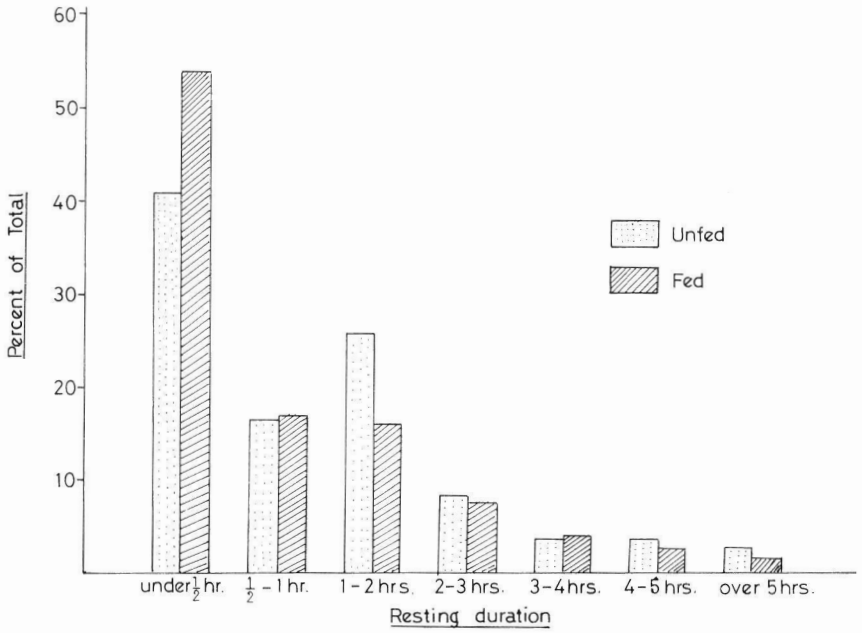

Fig. 5. Showing resting duration of *A. campestris* fed and unfed obtained during three nights in experimental huts in Jalan Baru, Penang during January 1972

670 observations were made and only 22% were found resting on the roof and 88% on the wall of which 54% were resting under 2 ft height. The results after spraying are normal as has been the experience in routine observations. The high percentage resting on the roof before spraying was probably due to the disturbance of the collectors and the flashing of the torch light when the mosquitoes might have been driven to the roof where there was less disturbance and they could go no further. It is relevant to mention here the number of observations do not represent the number of mosquitoes as the same mosquito would have been observed twice, once before feeding and once after feeding due to their moving to a different spot after feeding. If they had moved as a result of the disturbance, then the same mosquito could have been observed even more than twice. After spraying, when nearly 90% of the mosquitoes were killed in the hut and rested less than half an hour as presented later, the movement of individual mosquitoes would be minimal and the resting position observed gives a better picture of what happens in nature. The results for fed and unfed mosquitoes are presented separately and as was expected, 70% of the fed mosquitoes (35% of the total fed and unfed) were found resting below 2 ft after spraying.

Resting duration

To study the resting duration of fed and unfed mosquitoes, observations were made during three nights by noting them in their positions at half-hourly intervals. If it was seen at the same spot twice, then it would have rested at least for half hour and so on. Before spraying, a total of 494 observations were made. In the morning all mosquitoes in the huts and window traps were collected and the total collected during the same period was 230, which is a little less than half the total observations. If some mosquitoes had escaped from the hut, it is reasonable to presume that each mosquito was being observed at two different locations which is to be expected as each mosquito would change its first resting place after feeding.

The results presented in Figure 5 show that 41% of the fed and 54% of the unfed rested for less than half hour, 16% rested from half to one hour, 20% from one to two hours and becoming less and less for longer durations. Twelve unfed and four fed were observed to rest for over five hours. The average time computed for each mosquito was 54 minutes before feeding and 71 minutes after feeding, a total of 125 minutes (about 2 hrs) before and after feeding.

In about 670 observations made one month after spraying, one fed *A. campestris* was seen to rest between 1 to 1½ hours, 20 fed and four unfed between half to one hour and all the rest (over 96%) rested under half hour. During the six nights of observation, 437 *A. campestris* were collected from the sprayed hut of which 333 were found dead in the hut. This showed that a large number of *A. campestris* were being killed within half-hour of their coming to settle inside the hut.

Before spraying, the ratio of observations to the actual number of mosquitoes collected inside the hut was about 2:1 (490:230), whereas the same ratio was 1.5 : 1 (670:437) after spraying. This would mean that only half the mosquitoes were being observed twice after spraying unlike all the mosquitoes before spraying. This was confirmed by the fact that 57% of the *A. campestris* found dead in the hut were unfed showing that they were killed before they had a chance to feed, and were only observed only once.

The fact that no mosquito rested for over one and a half hours after spraying may indicate that they were being killed or left the hut within that time. Mortality figures in sprayed huts discussed later was a clear indication that a large percentage of vectors coming into the hut were picking up a lethal dose of DDT and being killed within the short period.

Daytime resting inside houses

A. campestris in this country has always been considered an endophilic (indoor resting) and endophagic (indoor feeding) vector. During six nights' observations in experimental huts it was found that only 32.6% of a total of 389 collected were found to rest inside the hut at 7 am, the majority leaving the hut through window traps during the night. Ordinary huts would probably be more attractive for the mosquitoes to stay indoors during the day, but Reid (1964) also states that although *A. campestris* has been known to be a highly endophilic species, probably the majority left houses to rest outside. The present findings support Reid's view.

Entry and exit

A. campestris was coming into experimental huts steadily right through the night as shown in Figure 3. In order to determine the time of exit, the window traps were emptied hourly, right through the night. Before spraying, 219 (about 80%) out of 263 collected in the window traps left the hut between 6 am and 7 am. During the other hours, a few were found to leave rather irregularly. After spraying, out of 381 collected from the window trap, only 45% left between 6 am and 7 am, the rest leaving at all hours of the night. It was also found that within two weeks of spraying, about 50% had left by 1 am and only 14% left after 6 am. Although most of those collected from the window traps died within 24 hours, the earlier time of exit may suggest some irritability to DDT which did not prevent them from picking up a lethal dose. There was no difference in the mortality rates of those leaving in the night compared to those leaving at the break of dawn.

Window traps had been set on each of the walls of the hut and the largest numbers left through the traps facing east.

Host preference

Reid and Weitz (1961) reported 63% of 27 *A. campestris* collected from day-time resting places had human blood. It has been almost impossible to collect *A. campestris* from day-time resting places to carry out precipitin tests. Therefore in 1973, a collection was made of fed mosquitoes from a net trap with two collectors and one cow acting as bait. The mosquitoes had an artificial but equal opportunity to feed on either man or cow. Of the 36 fed *A. campestris* collected from the net, only 8 (22%) had human blood and the rest bovid. Reid (1961) studying the attraction of mosquitoes to human and animal baits reported a man:calf ratio of 3.4:1 for *A. campestris.* Afifi (1965 unpublished) found that all 96 *A. campestris* collected during day-time from houses had human blood. In our experience too, in routine collections, most of the *A. campestris* are collected from man-biting collections, this species being very rare in animal bait collections where most of the other anophelines are abundant.

Transmission of malaria and results of dissections

During the two year period of study, a total of 2,136 *A. campestris* were dissected without finding a single sporozoite or oocyst infection. This was not unexpected as Reid (1962) reported that up to that time in over 15,000 dissections of this species, the sporozoite rate was only 0.33% when the malaria rate in the country was probably 20-40%. It was Reid's conclusion that *A. campestris* can only maintain a low level of transmission. At the time of the study, when the malaria rate in the area was less than 1% it was not surprising that no infected mosquito was found.

RESPONSE OF *A. CAMPESTRIS* TO RESIDUAL SPRAYING WITH DDT

After some preliminary observations in the two experimental huts lasting about five months to study the attractiveness of the huts for *A. campestris* to enter, one of the huts, was sprayed with DDT wdp at 2 gm/m^2, during May 1972. The walls and roof were sprayed, care being taken not to spray the entry louvres. The other hut was maintained as untreated control. Subsequent sprayings were carried out during November 1972, July 1973 and January 1974 with DDT emulsion at the same dose, in keeping with the change of formulation by the MEP in 1972.

Man-biting collections were continued in the sprayed and unsprayed huts monthly for an average of two nights per month. In addition, baits were made to sleep in the huts during three other nights of the month and collections were made hourly of dead mosquitoes on the floor in the sprayed hut and from window traps of both huts. Mosquitoes collected from window traps as well as those found resting inside the hut at 7 am were kept for 24 hour survival test.

Entry of A. campestris into sprayed hut

From the results presented in Table III and Figure 6 for collections carried out simultaneously in the sprayed and unsprayed huts, there appeared to be no significant difference in the numbers entering the sprayed hut compared to the unsprayed hut. One month and six months after spraying, the numbers in the sprayed hut were slightly higher than the unsprayed and on the other occasions the numbers in the unsprayed hut were higher. Observations were carried out in the huts for two years during which time there were four applications of DDT. The number of *A. campestris* collected during this period from the sprayed hut was 1,881 compared to 2,347 in the unsprayed hut. With about 50% to 75% of the collections from the sprayed hut being found dead on the floor, there was a possibility that some of these could have been missed, and the difference between the huts could not be of significance. Added to the fact that such a large number was collected from the sprayed hut is proof enough that the *A. campestris* in the area had not changed its behaviour from an indoor biter to an outdoor biter and that it will readily enter DDT sprayed houses. The negligible number of vectors collected biting indoor during routine collections after spraying may be due to a combination of many factors like (a) the very low densities of this species generally after spraying (b) that the vectors coming in were being killed by the DDT before they have a chance to bite and (c) in a kampong house the mosquitoes have a choice between one or two collectors and five or more occupants inside, whereas outdoors the collectors sit alone.

Mortality of A. campestris in sprayed hut

It has been possible to observe mortality in the sprayed hut after two successive cycles of DDT spraying, and the results are presented in Table II and for the first cycle only in Figure 6. After the first spraying, over 75% mortality was obtained up to the 6th month after spraying. During four of the monthly observations, the mortality was over 85%. On the completion of six months, the mortality dropped to 51%, and the hut was re-sprayed, this time with DDT emulsion. After the second spraying, the mortality remained high up to the 7th month after which it dropped to 55.4% and after eight months mortality was only 9.4%.

Usually the mortality within the first two weeks after the spraying was not so high, being about 65 to 75%, but increased after this period. This was probably due to the irritant effect of the fresh DDT deposit which might have driven away the mosquitoes before they

Table II. Mortalities of *A. campestris* in experimental hut after spraying with DDT 2 gm/m^2, obtained at Jalan Baru, Penang during 1972 and 1973.

No. of months after spray	No. dead on floor			No. found alive in hut at 7 am			No. found in window traps			Total collection			No. Survived			Mortality %
	F	U	T	F	U	T	F	U	T	F	U	T	F	U	T	
0-½ *	25	6	31	4	4	8	10	10	20	39	20	59	10	4	14	76.3
1	125	224	349	9	3	12	48	50	98	182	277	459	45	11	56	87.8
2	24	100	124	4	2	6	27	24	51	55	126	181	23	5	28	93.0
3	61	13	74	4	1	5	18	8	26	83	22	105	9	3	12	84.8
4	30	6	36	0	0	0	4	3	7	34	9	43	4	2	6	86.4
5	11	8	19	0	0	0	8	1	9	19	9	28	7	0	7	75.0
6	39	12	51	1	2	3	29	17	46	69	31	100	30	19	49	61.0
0-½ a	8	1	9	0	0	0	3	7	10	11	8	19	11	8	19	68.4
1	44	3	47	1	0	1	10	4	14	55	7	62	8	1	9	85.5
2	15	2	17	0	1	1	3	2	5	18	5	23	2	1	3	86.9
3	8	0	8	0	0	0	3	0	3	11	0	11	3	0	3	72.3
4	1	0	1	0	0	0	1	0	1	2	0	2	0	0	0	100
5	4	0	4	0	0	0	2	2	4	6	2	8	0	0	0	100
6	0	0	0	0	0	0	11	0	11	11	0	11	0	0	0	100
7	9	2	11	0	3	3	30	12	42	39	17	56	20	5	25	55.4
8	0	0	0	0	0	0	31	1	32	31	1	32	29	0	29	9.4
Total	404	377	781	23	16	39	238	241	379	665	534	1199	201	59	260	

* Sprayed with wdp

a Sprayed with emulsion

F = Fed, U = Unfed, T = Total

could pick up a lethal dose, most of the survivors being from window trap collections. Reid and Wharton (1956) reported, from a similar experiment in Negri Sembilan, Malaysia, where DDT emulsion had been used, 72% mortality during the first month, 32% during the second month and that DDT failed to kill *A. campestris* in subsequent months. However, in the MEPP in Selangor, Moorhouse & Chooi (1964) reported that *A. campestris* totally disappeared from the area after only two cycles of spraying with DDT emulsion.

During the 14 months of observation, a total of 1,199 *A. campestris* were collected from the sprayed hut, of which 781 (65%) were found dead in the hut. Of these 404 (51.7%) were fed and 382 (48.3%) unfed. Of the ones caught in the window trap, about 80-85% died within the 24 hour holding period. The results therefore are a clear indication that *A. campestris* was being killed in sufficient numbers and for a sufficiently long period by the DDT spraying.

Tables III. Parous rates of *A. Campestris* obtained in Jalan Baru, Penang, during 1972 and 1973.

Month	1972		1973	
	No. diss.	% Parous	No. diss.	% Parous
Jan	126	37.3		-
Feb	90	62.2	53	30.2
Mar			8	37.5
Apr			12	33.3
May	78	39.7	40	60.0
Jun	442	26.2	57	54.4
Jul	439	40.1	79	41.8
Aug	127	44.1	48	35.4
Sep	137	37.2	13	23.1
Oct	106	38.7	18	33.3
Nov	89	58.4	9	66.7
Dec	89	31.5	76	26.3

Months of spraying of Jalan Baru -

Feb 71, Jul 71, Jan 72, Jul 72, Feb 73, Aug 73, Dec 73.

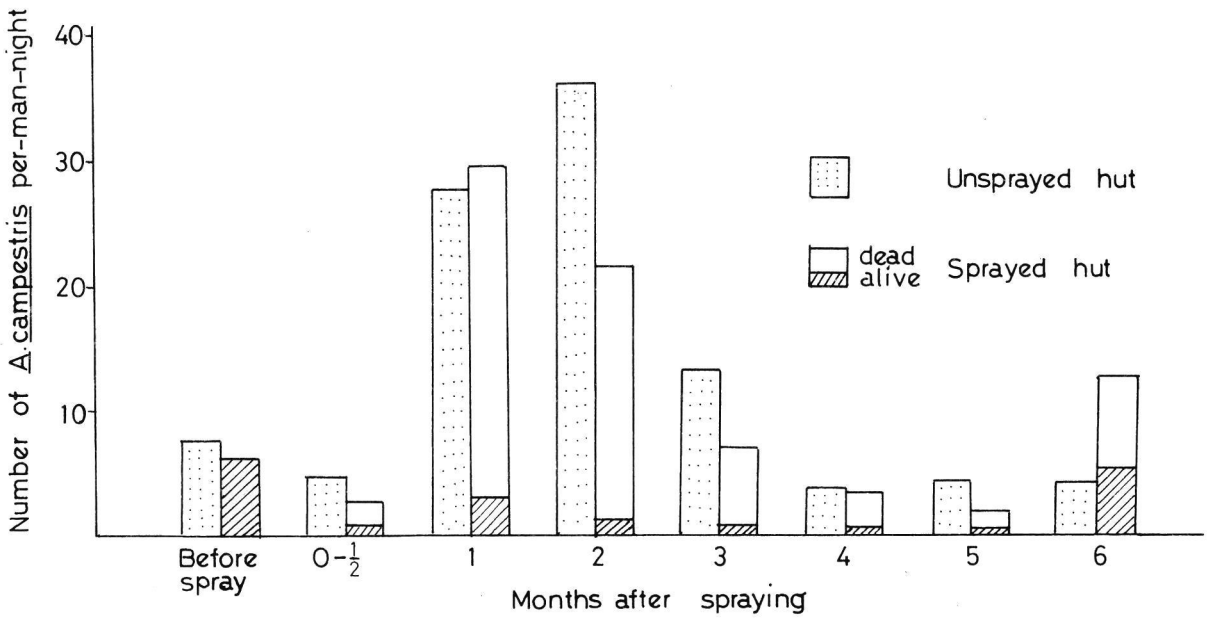

Fig. 6. Showing the number of *A. campestris* caught in sprayed and unsprayed huts at Jalan Baru, Penang.

SUSCEPTIBILITY OF *A. CAMPESTRIS TO DDT*

Several tests were carried out at Jalan Baru and in neighbouring kampongs from 1972 onwards to determine the susceptibility of *A. campestris* to DDT. When mosquitoes were available in sufficient numbers, a full series of tests were carried out exposing them to concentrations ranging from 0.25% to 4% DDT. When numbers were small, all were exposed to the discriminating dose of 4% DDT. When there were survivors to 4% DDT at one hour exposure, then 2 hour exposure with 4% DDT was tried. In mid 1972 several series of tests carried out at Jalan Baru with a total of 358 mosquitoes gave an LD_{50} of 1.4% DDT. No pre-spray figures are available from the area but Afifi (1966) reported an LD_{50} of 0.66% DDT for the species from Sabak Bernam, an unsprayed area in Selangor state. A test carried out during the present study, from the same area in 1972 (also before MEP spraying) although not with sufficient numbers, gave only 84.4% mortality with 4% DDT, similar to the figures from Jalan Baru. Being a rice growing area, there was probably extensive use of DDT between 1966 and 1972 in agriculture which may explain the later results. Wharton (1958) reported an LD_{50} of 1.3% DDT for laboratory bred *A campestris.*

From January 1972, in most of the tests carried out at Jalan Baru and neighbouring areas, there were a few survivors to one hour exposure to 4% DDT. Two hour exposure to 4% DDT did give 100% kill in all except in one instance in October 1972 when 3 out of 92 survived the 2 hour exposure.

The mortality regression lines for the Sabak Bernam tests in 1966 and the Jalan Baru tests in 1972 are given in Figure 7. The slope of the curve which is a rise per unit horizontal distance expressed as $2\left(\frac{LC_{84}}{LC\ 50} + \frac{LC_{50}}{LC_{16}}\right)$ is 0.51 for Sabak Bernam and 0.46 for Jalan Baru. The latter being less steep indicates a greater variability in the population and a shift to the right indicating an increase in tolerance. This in addition to the fact that 2 hour exposure to 4% DDT failed to give 100% mortality at least once, indicates a trend towards the species building up resistance to DDT in the area although still susceptible to DDT up to 1974.

DDT had been used as a malaria control measure in the South West District of Penang for over ten years before the MEP started, the spraying not being on a regular basis but carried out at times of malaria outbreaks. In addition, DDT would have been used extensively for agriculture on rice which is extensively grown here. Pre-spray figures for the area not being available, one cannot conclusively state that there is any change in the tolerance of *A. campestris* in the area to DDT although the results are suggestive of this fact, and the change if there was any was probably due to the earlier use of DDT for malaria control as well as in agriculture.

PAROUS RATES AND DAILY MORTALITY

Dissection for parous rates were carried out regularly during the two years and the results are presented in Table III. In over 2,000 dissections carried out during the period, the overall parous rate was 40.8 compared to 65% before spraying. It was difficult to correlate the monthly rates with the timing of spraying but generally the rates were higher 3 to 4 months after spraying. The daily mortality obtained by the formula $1-\sqrt[2]{\text{parous rate}}$ for a two day gonotrophic cycle was about 37% in 1972 compared to 24% in 1971.

There was an improvement in the spraying coverage in the area in mid-1972 which was mainly due to the change in formulation of DDT from wdp to emulsion which also resulted in far less wipe off of the DDT by the people. This was probably the main reason for the increased mortality in 1972 and 1973. The malaria situation had also shown a marked improvement in Jalan Baru in 1972 and 1973 as seen in Table I. In 1971 there were 63 cases which came down to 14 in 1972, 13 in 1973 and 2 in 1974. There was therefore reason to conclude that with a good spray coverage with DDT, transmission of malaria by *A. campestris* could still be interrupted in the area.

SUMMARY

Studies on the biology of *A. campestris* and its response to residual spraying with DDT in experimental huts at Jalan Baru, Penang, are presented. High density months were found to be May to August with peak in June/July and another smaller peak in December/January.

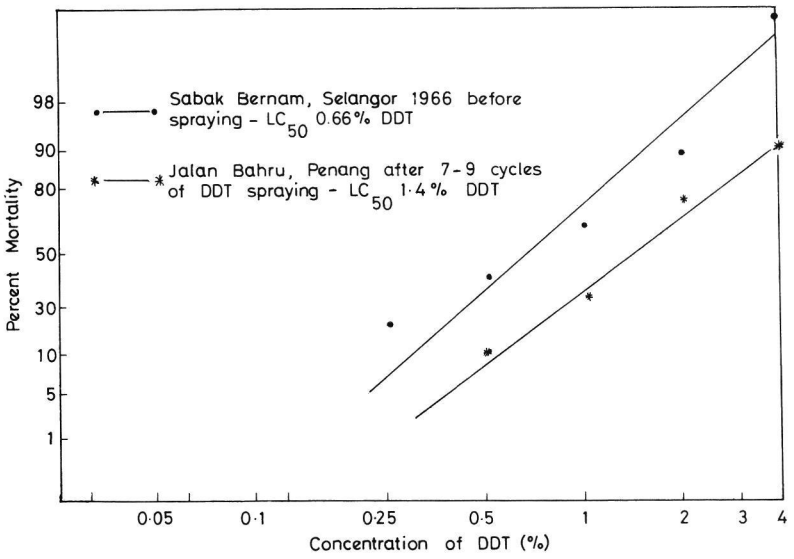

Fig. 7. Dosage mortality curve of *A. campestris* from Sabak Bernam, Selangor before spraying and from Jalan Baru, Penang after 4 years of spraying.

Indoor to outdoor biting ratio was 1.2 : 1 obtained with about 1,400 campestris during 140 man-nights. Indoor biting was fairly uniform right through the night with no marked peak, but increasing after midnight up to 4 am. Outdoor biting had a distinct peak from 9 pm to midnight and a smaller peak between 2 and 4 am. Average number of eggs laid by each female was 163 and the gonotrophic cycle was about two days.

Before spraying, it was seen that 56% rested on the roof and the rest on the wall, decreasing progressively with height. One month after spraying only 22% rested on the roof and 54% under 2 ft of the wall. Before spraying unfed mosquitoes rested for an average of 54 minutes and fed mosquitoes for 71 minutes. After spraying, only a few rested for more than half hour.

Of the *A. campestris* entering the hut, only 32.6% were found to remain inside the hut at 7 am the rest having left the hut by that time, the majority leaving between 6 am to 7 am before spraying. After spraying, about 45% left between 6 am and 7 am and 50% left before 1 am. Given the choice between cattle and human blood, 22% chose human and the rest cattle.

DDT at 2gm/m^2 gave a good kill of about 75% up to the end six months after which the mortality declined. There was no difference in the numbers entering the sprayed and unsprayed huts. The LC_{50} was about 1.4% DDT after 10 cycles of spraying with an odd mosquito surviving two hour exposure to 4% DDT. There was no evidence of any resistance in *A. campestris* at the time of reporting although there appears to be an increased tolerance. Dissections for parous rates are reported which could not be correlated with the DDT application in the area.

It is therefore concluded that *A. campestris* continues to enter sprayed houses to bite and would still be killed by residual spraying with DDT in the area up to the time of reporting.

ACKNOWLEDGEMENTS

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CARDIAC ARRHYTHMIAS IN ACUTE MYOCARDIAL INFARCTION

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INTRODUCTION

THE reduction in mortality in acute myocardial infarction from 30-35% to 20-25% is attributed to the early recognition and treatment of cardiac arrhythmias in the early phases of the acute coronary event (Kimball and Killip, 1968; Pantridge *et al.*, 1975). The more frequent use of continuous electrocardiographic monitoring, artificial cardiac pacing and electrical cardioversion has contributed in this reduction in mortality. In addition, there is now a better understanding of life-threatening arrhythmias and its role in the genesis or aggravation of cardiac failure and shock. In contrast, mortality from cardiogenic shock in acute myocardial infarction has however not changed despite modern facilities and drugs.

It is common to develop one or more types of arrhythmias following acute myocardial infarction. An incidence of 75%-95% of patients has been reported to develop some disorder of rate, rhythm or conduction as a complication (Julian *et al.*, 1964; Meltzer and Kitchell, 1966; Hurwitz and Eliot, 1964). Time lapse between onset of symptoms and hospital admission and the duration of monitoring are two important factors that influence arrhythmia detection.

This report is a prospective study of 164 patients with acute myocardial infarction seen between October 1977 and July 1979 in the Universiti Kebangsaan Division of the Coronary Care Unit, General Hospital, Kuala Lumpur. By continuous electrocardiographic monitoring for 24 hours, we report our experience of the incidence of the various types of arrhythmias in acute myocardial infarction in the local population.

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PATIENTS AND METHOD

All patients admitted with history and symptoms suggestive of acute myocardial infarction were included in the study. No selection was made regarding age, sex, race and severity of illness. The diagnosis was established by a) typical clinical history b) electrocardiographic abnormalities consisting of either new Q waves or typical evolutionary ST-T changes c) serum glutamate oxaloacetate transaminase rise of at least twice normal. Patients not fulfilling the above criteria and re-admissions were excluded from the study. Every patient was seen by one of us within 12 hours of admission. A standard 12 lead electrocardiogram was done on admission and the patient was started on continuous electrocardiographic monitoring without delay.

All arrhythmias detected on the monitors were noted and where possible, recorded. Deaths and complications of cardiac failure and shock occurring in the coronary care unit were documented. Cardiac failure was diagnosed in the presence of a) raised jugular venous pressure b) crepitations in the lung bases c) chest X-ray changes consistent with cardiac failure. Shock was diagnosed when the systolic blood pressure was less than 90mm. of Hg. in the presence of peripheral cyanosis, cold and sweaty skin and oliguria. Patients with cardiogenic shock and cardiac failure were classified as shock.

Monitoring system: Continuous electrocardiographic monitoring was obtained using the Hewlett Packard Model 78220 A/B Arrhythmia Monitoring System. Each bedside monitor was

interfaced to the central console in the nursing station allowing arrhythmia detection from both places. An alarm system sensitive to changes in heart rates, ectopics and life-threatening arrhythmias permits direct recording during appropriate events. The system in addition could display, on request, of a patient's heart rate and ectopics trends over the past 9 hours thus permitting evaluation of preceeding events and response to treatment.

RESULTS

There were 146 men (89%) and 18 women (11%) who fulfilled the criteria in the study. Table I shows the distribution of the 164 cases by race and sex. The age range was 26 years to 81 years, with a mean of 53.5 years.

Site of Infarction, Complications and Deaths: The site of infarction and its frequency by sex is shown in Table II. In this study, there were more anterior (69.8%) than inferior (40.2%) infarctions. In 120 patients (73.2%) no complications of cardiac failure and cardiogenic shock developed. These complications were more frequent with anterior (30.6%) than inferior (21.2%) infarctions (Table III). There were 16 deaths (9.8%), 11 patients with anterior and 5 with inferior infarctions, within 24 hours of admission. Of the 8 patients who developed cardiogenic shock, 5 died within 24 hours. There were 6 deaths (16.7%) out of the 36 patients who developed cardiac failure on admission. Refractory ventricular tachycardia and/or ventricular fibrillation and complete heart block were the immediate causes of death in the other 5 patients. This relatively low incidence of deaths seen with this series was because deaths occurring after 24 hours were excluded from the study.

Arrhythmias: 132 of the 164 patients (80.5%) monitored developed some disorder of rate, rhythm or conduction (Table IV). The incidence of arrhythmias varied with the clinical status of the patients. All patients with cardiogenic shock, 94.4% of patients with cardiac failure and 75% of patients with no complications developed arrhythmias. The occurrence of arrhythmias in relation to the site of infarction is shown in Table V.

Supraventricular Arrhythmias occurred in 54.8% of patients. Sinus bradycardia was more common in inferior infarctions whereas supraventricular tachycardia was seen more frequently in anterior infarctions. Bradycardia arising from sinus bradycardia, second degree heart block and complete heart block was seen in 23.2% of the patients. This was more common in inferior (13.5%) than anterior (9.7%) infarctions. Premature atrial contractions, atrial flutter and atrial fibrillation were less frequent, usually transient and did not require specific treatment.

Ventricular Arrhythmias was seen in 34.7% of patients. Unifocal premature ventricular contractions was the most common type seen (23.2%). Treatment of premature ventricular contractions with Lignocaine (Xylocard), either in a bolus injection or as a continuous infusion, was

Table I
Racial distribution of 164 Patients

Race	Sex				Total	
	Male		Female			
	No.	%	No.	%	No.	%
Malay	52	31.7	8	4.9	60	36.6
Chinese	34	20.7	6	3.7	40	24.4
Indian	58	35.4	4	2.4	62	37.8
Others	2	1.2	0	0	2	1.2
Total	146	89.0	18	11.0	164	100.

Table II
Distribution of patients by sex and site of infarction

Site of Infarction	Sex of Patient				Total	
	Male		Female			
	No.	%	No.	%	No.	%
antero-septal	62	37.8	10	6.1	72	43.9
Extensive Anterior	20	12.2	6	3.7	26	15.9
Inferior	64	39.0	2	1.2	66	40.2
Total	146	89.0	18	11.0	164	100

Table III

Incidence of Complications in relation to site of Infarction

Clinical Status of Patient	Site of Infarction			Total	
	Antero-septal	Ext. Anterior	Inferior	No.	%
No Cardiac Failure	50(0)	18(3)	52(2)	120	73.2
Cardiac Failure	18(3)	6(2)	12(1)	36	22.0
Cardiogenic Shock	4(1)	2(2)	2(2)	8	4.8
Total	72(4)	26(7)	66(5)	164	100

( ) Figure in brackets indicate number of deaths.

Table IV

Incidence of Arrhythmias [all types] in relation to the Clinical Status of the Patient

Clinical Status of Patient	Total Number of Patients	Patients with Arrhythmias	
		No.	%
No Cardiac Failure	120	90	75
Cardiac Failure	36	34	94.4
Cardiogenic Shock	8	8	100
Total	164	132	80.5

usually satisfactory. Mexiletene (Mexitil) was used when an unsatisfactory response was obtained. Ventricular tachycardia or fibrillation was seen infrequently (3.6%) in anterior infarctions only. Of the 6 patients who developed this arrhythmia, 2 showed it as a terminal event and was refractory to treatment.

Conduction Defects developed in 29.8% of the patients studied. It was more frequent in inferior infarctions (17.1%) than anterior infarctions (12.7%). 9 patients developed complete heart block, 3 of whom died.

DISCUSSION

It is now well recognised that arrhythmias of various types occur in 75%-95% of patients with acute myocardial infarction. In the pre-monitoring era, arrhythmias were considered to occur in only about 20% of patients with acute myocardial infarction, rather than the almost 100% incidence that is now reported (Master *et al.*, 1937). Early mortality in acute myocardial infarction which occurs within a few hours of the onset of symptoms is attributed to arrhythmias. Attempts to reduce this mortality rate should thus be directed to the early detection and treatment of arrhythmias. This became apparent after the widespread establishment of coronary care units with continuous electrocardiographic monitoring facilities. It is also recognised that the earlier the patient is admitted to the coronary care unit, the greater will be the incidence of arrhythmias detected. Certain arrhythmias are considered life-threatening which predispose to early deaths. They include severe bradycardia, advanced heart block, frequent ectopics, ventricular tachycardia and ventricular fibrillation. Treatment of arrhythmias in general serve to prevent this mortality and in addition prevents extension of infarct size and aggravation of cardiac failure.

Bradyarrhythmias are common after acute myocardial infarction (Jewitt *et al.*, 1967; Cristal *et al.*, 1975). The prevalence of bradycardia is dependent on the time monitoring is started. When seen within 30 minutes after infarction, Webb *et al.* (1972) found 77% of patients had bradycardia. Pantridge *et al.* (1975) in their series noted the incidence decreased to 34% when seen within 1 hour of symptoms. In this study, 23.2% of patients developed bradycardia and was more frequent in the inferior infarc-

tions. Delay in hospital admission is contributory to the low incidence. In our experience, the mean dealy in hospital admissions is 11.7 hours (Ng *et al.*, 1979). The significance of the bradyarrhythmias, sinus bradycardia or advanced heart blocks, is their association with an increased morbidity and mortality. This is attributed to hypotension with its adverse haemodynamic sequelae, enlargement of infarct size and causing electrical instability that may provoke genesis of escape rhythms such as ventricular tachycardia and ventricular fibrillation (Moroko *et al.*, 1971). Bradycardia is significantly more common in patients with inferior myocardial infarction than in those with infarctions of other sites (Adgey *et al.*, 1968; Grauer *et al.*, 1973). In the early phases of acute myocardial infarction, hypotension and electrical instability secondary to bradycardia frequently respond to an increase in heart rate. This is possible with atropine or the use of a pacemaker when the drug is ineffective.

Tachyarrhythmias in acute myocardial infarction are due to sinus tachycardia, paroxysmal atrial tachycardia, atrial flutter, atrial fibrillation or ventricular tachycardia and fibrillation. Sinus tachycardia is reported to occur in 20%-53% of patients with acute myocardial infarction (Julian *et al.*, 1964; Jewitt *et al.*, 1967). This arrhythmia can arise from anxiety, pain or extensive myocardial damage resulting in cardiac failure or shock. As a reflection of the extent of myocardial dysfunction, it is seen more frequently with anterior than inferior infarctions where the occurrence of such complications are higher. Mortality is therefore higher in these patients. With supraventricular tachycardia, paroxysmal atrial tachycardia and paroxysmal junctional tachycardia, the occurrence is infrequent. It is usually transient lasting from several munutes to a few hours. Atrial fibrillation and atrial flutter are uncommon. They arise from a concommitent infarction of the atrium or secondary to left ventricular failure. When associated with rapid ventricular rates, the prognosis may be worsened by the undesirable effects on cardiac output either precipitating or aggravating cardiac failure and also because severe cardiac damage is usually present. In 24 hours monitoring of the 164 patients in this study, sinus tachycardia was observed in 33 patients (20.1%). Less than 5% of patients developed atrial fibrillation (4.9%) and atrial flutter (2.4%). Ventricular tachycardia and ventricular fibrillation occur in 2%-6.4% of patients. Frequency of detection is dependent on delay in admission time. Their occurrence is increased in cases complicated by cardiac failure or shock and thus seen usually as a terminal event preceeding "cardiac arrest".

The incidence of developing premature ventricular contractions (all types) ranges from 58%-93% depending on interval from onset of symptoms and duration of monitoring (Pantridge *et al.*, 1975). In this study, 31.1% of the patients developed premature ventricular contractions. This low incidence in comparison to other reported series may be attributed to the short duration of monitoring. Non-detection of this arrhythmia by the observer is also contributory. Certain types of premature ventricular contractions are now identified as those that preceed ventricular tachycardia or ventricular fibrillation. They include; ectopic beats occurring greater than 5 per minute, multifocal nature of the beats, coupled beats or salvos (three or more in a row) and ectopics that show a "R on T" phenonmenon (Lown *et al.*, 1967). Suppression of these arrhythmias may prevent the high risk of developing ventricular tachycardia or fibrillation. This forms the basis for immediate or prophylactic anti-arrhythmic therapy in the attempt to reduce coronary care mortality. Prophylactic use of Mexiletene (Achuff *et al.*, 1977) and Disopyramide (Zainal *et al.*, 1976) have been shown to effectively reduce ventricular arrhythmias following myocardial infarction.

Continuous electrocardiographic monitoring has increased awareness to early arrhythmia detection with its clinical implications in acute myocardial infarction. Being an observer monitoring system, and despite well trained coronary care unit nurses, non-detection of warning arrhythmias occur. Vetter and Julian (1975) demonstrated in their study using a computer analysis system, the detection of 99% of potentially serious ventricular arrhythmias as compared to the detection of less than 50% of these arrhythmias in the conventional observer monitoring system. This limitation results in patients not receiving anti-arrhythmic therapy or delayed because of detection failure.

SUMMARY

Cardiac arrhythmias occur in the majority of patients after acute myocardial infarction. The incidence of arrhythmias is affected by the time delay before hospital admission and the duration of monitoring carried out. 164 patients with acute myocardial infarction are studied with reference to the types and incidence of arrhythmias occurring in 24 hours of continuous monitoring. The local experience is compared with other series and the significance of certain types of arrhythmias is discussed.

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THE SIGNIFICANCE OF ATRIAL FIBRILLATION IN RHEUMATIC MITRAL STENOSIS: AN ECHOCARDIOGRAPHIC STUDY

K.T. SINGHAM & M. ARIFFIN

INTRODUCTION

THE onset of atrial fibrillation in patients with mitral stenosis is associated with progression of the severity of the disease. The present study was undertaken to correlate left atrial size, severity of mitral stenosis and the occurrence of calcified and/or rigid fibrotic mitral valves with the presence of atrial fibrillation or sinus rhythm using reflected ultrasound to evaluate the mitral valve.

MATERIAL AND METHODS

Two hundred and fifty patients with rheumatic heart disease echocardiographically confirmed to have mitral stenosis seen over a 2 year period May 1976 to June 1978 were admitted into the study. Echocardiograms were performed using a Smith-Kline Ekoline 20A ultrasonoscope using a 15 mm diameter 2.25 mHz transducer prefocused at 10 cm and a repetition rate of 1000 per second permitting an examination of up to 20 cms tissue depth with excellent resolution. Simultaneous electrocardiograms were recorded in all patients. Echocardiograms were recorded using either a polaroid photographic system or a cambridge multichannel fiberoptic photographic strip chart recorder. The patients were examined either supine or propped up. The transducer was positioned in the 3rd or 4th left intercostal space parasternally and a systematic examination of the heart was performed by a standard technique (Feigenbaum, 1976).

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The criteria used to diagnose mitral stenosis (Fig. 1) was the presence of a slow diastolic closure rate of the anterior leaflet of the mitral valve associated with synchronous movement of both leaflets (Duchak *et al.*, 1972). The severity of the stenosis were assessed using the diastolic closure rate of the anterior mitral valve leaflet (Feigenbaum, 1976). Mild mitral stenosis was said to be present when the anterior mitral valve leaflet diastolic closure rate was between 26 mm/sec to 35 mm/sec. Moderate mitral stenosis was defined as an anterior mitral valve leaflet diastolic closure rate of 15 to 25 mm/sec. and severe mitral stenosis was defined as an anterior mitral valve leaflet diastolic closure rate of less than 15 mm/sec. (Feigenbaum, 1976). Mitral valve calcification was noted to be present if either anterior and/or posterior leaflet was found to have multiple layered echos (Fig. 2). The

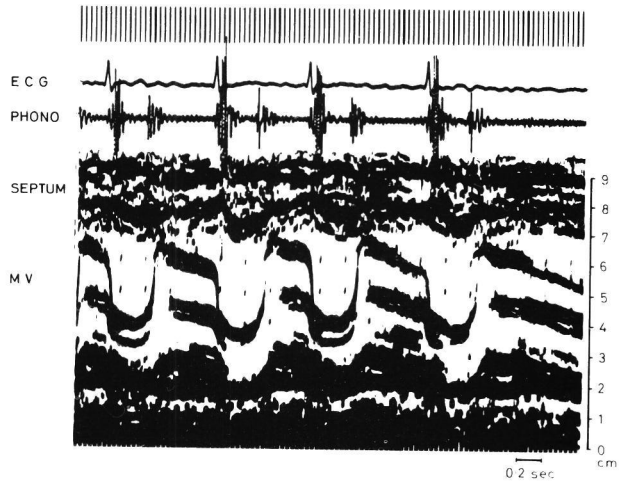

Fig. 1. Mitral stenosis with atrial fibrillation. [MV = mitral valve]

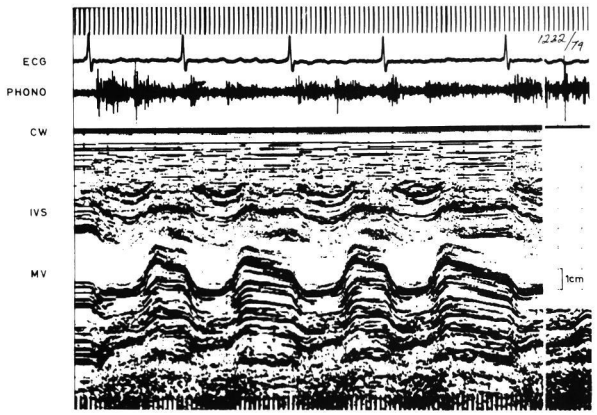

Fig. 2. Mitral stenosis with heavy calcification and atrial fibrillation [MV = mitral valve; IVS = interventricular septum; CW = chest wall].

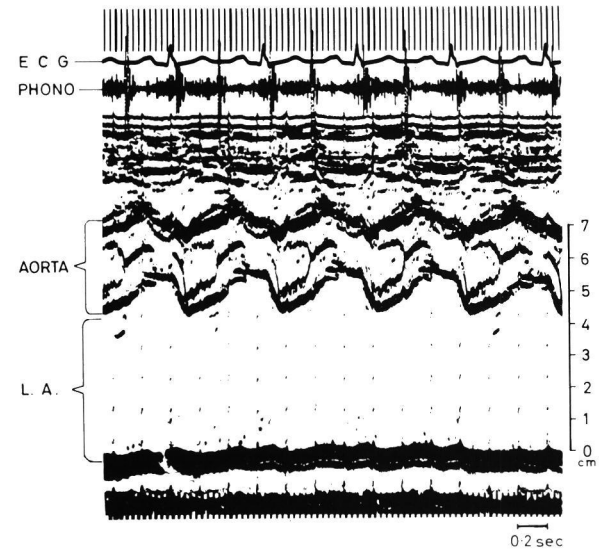

Fig. 3. Enlarged left atrium [LA = left atrium].

valve was assessed as rigid if the amplitude of opening of the anterior mitral valve leaflet was less than 20 mm. Left atrial enlargement was considered to be present if the anteroposterior diameter measured by ultrasound exceeded 4 cms (Fig. 3). The data obtained were subjected to statistical tests of significance.

FINDINGS

The findings in this study are summarised in Tables 1, 2 and 3. In comparing the groups with rigid mitral valves, calcified mitral valves and pliable mitral valves in Table 1 there is an overall significant difference in the occurrence of sinus rhythm or atrial fibrillation (x^2 = 31.6825; $p<0.001$). A comparison of patients with rigid mitral valves with those with calcified mitral valves shows no statistical difference between the two as to the occurrence of atrial fibrillation or sinus rhythm (x^2 = 0.0148 with Yate's correction $p>0.05$). The overall significant difference observed in Table 1 is contributed by the difference between those with pliable mitral valves as compared with rigid and calcified mitral valves taken together (x^2 = 29.7697 with Yate's correction $p< 0.001$). The data suggests that while patients with rigid and calcified mitral valve stenosis tend to be in atrial fibrillation more frequently, those with pliable mitral valves tend to be in sinus rhythm.

A comparison of the three grades of severity of mitral valve stenosis as to the occurrence of sinus rhythm or atrial fibrillation (Table 1) shows a statistically significant result at the 5% level of significance (x^2 = 8.2583; O.O2>p> O.O1). A comparison of the groups with moderate and severe degrees of stenosis as to the occurrence of atrial fibrillation or sinus rhythm produced a non-significant result (x^2 = O.O185 with Yate's correction p>O.O5). However a comparison of patients with mild mitral stenosis against those with moderate and severe stenosis taken together produced a significant result (x^2 = 7.1OO6 with Yate's correction p<O.O1). Examination of the data suggests that a larger proportion of those with mild mitral stenosis tend to be in sinus rhythm compared to those with moderate and severe mitral stenosis. A test for linear trend in proportions observed in Table II was carried out as follows: Total x^2 = 8.2583 O.O2> p> O.O1; Linear trend x^2 = 6.5060 O.O2> p> O.O1; Deviations x^2 = 1.7523 O.20> p> O.1O.

Table I

Echocardiographic assessment of pathological changes on the valve in Mitral Stenosis

Rhythm	Rigid valves	Calcified valves	Pliable valves	Total
Atrial fibrillation	19	19	56	94
Sinus rhythm	7	9	140	156
Total	26	28	196	250

Table II

Echocardiographic assessment of the severity of mitral stenosis

Rhythm	Mild Stenosis	Moderate Stenosis	Severe Stenosis	Total
Atrial fibrillation	5	20	69	94
Sinus rhythm	28	31	97	156
Total	33	51	166	250

Table III

Left Atrial Size in Mitral Stenosis

Rhythm	Enlarged Left atrium	Normal Left atrium	Total
Atrial fibrillation	55	39	94
Sinus rhythm	50	106	156
Total	105	145	250

At a significance level of 5 per cent the evidence suggests that there is a significant linear trend in the increase in proportions of cases with atrial fibrillation.

An analysis comparing patients with a normal sized left atrium and those with a large left atrium revealed a significant difference between the two as to the occurrence of sinus rhythm or atrial fibrillation ($x^2 = 16$; $p < O.OO1$). Examination of the data suggests that a greater proportion of those with a large left atrium have atrial fibrillation and that there is a higher proportion of patients with sinus rhythm amongst those with normal sized left atria. (Table III).

DISCUSSION

The natural history of rheumatic mitral stenosis has been well documented since the advent of cardiac catheterization and cardiac surgery (Wood, 1954; Goodwin *et al.*, 1955; McDonald *et al.*, 1967). It is well recognised clinically that the onset of atrial fibrillation is related to the occurrence of increasing effort dyspnoea of a moderate degree. However, the significance of atrial fibrillation in relationship to the pathological changes occurring in the valve in the clinical setting has not been worked out. Earlier studies have indicated a higher incidence of atrial fibrillation in patients with an enlarged left atrium and rheumatic mitral valve disease. This is confirmed in this study as well. In keeping with previous clinical studies (Hurst *et al.*, 1974) this echocardiographic study has demonstrated that a larger proportion of patients with mild mitral stenosis tend to have sinus rhythm whereas those with moderate to severe stenosis tend to have an increasing incidence of atrial fibrillation. In addition to this, it has been shown in this study that the presence of calcified or rigid mitral valves predisposes to the presence of atrial fibrillation more frequently than those with pliable mitral valves who tend to have sinus rhythm.

Evaluation of the patients with mitral stenosis by echocardiography is thus essential preoperatively as has been borne out by this study as mitral commissurotomy can be performed in virtually all patients with moderate to severe mitral stenosis and a mitral valve mobility of greater than 20 mm, in the absence of calcification. However, presence of calcification or rigid valves indicates that the valve is unsuitable for commissurotomy.

SUMMARY

Two hundred and fifty patients with echocar-

diographic evidence of mitral stenosis were analysed to correlate the presence of atrial fibrillation or sinus rhythm with the severity of the mitral stenosis, left atrial size and the presence of mitral valve calcification or heavy fibrosis resulting in rigid stenotic mitral valves. There appears to be a higher probability of the occurrence of atrial fibrillation in patients with calcified or rigid valves than those with pliable mitral valves. Patients with mild mitral stenosis tend to be in sinus rhythm compared to those with a more severe degree of mitral valve stenosis. As the mitral stenosis progresses from a mild to severe degree there is a significant linear trend in the increase in proportions of cases with atrial fibrillation. It appears that a greater proportion of those with large left atrial tend to have atrial fibrillation.

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EBSTEIN'S ANOMALY OF THE TRICUSPID VALVE: A REPORT OF 10 CASES

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INTRODUCTION

THE finding of a tricuspid valve which has been displaced into and greatly reducing the size of the right ventricular cavity was first noted during an autopsy of a young man by the German physician, Wilhelm Ebstein in 1866. It was some eighty three years later, in 1949, that the first case was diagnosed antemortem by Tourniaire, Deyrieux and Tartulier in France. The diagnosis has been made with increasing frequency antemortem in the last twenty years.

We are reporting our clinical experience with 10 cases of Ebstein's disease diagnosed at the University Hospital, Kuala Lumpur.

MATERIAL AND METHOD

This study includes all patients diagnosed to have Ebstein's anomaly at the University Hospital, Kuala Lumpur from 1967-1979. At least one 12-lead electrocardiogram, chest radiograph and cardiac catheterization were performed on all patients. Three patients had echocardiogram performed as well.

RESULTS

Sex and Age

There were 2 males and 8 females in this series; the youngest being 1 month and the eldest 44 years of age at diagnosis.

Family history

There were no instances of familial Ebstein's anomaly in our series. Gueron *et al.* (1966) reported two siblings with this condition and two years later Donegan *et al.*, (1968) reported a 6 year old boy with a 29 year old maternal uncle suffering from Ebstein's anomaly. Simcha and Bonham-Carter (1971) noted 2 families in which more than one member were similarly affected. Watson (1974) in a collected series of 505 cases found a family with 2 sisters clinically diagnosed as having the condition. Richard Emanuel (1976) studied 120 first-degree relatives of 26 patients with Ebstein's anomaly and found no case in any of them.

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Associated lesions

Associated cardiovascular anomalies other than interatrial communications were not found in this series. Three patients had patent foramen ovale. In the assembled series of Hamish Watson 48% were found to have associated lesions, the most frequent being defects in the interatrial septum.

Symptoms

All of our patients were symptomatic at the time of diagnosis. Effort dyspnoea and easy fatiguability were dominant symptoms in 7 patients. Orthopnoea was present in one patient. Two patients had transient syncopal attacks and palpitations with documented attacks of paroxysmal atrial tachycardia was found in another. Five of 10 patients were noted to have cyanosis prior to first examination.

PHYSICAL FINDINGS

Peripheral examination

Cyanosis was found in 5 patients. Two of the three children in this series were noted to have cyanosis soon after birth while the others developed cyanosis at 3 years of age. This is in keeping with the findings of larger series where cyanosis usually appears insidiously between 3 and 12 years of age (Simcha *et al.*, 1971). Four patients had clubbing of the finger tips.

Five of our patients were in atrial fibrillation at the time of first examination. Pulses were

generally small in volume. Three patients with pericardial effusions exhibited pulsus paradoxus. Blood pressure readings were normal. Elevated jugular venous pressure was noted in 7 patients. Contrary to what is generally believed however, only 1 of them demonstrated a large 'v' wave secondary to tricuspid regurgitation. No patient had large 'a' waves in the jugular veins. Rapid 'y' descent was noted in the three patients with pericardial effusion.

Central examination

Cardiomegaly was noted in 9 patients. Cardiac pulsations were however much reduced in only 7 patients. In 3 patients active pulsations were noted in the second and third left parasternal spaces, this being subsequently found to be due to active pulsations of the right ventricular outflow tract. Diminished intensity of heart sounds was noted in only 4 of the 10 cases. A 3rd heart sound was heard in all but on patient. Only half of our patients exhibited a soft ejection systolic murmur in the left sternal edge. No patient had any diastolic murmur.

Radiologic examination

Chest radiographs showed cardiomegaly in all nine who had clinically detectable enlargement of the heart (Fig. 1). The pulmonary vasculature appeared normal in 9 patients; however, marked oligemia was noted in one. Fluoroscopy was done in four patients and a consistent finding was generalised poor pulsation of the heart with the exception of the very active right ventricular outflor tract.

Electrocardiography

The suggestively diagnostic pattern of complete right bundle branch block with abnormally low R and S waves over the right praecordium was not found in any of our patients. In keeping with the twenty proven cases assembled from the literature by Keith (1978) however, R and S waves measuring less than 7 mm in the right praecordial leads were noted in 9 of our cases. Abnormalities of the P waves consisting of either increases in amplitude and/or duration were seen in all 5 patients with sinus rhythm. Five patients had atrial fibrillation and one exhibited paroxysms of supraventricular tachycardia. The mean QRS axis ranged from $+10^{o}$to $+150^{o}$. None of our patients exhibited Wolff-Parkinson-

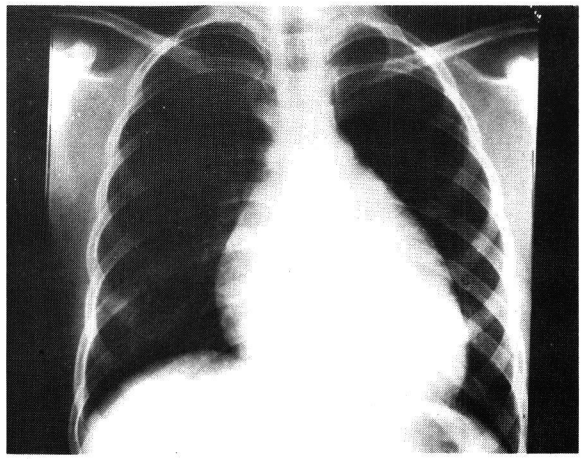

Fig. 1. Plain chest x-ray showing cardiomegaly with pulmonary oligemia.

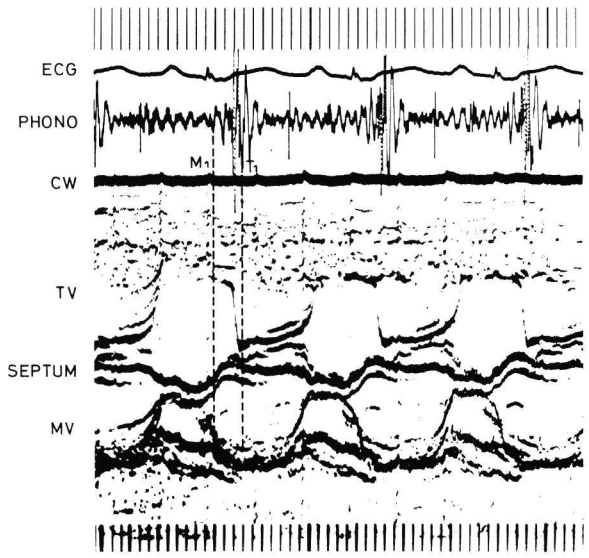

Fig. 2. Echocardiography showing a delayed closure of the tricuspid valve and a slow tricuspid valve closure rate; q^{T}_{1} = 40 mSec; q^{T}_{1} = 160 mSec; q^{T}_{1} - q^{M}_{1} = 120 mSec. [M_1 = mitral valve closure; T_1 = tricuspid valve closure; TV = tricuspid valve; MV = mitral valve, CW = chest wall].

White syndrome, a feature found in about 10 per cent of patients with Ebstein's anomaly of the tricuspid valve.

Echocardiography

Echocardiography was done in 3 patients. In two patients, delayed closure of the tricuspid valve was demonstrated (Fig. 2). This, and an abnormally anterior position of the anterior leaflet of the tricuspid valve during diastole (Lundstrom, 1973) have been deemed to be features consistently found in the echocardiograms of patients with this condition. In one patient a significant pericardial effusion was detected at echocardiography.

Cardiac catheterization

All but one patient underwent right heart catheterization. In 8 patients the catheter was noted to be coiled up in the abnormally dilated right atrium. The right atrial mean pressure exceeded 15 mmHg in 5 patients. Probe patency of the foramen ovale was noted in 3 patients and arterial desaturation detected in 6 patients. A feature common to all patients catheterized was the difficulty encountered in entering the right ventricle followed by the showers of ventricular extrasystoles at the time of catheter manipulation in the ventricle. Electrode catheter recordings of simultaneous intracardiac electrocardiograms and pressures were done in 6 patients. Confirming Hernandez's experience (1958), this procedure detected the atrialised portion of the right ventricle in 5 patients (Fig. 3).

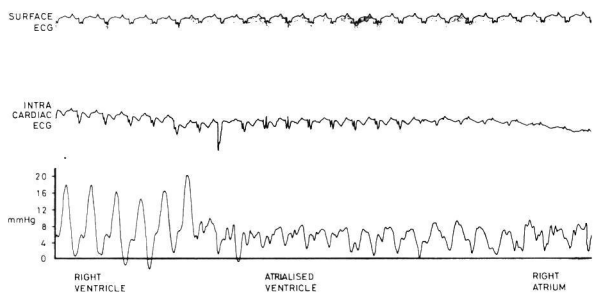

Fig. 3. Intracardiac electrocardiogram demonstrating the atrialised portion of the right ventricle.

Angiocardiography

Selective angiography was done in all 10 patients. In all cases a large right atrium occupying over half the cardiac shadow was demonstrated (Fig. 4). Also consistently found was the late emptying of the right atrium into the rudimentary right ventricle. The tricuspid valve was displaced laterally and to the left (fig. 4) and its relation to the annulus was shown as two notches at the inferior cardiac border.

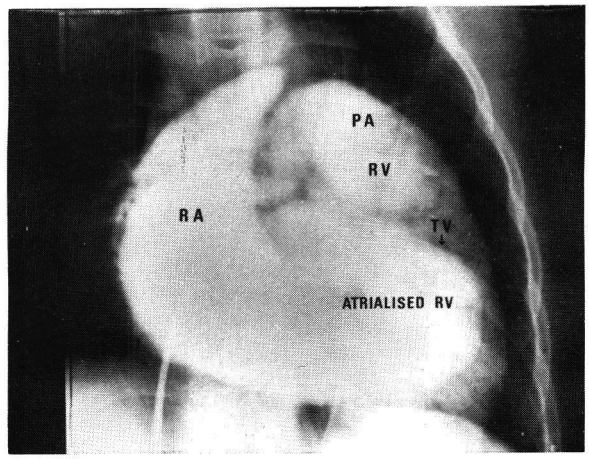

Fig. 4. Right atrial angiocardiogram showing a very large right atrium with the tricuspid valve being displaced into the right ventricle [PA = pulmonary artery; RV = right ventricle; RA = right atrium].

DISCUSSION

Ebstein's anomaly of the tricuspid valve is a relatively uncommon condition. If 61 centres in the cooperative study guided by Watson (1974)

only 17 collected more than 10 cases. The prognosis varies considerably; some patients live a completely normal life, the anomaly being an incidental finding at autopsy. The oldest patient recorded was 79 years old (Makons and Vander Veer, 1966), while at the other end of the spectrum, an infant died at 3 days of age from complications of the disease (Keith, 1978). The majority of deaths occur between the second and fourth decades of life. Six of our patients lived beyond 20 years of age while two were seen in infancy.

The sex ratio in our population of Ebstein's anomaly is probably not a true reflection of the sex incidence of this condition. In the cooperative study of Watson (1974), there were 258 males and 247 females, confirming the impression obtained from earlier smaller series that there is no difference in the sex incidence of this malformation (Vacca *et al.*, 1958 and Ganton & Blount, 1962).

There were no familial cases in our series and no obvious predisposing causes could be elicited in our patients. An interesting report of this latter aspect of the disease was made by Nora (1974) who noted that four of eight babies with congenital heart disease born to mothers exposed to lithium during pregnancy had Ebstein's disease. This is a sobering thought considering the number of young females in the reproductive age group who are on lithium carbonate therapy for manic depressive psychosis.

The clinical presentation of our patients are no different from those of previous series. Seven of the 10 patients presented with symptoms of effort dyspnoea of long standing. In the large series of Watson (1974) of the 35 cases under 1 year, 86% were in functional class III or IV by the New York Heart Association's classification. Seventy one per cent of those between one and twenty five years of age were in functional class I and II, while 60% of those over 25 years of age also had little or no disability.

No single physical sign or groups of signs are pathognomonic of this condition. While the presence of a large silent heart is frequently quoted as a usual finding, in 3 of our patients active pulsations were noted in the pulmonary area. These active pulsations transmitted from the outflow tract of the right ventricle should not be misinterpreted as evidence of right ventricular hypertrophy. Although tricuspid regurgitation can be found in this disease, it is not invariable. A large 'v' wave in the jugular veins and an enlarged pulsatile liver, were noted in only 1 of our patients. Takayasu in 1978 reported 26 patients with Ebstein's anomaly, only 4 of whom had dominant tricuspid incompetence. Eight of their patients had dominant tricuspid stenosis while 14 were classified as mild cases.

Just as no physical sign is diagnostic, the common investigatory tools are seldom able to confirm the diagnosis of Ebstein's anomaly of the tricuspid valve. In many cases, the chest radiograph and electrocardiograph may suggest the diagnosis. However, cardiac catheterization and angiography are usually required to confirm it. While cardiac catheterization was at one time deemed very dangerous in this condition, recent experience suggest that it is not very much more hazardous to catheterize these patients than other sick patients with other congenital or acquired heart disease as is borne out by our experience. Clues to the diagnosis are the tendency for the catheter to coil in the grossly enlarged RA, difficulty in entering the abnormally positioned tricuspid valve and the showers of ventricular extrasystoles associated with the procedure. In Watson's series, no less than 100 of 363 patients undergoing catheterization experienced paroxysmal dysrhythmias. Intracavitary electrocardiography may provide convincing evidence of the presence of an abnormally positioned tricuspid valve associated with atrialisation of the right ventricle. Selective angiocardiography clearly identifies the displaced tricuspid valve.

In recent years, echocardiography has proven to be useful in this condition. Two of our 3 patients who underwent this examination demonstrated what are now considered to be specific echocardiographic signs of Ebstein's anomaly which are the ability to record the anterior tricuspid leaflet further to the left of the left sternal border; and abnormally prolonged interval between the closure points of the tricuspid valve and the mitral valve demonstrating delayed tricuspid valve closure (Farooki *et al.*, 1976).

Management of all our patients were entirely

conservative. Symptomatic patients were placed on digoxin and diuretics and any infections, especially chest infections, were aggressively treated. None of our patients required long term antiarrhythmic therapy.

Surgical treatment of this condition is presently limited to a few selected cases. Its role and the procedure of choice for its correction are not yet clearly defined. At present, surgery seems to be indicated in patients with intractable congestive heart failure and those with repeated, arrhythmias especially when they are difficult to control (Watson, 1974 and Keith, 1978).

The prognosis of this condition is variable. However, life expectancy is considerably reduced in patients with Ebstein's anomaly as a whole. Hansen (1977) in a long-term follow up of 22 patients identified cyanosis due to a right-to-left shunt through an atrial septal defect as the best guide to distinguish the group with a good from the one with a bad prognosis. Right sided heart failure and dyspnoea at rest, often associated with palpitations, praecordial pains and syncope are grave prognostic findings.

SUMMARY

The clinical features, plain film radiological findings, electrocardiographic findings, echocardiographic changes, haemodynamics and angiocardiographic features of 10 patients with Ebstein's anomaly of the tricuspid valve are described. The ages of the patients varied between 1 month to 44 years. There were 2 males and 8 females. Common symptoms were effort dyspnoea, palpitations and cyanosis. Cardiomegaly with an obvious third heart sound was present in majority of patients. Echocardiography showed an obvious delay in tricuspid valve closure and angiocardiography demonstrated characteristic displacement of the tricuspid valve into the right ventricular cavity.

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LOW INCIDENCE OF SELECTIVE IgA DEFICIENCY IN NORMAL MALAYSIANS

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INTRODUCTION

IN populations residing in the temperate regions selective IgA deficiency is the most common of the primary immunodeficiency diseases occurring in about 1:500 to 1:700 individuals (Bachmann, 1965; Hanson, 1968; Hobbs, 1968; Johansson *et al.*, 1968; Koistinen, 1975). The condition is characterized by serum IgA levels less than 5 mg/100 ml with normal serum levels of the other class of immunoglobulins and absence of T cell deficiency. In many of the individuals with selective IgA deficiency, thymus defects of varying severity are present and therefore some degree of T-cell hypofunction is expected (Horowitz & Hong, 1975; Buckley, 1975).

The deficient serum IgA is usually associated with absence of secretory IgA from the body secretions but occasional individuals possess the capacity for normal production of secretory IgA (Bellanti *et al.*, 1966). Also, individuals with secretory IgA deficiency in the presence of normal serum IgA have been recorded (Krakaeur *et al.*, 1975).

Ammann & Hong (1971) reviewed the clinical features of 205 patients with IgA deficiency and found that autoimmune disorder were present with greates frequency and also, many patients experienced recurrent sinopulmonary infections and gastrointestinal disorders. A surprising observation was that about 10 per cent of the individuals with selective IgA dificiency were clinically normal. Similar observations had also been made by other investigators (Hanson, 1968; Koistinen, 1975).

The exact mechanism by which IgA deficiency occurs remains unclear but at least two separate mechanisms have been shown to occur. In one, there is insufficient helper T cell activity for IgA antibodies because of the defect in thymus development, and in the second, B lymphocytes destined to produce IgA are arrested at an early stage of development. The selective IgA dificiency can occur sporadically but autosomal dominant, autosomal recessive, intermediate polygenic modes of inheritance and chromosome abnormality have been reported (Nell *et al.*, 1972; Koistinen, 1976; Horowitz & Hong, 1977). Environmental factors, too, can be important in its development. Lewkonia *et al.* (1976) noted the presence of IgA deficiency in one of the monozygotic twins. In some individuals IgA deficiency develops following penicillamine or phenytoin therapy (Hjalmarson *et al.*, 1977; Stanworth *et al.*, 1977).

There is very little information on selective IgA deficiency in Malaysians, or for that matter for populations normally resident in the tropics (Yadav, 1977). Some individuals with selective IgA deficiency have the potential of forming anti-IgA antibodies with the resultant and sometimes fatal anaphylactoid reactions on transfusion with IgA containing plasma (Vyas *et al.*, 1969), and therefore it is important to konw the incidence of IgA deficiency in normal Malaysians.

The aims of this study was to determine the normal range of serum IgA level in Malaysians from the urban (Chinese, Malay & Indian) and rural (Malay and Orang Asli) areas with special reference to low or absent levels of serum IgA. The observations show that selective IgA deficiency is uncommon in healthy Malaysian blood donors.

MATERIALS AND METHODS

Blood Samples: Sera from 2,025 healthy donors were obtained from the Blood Bank, University Hospital, University of Malaya; the Gombak Orang Asli Hospital, Selangor; through the cooperation of secondary schools in Petaling Jaya, Selangor and through the cooperation of

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the Filaria Unit, Sungei Patani, Kedah. The sera were kept frozen at -20°C until required.

Quantitative Determination of Immunoglobulin: The sera was assayed for immunoglobulin A by the single radial immuno-diffusion method (Mancini *et al.*, 1965) as previously described (Yadav, 1977; Yadav & Shah, 1978). The agar diffusion plates incorporating H-chain specific rabbit antisera were either prepared in our laboratory or the immunodiffusion plates were purchased from a commercial source (Behringwerke, Germany). Standards from the World Health Organisation or commercial sources were used.

RESULTS

Selective IgA deficiency was not observed in 2,025 sera analysed for IgA from urban and rural Malaysians. (Table I). The serum IgA level ranged from 57 to 846 mg/100 ml in rural and 45 to 430 mg/100 ml in urban folks. The frequency histogram of serum IgA was skewed to the right for the samples from the rural population. The mode was between 121-200 mg/100 ml for urban Malaysians, 161-240 mg/100 ml for rural Malays and 321-360 mg/100 ml in the Orang Asli. For the total sample the mode fell between 161-200 mg/100 ml. The mean serum IgA level for urban sample was 200 mg/100 ml which was significantly lower than the mean value of 267 mg/100 ml for the rural sample.

DISCUSSION

Selective IgA deficiency occurs in 1:700 healthy individuals in Sweden (Bachmann, 1965; Hanson, 1968; Johansson *et al.*, 1968), 1:310 in school children 5-19 years old and 1:454 in hospital patients 0-19 years old in Canada (Collins-William *et al.*, 1972), 1:398 in rheumatoid arthritis patients and 1:1255 in blood donors in Norway (Natvig *et al.* 1971), 1:2190 in blood donors in France (Frommel *et al.*, 1973) and 1:396 in blood donors in Finland (Koistinen, 1975). It is believed that the marked difference in the frequency of selective IgA deficiency may be caused by genetic factors in different ethnic groups (Koistinen, 1975). However, it is also possible that the low incidence in some groups is because IgA deficient individuals would not survive through early life in a pathogenically hostile environment. In Malaysia the analysis of 2,025 sera from healthy blood donors has not revealed a single case of IgA deficiency. Previously, we have reported that in a 10 years old girl with bronchiectasis, chronic diarrhoea and recurrent episodes of otitis media, the serum IgA level was low (31 mg/100 ml) and the other classes of immunoglobulins were markedly elevated (Yadav *et al.*, 1977). Since IgA is the first line of defense of the secretory system which primarily protects the respiratory and gastrointestinal tracts, uncontrolled antigenic assault in those areas in individuals with low or absent protective IgA would result in development of clinical disease. In the tropics relatively more opportunities are prevalent for assault from a variety of viral, bacterial, fungal, helminthic and other agents. In view of the above it is questionable whether asymptomatic selective IgA deficiency can be present in the tropics. Thus, in the temperate regions the significant number of individuals with asymptomatic selective IgA deficiency (Koistinen & Sarna, 1976; Horowitz & Hong, 1975) do not develop clinical disease presumably because environmental infective agents are relatively uncommon and secondly, the compensatory mechanisms including secretion of IgM (Thompson, 1970) on the mucosal surface are adequate under the conditions, to exclude the entry of pathogenic antigens.

In an analysis of 606 sera from adult out- and in-patients seeking treatment for a variety of disorders e.g. bronchitis, tuberculosis, asthma, gastritis, gastroenteritis, appendicitis, cholecystitis, typhoid, malaria, aches & pains, coughs & colds, and others, serum IgA levels were never less than 35 mg/100 ml (Yadav, unpublished). This observation leads us to believe that patients with selective IgA deficiency may get life threatening infections in early life.

In the newborn IgA in serum ($<$0.8 mg/ml) was present in 36.4, 40.5, 31.6, and 62.5 per cent of full term Chinese, Indian, Malay and Orang Asli, respectively (Shah & Yadav, 1977). It is not known how soon after birth the infants attain protective levels of serum IgA and more significantly when the secretory IgA on mucosal surfaces reaches optimal levels. However, in a preliminary analysis of the serum immunoglobulins in 497 infants aged 1 month to 4 years admitted to the University Hospital for various

Fequency Distribution of Serum IgA Concentration of Malaysians aged 11 to 60 years

Table I

Race	Serum IgA Concentration mg/100 ml*													
	Total Samples	5	5-40	41-80	81-120	121-160	161-200	201-240	241-280	281-320	321-360	361-400	401-440	441-900
URBAN														
Chinese	466	0	0	3[a]	73	112	123	54	36	39	21	4	1	0
Indians	390	0	0	4	38	54	78	62	47	50	47	7	3	0
Malays	326	0	0	3	32	92	89	46	27	22	8	6	2	0
RURAL														
Malays	605	0	0	5	15	78	129	111	85	74	35	33	21	19
Orang Asli (Aborigines)	238	0	0	0	6	12	4	10	23	30	36	32	22	63
Total	2,025	0	0	15	164	348	423	282	218	215	147	82	49	82
Per cent		0	0	0.7	8.1	17.2	21.0	13.9	10.8	10.6	7.3	4.0	2.4	4.0

* Multiply by 0.5952 to convert to IU/ml.

[a]Number of individuals.

gastrointestinal disorders it was noted that 33 infants (6.6 per cent) had less than 5 mg/100 ml IgA in serum (Yadav & Iyngkaran, unpublished). The majority of the infants presented with acute infective gastroenteritis, cow's milk protein-sensitive enteropathy or malabsorption as their primary clinical feature. Transient IgA deficiency is present in many infants and in some is thought to predispose to atopy, possible by allowing penetration of antigens through mucosal membrane barriers (Soothil, 1974). However, the atopy has also been observed in infants with normal serum IgA. Thus, other factors including genetic constitution and pathogenicity of infective agents may be important in the development of the gastrointestinal defects. However, we have no information on the incidence of transient IgA deficiency in normal Malaysian infants and children, and therefore are unable to comment on the overall significance of the deficiency on the development of atopy in children.

SUMMARY

Immunoglobulin A level were assayed according to the Mancini's method in 2,025 sera from clinically healthy donors of four racial origins (Malay, Indian, Chinese, Orang Asli) residing in urban (1,182 individuals) and rural (843 individuals) parts of Malaysia. The serum IgA level ranged from 45 to 430 mg/100 ml for urban and 57 to 846 mg/100 ml for rural folks. The frequency distribution of the serum IgA concentration for the rural population was skewed to the right. No case of selective IgA deficiency was noted in the samples. It is suggested that the incidence of asymptomatic IgA deficiency is low in the tropics compared to its incidence in the temperate regions, because the prevalence of pathogens in the tropics would eventually result in an uncontrolled antigenic assault on the mucosal surface resulting in the development of disease which may be fatal.

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NEUROBLASTOMA IN MALAYSIAN CHILDREN

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INTRODUCTION

NEUROBLASTOMA, one of the commonest tumours in childhood accounts for 11 to 14 per cent of all malignant solid tumours in children in the USA, UK and Australia (Dargeon, 1962; Bodian, 1959; Jones and Campbell, 1976). The overall 2 year survival rate has remained the same despite the use of chemotherapy (Leiken *et al.*, 1974).

Previous studies have mainly been in Caucasian children and information is not available on the epidemiology, clinical features, response to treatment and clinical vagaries such as the tendency to undergo spontaneous maturation and regression (Evans *et al.*, 1976) in Malaysian children with neuroblastoma.

This study reviews (1) the epidemiological and clinical features (2) the pathological staging and (3) the response to treatment and outcome in children with neuroblastoma seen at the University Hospital, Kuala Lumpur over a 10 year period.

MATERIALS AND METHODS

All children with neuroblastoma admitted to the Paediatric Unit, during the period 1968 through 1977 were reviewed. The diagnosis was based on biopsy findings or a combination of radiological, biochemical and bone marrow abnormalities in the absence of tissue confirmation in patients with widespread disease. Since 1973, combination chemotherapy which includes vincristine, adriamycin and cyclophosphamide, has been used together with the other modalities of treatment in the management of patients with advanced disease. Details of the illness, physical findings, results of investigations, pathological staging and response to treatment and subsequent outcome were documented and compared with other series.

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RESULTS

Epidemiology

During the index period, 16 children with neuroblastoma were admitted to the Unit. The total number of paediatric hospital admissions during this period was 24,532 cases. Neuroblastoma accounts for 0.65 per 1000 hospital paediatric admissions and 13.4 per cent of all malignant solid tumours in childhood.

Ethnic Distribution

The 16 children comprised 8 Chinese, 4 Malays, 3 Indians and 1 Orang Asli (aborigine). Chi-square analysis revealed no significant association between race and incidence of neuroblastoma among inpatients as seen in Table I.

Sex

In our series there were 10 males and 6 females. Chi-square analysis revealed no significant association between sex and the incidence of neuroblastoma among inpatients ($X^2=0.0274$, $df=1$ $P>0.5$).

Age at diagnosis

The mean age at diagnosis was 41.6 ± 33.2 months, SD; the youngest patient was 2 months

Table I

Ethnic Distribution of Neuroblastoma

Race	No. of Cases	No. of admissions 1068 - 1977
Chinese	8	12,040
Non-Chinese	8	12,492
Total	16	24,532

$X^2 = 0.006$,
df = 1,
$0.95 > p > 0.90$

old and the oldest 11 years respectively. Approximately 70 per cent of cases occurred by age of 4 years as in other series (Evans *et al.*, 1969).

Clinical Features

The average duration of symptoms prior to diagnosis was 4.5 weeks and ranged from 2 weeks to 3 months.

The commonest symptoms were fever, abdominal distension, anorexia and weight loss; the commonest signs were hepato-splenomegaly, proptosis, abdominal mass and fever as seen in Table II.

Table II

Presenting Symptoms and Signs in 16 patients with Neuroblastoma

Symptoms	No. of cases
Fever	11
Abdominal distension	8
Anorexia	7
Weight loss	6
Abdominal pain	3
Abdominal mass	3
Swelling of eye/face	3
Neck swelling	2
Blindness, mass at front of chest, loin pains, maxillary swelling, diarrhoea arthralgia, scalp mass	single cases

There was no association with hypertension or opsoclonus

Investigations

The mean haemoglobin level was 9.5 gdl $\pm$3.5 g/dl, SD and ranged from 2.3 g/dl to 19.0 g/dl; it was less than 10 g/dl in 9 of the 16 children. The mean white cell count was 10,306.25 $\pm$ 2,466.7 per cumm and ranged from 7000-14,200 per cumm. The platelet count was normal except in 2 patients with levels of 21 x 10^9/1 and 56 x 10^9/1 respectively. The ESR was elevated in 4 of 8 children and ranged from 82-126 mm/HR. Urine examination was generally normal except in 4 patients who had white cell counts ranging from 20-125 cells/mm^2 but viable counts were not significant. The urinary VMA screening test was positive in 13 of 14 cases and negative in 1 patient with a highly undifferenciated metastatic neuroblastoma. Blood urea was elevated in 1 of 12 cases.

Chest X-ray revealed either lung, hilar or mediastinal metastases in 6 patients and destruction of the sternum in 1 instance. Skeletal survey revealed abnormalities in 6 cases (3 also had chest X-ray abnormalities) which included dehiscence of cranial sutures by meningeal metastases, demineralisation of the sella turcica, erosion of the skull and roof of orbit, destruction of the nasal bones and metastases in the pelvis, long bones, maxilla, mandible and spine. Intravenous pyelogram disclosed downward displacement of the kidney in 11 cases calcification in 2 and hydronephrosis in 1 case respectively. Liver scan revealed cold areas in 4 of 5 cases studied. The bone marrow was infiltrated by tumour cells in 10 of 13 cases studied. The diagnosis was confirmed by biopsy in 9 cases and from a combination of radiological, biochemical and bone marrow abnormalities, without tissue confirmation in 7 patients. The pathological staging proposed by Evans et al. (1971) was adopted and of the 16 children reviewed 1 had stage III disease, 11 had stage IV disease and 4 had stage IV-S disease. The outcome of treatment in these patients is recorded in Table III.

The patient with stage III disease had inoperable tumour which responded well to chemotherapy and radiotherapy and no evidence of residual tumour was detected at surgery 3 months later. He was maintained on continuation chemotherapy but was subsequently lost to follow up after he developed metastases at 9 months.

Table III

Clinical staging and outcome of treatment in 16 cases of Neuroblastoma

Stage	No. of cases	Outcome
III	1	Metastases at 9 months, lost to follow up.
IV	11	4 died within 6 months; 6 lost to follow up. 1 alive and well at 9 months
IV-S	4	1 died of septicaemia while in remission. 1 refused treatment. 2 alive and well (2½) and 3 years later respectively).

Four of 11 patients with stage IV disease died within 6 months 2 within a few days; 6 patients were lost to follow up and 1 is alive and well on a vincristine, adriamycin, cyclophosphamide (VAC) regime 9 months after radiotherapy for a mediastinal neuroblastoma eroding the sternum.

2 of 4 patients with stage IV-S disease have survived 2½ years and 3 years respectively with minimal chemotherapy and radiotherapy. One patient refused treatment while another died of pseudomonas septicaemia at 3 months while on 2 weekly VAC regime following surgery and radiotherapy; autopsy revealed no evidence of tumour.

DISCUSSION

The present study reveals that neuroblastoma in Malaysian children behaves in much the same manner as in Caucasian children. The frequency of this tumour in relation to the other childhood malignancies and the epidemiological and clinical features appear to be similar to that of other series (Dargeon, 1962; Bodian, 1959; Jones and Campbell, 1976).

A significant proportion of our patients were anaemic at presentation but this was not related to bone marrow infiltration. The VMA screening test, positive in 93 per cent of our patients compares well with the positive rates reported in other series (77% McKendrick and Edwards; 96% Gitlow *et al.*, 1970; Voute *et al.*, 1975). The prognosis of patients without increased catecholamine excretion is poor and is associated with a highly undifferenciated form of neuroblastoma (Voute *et al.*, 1975) which usually arises in the midline such as the coeliac axis or pelvis area. Almost all our patients presented with metastases compared with two-thirds in other series (Evans *et al.*, 1978); none of our children had stage I or II disease. Metastases in the liver are mainly found in infants up to 6 months and skeletal metastases in older children (Wieberdink, 1957). Although papilloedema, scalp nodules,. dehiscence of sutures and erosion of orbit and skull have been observed in some cases metastases have not been found to invade the brain.

Prognosis appears to correlate with age and extent of disease. The outcome in our patients has been poor because of the advanced stage of their illness. Only one of our stage IV patients appears to be disease free at 9 months. The poor prognosis in stage IV patients has been observed in other centres (Evans *et al.*, 1978).

A favourable prognosis has been observed in Stage IV-S disease as in other series (Evans *et al.*, 1978). The reason for this is not clear but may be related to a unique interaction between the host and the tumour (Jones and Campbell, 1976) and as a rule these patients need little if any treatment as spontaneous regression usually ensues. In advanced cases a short course of chemotherapy and/or low dose radiation may initiate regression of disease. Significant bone marrow infiltration warrants chemotherapy such as delivered to patients with overt bone metastases but caution needs to be exercised in over zealous treatment as this may lead to myelosuppression or immunosuppression and increased mortality from infection.

One of the major problems encountered in the management of malignancies in Malaysia appears to be the problem of follow up. Eight of the 16 cases studied were lost to follow up and they were from the lower socio-economic group emphasising that social and economic factors are important considerations in cancer therapy programmes.

SUMMARY

A review of 10 years experience of neuroblastoma in the University Hospital, Kuala Lumpur

reveals no significant differences in either the epidemiological or clinical features between Malaysian and Caucasian children. The prognosis of patients with stage III and stage IV disease remains poor despite surgery, radiotherapy and chemotherapy. With limited treatment a favourable outcome is recorded in infants with stage IV-S disease.

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EXPERIENCE WITH SKIN REACTIONS TO VARIOUS ALLERGENS IN BRONCHIAL ASTHMA

A. ZULKIFLI & CHEN KWAI WENG

INTRODUCTION

ASTHMA is a disorder characterised by partial obstruction of the airways, reversible either spontaneously or as a result of treatment (American Thoracic Society, 1962). It is classified into the intrinsic and extrinsic asthma. In the extrinsic type, the clinical features, skin and laboratory tests showed that the allergy is of Type I and Type III.

Tests to detect the allergens include the scratch, intradermal and pin prick skin tests (Herxheimer, 1975). Skin testing is feasible routinely as an outpatient procedure. The highest positive skin tests occur in the extrinsic group reacting to a wider range of allergens than in the intrinsic group.

Once the skin tests identify the allergens, then can be avoided; the patients may be densensitised or treated by disodium cromoglycate. This study helped to identify such allergens in 74 patients using the pin prick skin tests.

MATERIALS AND METHODS

All asthmatic patients, seen in the Medical Unit, Universiti Kebangsaan Malaysia in 1978, that satisfy the criteria of the American Thoracic Society (1962) for bronchial asthma were included in this study. Based on this criteria, 74 patients were selected. We obtained a complete history and performed a clinical examination on every patient. We examined the blood haematologically urine and stool microscopically, and did x-rays of the chest and sinuses as well as an ECG. Antihistamines were stopped 48 hours prior to the tests as they inhibit the reactions to the tests.

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We performed the pin prick tests on the right forearm by pricking an ordinary pin into the outermost layer of the skin through a small drop of the allergen to be tested. Care was taken that bleeding did not occur. The distance between each test sites were at least 5 cm. apart and were numbered. A positive result is a wheal of at least 5 cm. diameter, read after 15 minutes. A control test using normal saline was done simultaneously on the same arm (Herxheimer, 1975).

History of allergies that precipitated asthmatic attacks and that of collateral allergies were obtained. The results were tabulated and analysed.

RESULTS AND DISCUSSION

74 patients, 39 males and 35 females, aged between 8 and 62, comprising 30 Malays, 26 Chinese and 18 Indians, were studied. The results of our positive skin tests (Table I) are compared with other authors (Cua-Lim, 1974), Pepys (1977). Household dust topped the list which was also the experience of others (Ch, r-pin, 1974) 70% (Lewandoska, 1974) 80%, (Hobday, 1974) 60% and (Pepys, 1977) 70%. Of the food tested, shrimps (19%) topped the list which in Cua-Lim's (1975 experience were crabs (17%) and shrimps (15%). The common allergens involved, such as household dusts and mites, may be reduced by vacuuming the room and by changing the linen frequently. This brings about an eight fold reduction in the number of airborne mites. In hospital where linens are changed frequently, the frequency of attacks of asthma are reduced. Occupational history and history of pets kept as well as food habits are often neglected facet of history-taking, may provide the clue in some patients. Complete avoidance of pollen is just not possible in this country. Hyposensitisation of allergens, such as pollen, may meet with success as in some Western countries. Hence in patients with an allergic history, skin testing helps in management. Where avoidance is impossible or desensi-

Table I

Incidence of positive skin tests with various allergens in authors series compared with others

ALLERGENS	Cua-Lim [1974] %	Pepys [1974] %	Author's series [1978] %
Household Dust	39	70	81
Grass Pollens	—	66	32
D. pteronyssinus	34	69	75
Asp. fumigatus	—	16	21
Animal Dander	—	38	—
Cat Fur	13	—	35
Chicken Feather	61	—	11
Dog Hair	47	—	15
Food	—	16	—
Shrimps	15	—	19
Egg	6	—	5
Crab	17	—	5

Table II

Number of patients with positive skin tests according to age group

Age Group	Number of cases reacting with one allergen	Number of cases reacting with more than one allergens
0 — 9	6	2
10 — 19	12	8
20 — 29	20	8
30 — 39	12	4
40 — 49	6	4
50 — 59	4	0
60 and above	0	0
Total	60	24

Table III

Average number of allergens causing positive skin reaction by age group

Age	Average number of Allergens
0 — 9	2.5
10 — 19	4.5
20 — 29	5.2
30 — 39	2.6
40 — 49	3.0
50 — 59	2.5

tisations fail, disodium cromoglycate will be of aid in some asthmatic patients. Monovalent allergy is better inhibited than multiple allergies. The incidence of positive skin tests (Table II) is highest in the age group 10-29 (55%). The average number of allergens causing positive reactions (Table III) is highest in the age group 10-29. Thus extrinsic asthma produced the most positive tests under the age of 30 years, reacting with a wide range of allergens. This tallies the experience of Pepys (1971).

Rhinitis was found in one half of our patients. Pepys (1971), Cua-Lim (1974) and Charpin (1977) found rhinitis in 36%, 60% and 49% respectively in their series. 20% of patients had eczema, though Charpin's (1977) figure was higher (35%). About half of those with infantile eczema developed asthma (Pepys, 1977).

SUMMARY

This study was proposed to determine the allergic states of patients in the Medical Unit University Kebangsaan Malaysia that satisfy the American Thoracic Society (1962) criteria for bronchial asthma. 74 patients, 39 males and 35 females, were selected. We performed pin prick skin tests on them. It was noticed that the extrinsic group of patients showed the highest positive skin tests with a wide range of allergens. The commonest allergens were in our experience. *D. pteronyssinus* in dusts and shrimps among food. The highest reactors belong to age group 10-29. Rhinitis tops the list of collateral allergic conditions. This being a pilot study, it is hopefully believed that it will be

taken advantage of by other clinicians before attempting desentisation procedure.

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IDENTIFICATION OF TRIGGER MECHANISMS IN BRONCHIAL ASTHMA

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INTRODUCTION

BRONCHIAL asthma is regarded as variable airway obstruction which presents clinically as wheezing and dyspnoea. Variability is considered with a 20% change in the index of resistance to air flow. This is unlike chronic obstructive airway disease, emphysema and chronic bronchitis, which is irreversible airways obstruction without variability (Starling, 1978).

The classification of bronchial asthma into extrinsic (allergic) and intrinsic (late onset) types is required to assess prognosis and management. In the assessment of patients with bronchial asthma, the identification of causative factors or trigger mechanisms is of vital importance in their management. The trigger mechanisms are grouped under three categories (Starling, 1978), which are allergic factors, infections and non-specific factors such as exercise and temperature changes. The latter mechanisms once identified could be avoided and treated where ever possible.

The purpose of this study is to identify the various trigger mechanisms of bronchial asthma in Malaysian patients admitted to the Medical Unit, Universiti Kebangsaan, Malaysia.

PATIENTS AND METHODS

All consecutive patients seen in the Medical Unit of Universiti Kebangsaan Malaysia between January 1976 and December 1978, that fulfilled the criteria of The American Thoracic Society (1962) for bronchial asthma were included in the study. No selection was made regarding age, sex, race or severity of illness. Re-admissions and doubtful diagnoses were excluded from the study. Each patient was seen by the authors on admission or in the clinic. A history of trigger mechanisms was obtained from the patient; this was subsequently confirmed by the relatives when possible. Family history of bronchial asthma and history of allergies in the patient and his relatives were documented. In addition to the clinical examination, x-rays of the chest and nasal sinuses, routine examination of blood, urine and stools were performed.

RESULTS AND DISCUSSION

148 patients, 79 males and 69 females, fulfilled the criteria and formed the subjects of this study. There were 42% Malays, 33% Chinese and 25% Indians. As in Singapore, asthma is less common in the Chinese (Gregg, 1977) than in the other two races. In 38% of cases, the illness started before the age of 10 years and in 89% before the age of 40 (Table I). In Herxheimer's (1975) experiences the age of onset of below 15 and 35 were 54% and 85% respectively. However in Nigeria and India (Gregg, 1977) the incidence of the age upon onset in children is less common. Hence asthma affects many children, interfering with their attendance in school. Inadequate treatment render them physically and emotionally handicapped. Parents are told that their children will grow out of the asthma and hence the danger of undertreatment. If the age of onset is under five, in 40% - 50% of patients the asthma disappeared by the age of 15 (Jones, 1976).

Family history of asthma was obtained in half of the patients which is the experience of Herxheimer (1975), while in Mornig's (1973) series, it occurred in one third. Other diseases which mimic bronchial asthma have to be excluded. The likelihood of developing asthma is higher in relatives of asthmatics than in control (Jones, 1976). In 56% of the patients, allergies

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occurred below the age of 30 (Table II) and the allergies were often multiple. Therefore allergies occurred in the younger age group, sensitive to a wider range of allergens. A history of collateral allergy was obtained in 81% of cases, and rhinitis accounted for 52% of the cases. The experiences of Cua Lim (1974) were 72% for collateral allergy and 60% for rhinitis. However, (Gregg, 1977) rhinitis is less frequently seen among asthmatics in Singapore.

Table I

Age of first attack in 148 cases of Bronchial Asthma

Age	Number of cases
0 — 9	58
10 — 9	35
20 — 29	20
30 — 39	19
40 — 49	8
50 — 59	4
60	4
Total	148

Table II

History of allergy in 148 asthmatic patients by age group

Age group	Allergic to one factor	Allergic to more than one factor
0 — 9	5	0
10 — 19	23	19
20 — 29	55	25
30 — 39	17	12
40 — 49	18	14
50 — 59	2	
60 and above	0	
Total	120	70

Table III shows the incidence of precipitating factors in the authors' series as compared to the other workers. Weather changes appeared significant in our findings. Emergency admissions for asthma in Brisbane and Hong Kong (Gregg,

Table III

Incidence of precipitating factors of author's series compared to others

Precipitating Factors	Turner-Warwick %	Cua Lim [1974] %	Jones [1976]	Godfrey [1977] %	Author's series [1978] %
Weather	—	—	59	—	42
Emotion	45	35.1	60	—	20
Exercise	50	—	97	—	40.5
Infection	43	—	56	40	50
Rhinitis	—	—	—	60	52
Allergens	—	—	73	—	81

1977) are related to temperature and humidity. Emotions was less important in our patients if compared to that of other authors (35 - 60%, Table III). Allergy and infections trigger the attack which then persist possible because of anxiety. However, Luparello (1968) induced attacks of asthma in 50% of patients by injecting normal saline which the patients imagined was an allergen. Exercise caused attacks in 40% of our patients who were mainly adults. In Godfrey's (1977) experience it was 97% and his patients were mainly children. This is explained on the basis (Godfrey, 1977) that adults did not exercise adequately to bring on an attack. Infections were responsible for 40 - 50% of the attacks in the same series (Table III). Severity of asthma and mortality from status asthmaticus were highest in those with an infective factor (Gregg, 1977). In certain patients (Howell, 1971) the first attack of asthma followed an acute bronchial infection. Allergic rhinitis occurred in the majority of patients as in Brompton Hospital (Gregg, 1977) and Manila experience (Cua Lim, 1974). However it is less common in Nigeria and Singapore (Gregg, 1977). If the allergens are identified they can be treated early. The important allergens constituted household dust (52%) pollen (38%) and food (25%). Household dust can be reduced by vacuuming and frequent change of linen. Pollen desensitisation is effective in some patients. Avoidance of allergenic foods such as eggs, shrimps and crabs will be yet another important step towards the control of the disease. Histor

of allergies guide the skin sensitivity tests to be performed, thus identifying the allergens. The use of disodium cromoglycate will be advantageous in those in whom desensitisation is difficult or in cases where allergens are unavoidable.

SUMMARY

The study was proposed to identify trigger mechanisms in bronchial asthma in Malaysian patients. All consecutive patients, seen in the Medical Unit, Universiti Kebangsaan Malaysia between 1976 and 1978, satisfying the American Thoracic Society criteria for bronchial asthma formed the subjects of the study. Analysis of 148 patients, 79 males and 69 females, consisting of 42% Malays, 33% Chinese and 25% Indians lead to the following tentative conclusions. While familial incidence was clearly noted, history of allergy was equally evident. Exercise, infections including rhinitis as precipitating factors were also observed in a significant number of patients. The influences of climatic variations and emotional disturbances constituted important predisposing factors in the study. In the light of our findings and their role in the management of patients we hopefully believed to achieve better results.

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INFLUENZA HI ANTIBODIES IN PIG AND MAN IN MALAYSIA [WITH SPECIAL REFERENCE TO SWINE INFLUENZA]

DORA S.K. TAN, MOHAMED OMAR & T.C. YAP

INTRODUCTION

AFTER the pandemic of swine influenza which killed millions of people in 1918-19 subsided, other influenza types came into prominence and swine influenza appeared to have lost world attention until January 1976 when an outbreak of influenza occurred in an army camp in Fort Dix, New Jersey, U.S.A. In this outbreak, an army recruit died of viral pneumonia without bacterial complications. Eleven virus isolations were made of which four, including the isolate from the fatal case, were identified as related to the swine influenza-like virus, Hsw1N1.

This started a world-wide concentration on the potential dangers of swine influenza spreading from pig to man, and possibilities of new recombinants between Hsw1N1 and the human H3N2 subtypes in pigs emerging. Sera of pigs from various countries were tested by WHO for antibodies against Hsw1N1 and H3N2 subtypes and attempts at isolating these viruses from pigs were also made in some countries.

This article reports a study of the prevalence of influenza caused by Hsw1N1 and the H3N2 subtypes (antigenically similar to A/Hongkong/68) in pig and man in Malaysia. The object is to determine the importance of the pig as a reservoir for influenza viruses in this country and the possible transmission of the disease from pig to man.

MATERIALS AND METHODS

The presence of influenza antibodies was examined in sera collected from: (1) 173 pigs (94 porkers, 6 months old and 79 sows, 2 to 3 years old) between June 1976 and November 1977 at the Government Abbatoir at Shah Alam, Selangor, (ii) 60 pig slaughterers of the same abbatoir in January 1977 (iii) 65 veterinary laboratory workers of the Veterinary Diagnostic Laboratory, Petaling Jaya, in February, 1977.

The test used was the haemagglutination-inhibition (HI) microtitre technique. The sera were inactivated at 56°C for 30 minutes prior to treatment with Receptor Destroying Enzyme (RDE) to remove non-specific inhibitors. The method adopted was that recommended by the WHO International Influenza Center for the Americas. The antigens used were A/Swine/1976/31 (Hsw1N1), A/New Jersey/8/76 (Hsw1N1), A/Port Chalmers/1/73 (H3N2), A/Victoria/3/75 (H3N2) and B/Hongkong/5/72. Eight units of the viral antigens were used in the HI test.

Virus isolations were attempted from throat washings of 107 pigs. They were immediately placed and transported to the laboratory in a flask containing wet ice to be inoculated into primary monkey kidney cells. At least one blind passage was made.

RESULTS

Of 173 pig sera examined, 13.3% had antibodies to A/Swine/1976/31 (Hsw1N1) virus and 13.9% to A/New Jersey/8/76 (Hsw1N1) virus, both with a geometric mean titre (GMT) of 45, 22.5% had antibodies to A/Port Chalmers/1/73 (H3N2) virus with a GMT of 24 and 10.4% had antibodies to A/Victoria/3/75 (H3N2) virus with a GMT of 29 (Table 1). Sows, 2 to 3 years old had significantly higher rates (range $p<.001$ to $<.01$) than porkers aged 6 months. No antibodies to B/Hongkong15/72 virus were detected at all Although the rates between the two Hsw1N1 antibodies were similar, those between the two H3N2 antibodies were significantly different ($p<.01$).

In the human group, none showed antibodies to A/Swine/1976/31 (Hsw1N1) virus but 8%

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TABLE I

DISTRIBUTION AND GMT* OF INFLUENZA HI ANTIBODIES IN PIG SERA

GROUP	A/SWINE/31 (Hsw1N1)			A/NEW JERSEY/76 (Hsw1N1)			A/PORT CHALMERS/73 (H3N2)			A/VICTORIA/75 (H3N2)			B/HONGKONG/72		
	EXAM	%	GMT*	EXAM	%	GMT	EXAM	%	GMT	EXAM	%	GMT	EXAM	%	GMT
Pigs (A) †	94	9.5	43	94	7.4	44	94	11.7	25	94	4.2	34	94	0	5
Pigs (B) †	79	17.7	46	79	21.5	45	79	35.4	23	79	17.7	23	79	0	5
TOTALS	173	13.3	45	173	13.9	45	173	22.5	24	173	10.4	29	173	0	5

* Geometric Mean Titre expressed as reciprocals. Titres less than 1:10 arbitrarily assigned a value of 1:5 or Log_{10} = 0.7 in the calculation of GMT.

† Pigs (A) : Porkers, about 6 months old. Pigs (B) : Sows 2-3 years old.

TABLE II

DISTRIBUTION AND GMT* OF INFLUENZA HI ANTIBODIES IN HUMAN SERA

GROUP	A/SWINE/31 (Hsw1N1)			A/NEW JERSEY/76 (Hsw1N1)			A/PORT CHAL-MERS/73 (H3N2)			A/VICTORIA/75 (H3N2)			B/HONGKONG/72		
	EXAM	%	GMT*	EXAM	%	GMT	EXAM	%	GMT	EXAM	%	GMT	EXAM	%	GMT
Pig Slaughterers	60	0	5	60	10.0	18	60	90.0	20	60	93.3	20	60	13.3	16
Veterinary workers	65	0	5	65	6.2	10	64	98.4	25	63	100.0	28	63	6.3	3
TOTALS	125	0	5	125	8.0	14	124	94.4	23	123	96.7	24	123	9.8	10

½ Geometric Mean Titre expressed as reciprocals. Titres less than 1:10 arbitrarily assigned a value of 1:5 or Log_{10} = 0.7 in the calculation of GMT.

TABLE III

PERIODICAL DISTRIBUTION OF INFLUENZA HI ANTIBODIES IN PIG SERA

PERIOD	A/SWINE/31 [Hsw 1N1]			A/NEW JERSEY/76 [Hsw 1N1]			A/PORT CHALMERS/73 [H3N2]			A/VICTORIA/75 [H3N2]			B/HONG- KONG/72		
	EXAM	POS	%	EXAM	POS	%	EXAM	POS	%	EXAM	POS	%	EXAM	POS	%
JUNE -JULY 1976	36	0	0	36	2	5.6	36	4	11.1	36	4	11.1	36	0	0
AUG - SEPT 1976	53	17	32.1	53	13	24.5	53	10	18.9	53	12	22.6	53	0	0
JAN -FEB 1977	25	0	0	25	5	20	25	0	0	25	2	8.0	25	0	0
JUN - JULY 1977	30	5	16.7	30	4	13.3	30	13	43.3	30	0	0	30	0	0
AUG - NOV 1977	29	1	3.4	29	0	0	29	12	41.4	29	0	0	29	0	0
TOTALS	173	23	13.3	173	24	13.9	173	39	22.5	173	18	10.4	173	0	0

(10.0% in pig slaughterers and 6.2% in veterinary workers) had antibodies to A/New Jersey/8/76 (Hsw1N1) virus with a GMT of 14 (Table II). This difference is significant.

The antibody rates to both A/Port Chalmers/1/73 (H3N2) and A/Victoria/3/75 (H3N2) viruses were similarly high in the human group (94.4% and 97.7%, respectively) with GMT values of 23 and 20 respectively. The antibody rate to B/Hongkong/73 virus was low in percentage (9/8%) and GMT (10). The rates between the pig slaughterers and the veterinary workers were similar for all the antigens tested.

The rates of different batches of pigs slaughtered at different periods of time varied considerably (Table III). A/Swine/31 antibody rates varied alternately from low to high ranging from zero to 32.1%. The pattern (Figure) adopted by A/New Jersey/76 antibody rates, however, simulated a curve with the highest point in late 1976 (period B) and decreasing to zero towards the end of 1977 (E).

The mode of variation between the antibody rates to the two H3N2 subtypes was markedly different. Although there were similarly low to moderate rates against these subtypes in pigs slaughtered in 1976 (A and B), those slaughtered during the latter months of 1977 (D and E) showed high rates (41.4% to 43.4%) to A/Port Chalmers/73 virus but none at all to A/Victoria/75 viruses.

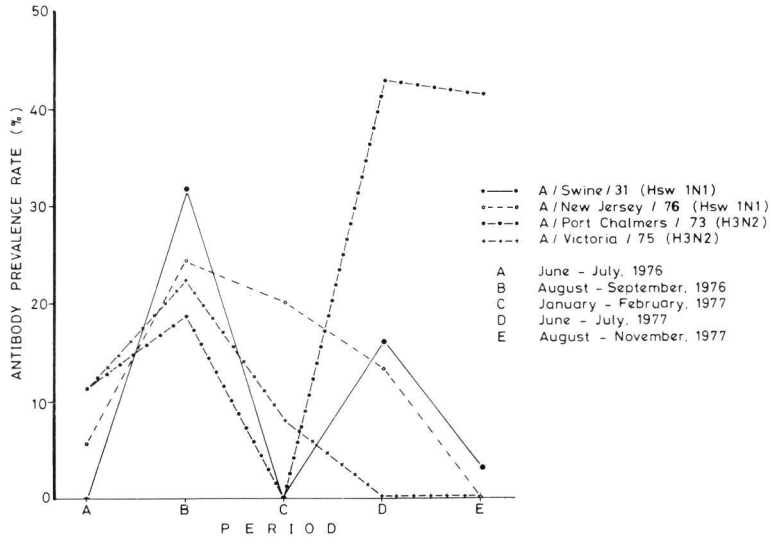
Only 3.3% (4/107) of throat swab specimens from the pigs yielded an agent which, however, was too low in titre for identification by the HI test. This could be attributed to a breakdown in the -70°C deep-freezer in which the specimens were stored.

DISCUSSION

The antigenic drift demonstrable between the two Hsw1N1 viruses, A/Swine/31 and A/New Jersey/76 (Kendal *et al,* 1977). and between the two H3N2 viruses, A/Port/Chalmers/73 and A/Victoria/75 (Pereira, 1979), was clearly shown in the results obtained in this study in which cross-reactions between similar subtypes were not evident.

The pigs examined showed persence of influenza infection with both the Hsw1N1 strains and both the H3N2 strains studied but none at all with B/Hongkong/72 virus (Table I). The older sows were more highly infected than the younger porkers as expected. The GMTs to the Hsw1N1 strains (45) were higher than those to the H3N2 strains (24 and 29 respectively) possibly indicating a more recent infection by the former strains. The periodical distributions of influenza antibodies in the pig sera appear to indicate a

FIGURE
PERIODICAL DISTRIBUTION OF INFLUENZA HI ANTIBODIES IN PIG SERA



wide variation of prevalence at different periods during 1976 and 1977 (Figure). Whereas the activity of all the viruses examined varied in a similarly fashion in 1976, the year 1977 saw a much greater activity of A/Port Chalmers/73 virus than of the other viruses, especially during the mid-year. Whether this could be related to an increase in human influenza-like cases reported to be occurring in some parts of Malaysia at that time, but from whom no specimens for investigation could be obtained is not known.

In the human group, no significant differences could be detected in the rates between the pig slaughterers and the veterinary workers (Table II). The former had been in direct contact almost daily with the pigs examined for at least one year. The latter comprised laboratory workers who rarely, if ever, came in direct contact with pigs, and therefore serves as a control group. The results, therefore, appear to indicate absence of transmission of infection from pig to man in this study and that the antibodies to A/New Jersey/76 in both human sub-groups had been acquired from human contact, albeit in the absence of an overt swine influenza outbreak in the population (An antibody survey, which will be carried out in 1980 on sera collected from 1977 to 1979 will hopefully show whether or not A/New Jersey/76 virus has indeed been circulating among Malaysians during this period). Almost all the people examined were younger than 50 years of age which explains the absence of A/Swine/31 antibodies in their sera (Tan & Omar, 1974). As the results of virus isolation from pig throat specimens cannot be relied upon due to the breakdown of the -70°C deep-freezer in which the specimens were stored, it cannot be determined for sure whether the infection in the pigs was currently active or not.

SUMMARY

The presence of influenza HI antibodies was examined in sera collected from 173 pigs (94 porkers, 6 months old and 79 sows, 2 to 3 years old) at the Shah Alam abbatoir, 60 pig slaughterers of the same abbatoir and 65 veterinary workers of the Veterinary Diagnostic Laboratory, Petaling Jaya.

The pig sera showed an prevalence rate of 13.3% to A/Swine/1976/31 (Hsw1N1) virus and 13.9% to A/New Jersey/8/76 (Hsw1N1) virus, both with a GMT of 45; 22.5% to A/Port Chalmers/1/75 (H3N2) virus with a GMT of 24 and 10.4% to A/Victoria/3/75 (H3N2) virus with a GMT of 29. No B/Hongkong/72 antibodies were detected. The rates to all the viruses studied were higher in the older pigs than the younger ones and varied considerably with different periods of time.

The human sera showed no antibodies to A/Swine/31 (Hsw1N1) virus but 8% showed antibodies to A/New Jersey/76 (Hsw1N1) virus with a GMT of 14. Very high rates of A/Port Chalmers/73 (H3N2) antibodies (94.4%) with a GMT of 23 and A/Victoria/75 (H3N2) antibodies (96.7%) with a GMT of 24 were found in the human group. B/Hongkong/72 antibodies were of much lower prevalence (9.8%) with a GMT of 10.

The abbatoir and veterinary workers had similar antibody distributions for all the virus strains examined although the former group had been in constant and direct contact with the pigs and the latter had not. It may be concluded from this that the pigs were not transmitting any influenza to their slaughterers and that the presence of A/New Jersey/76 antibodies detected in man might be attributed to the virus actually circulating among the population, albeit in low amounts and without causing an overt outbreak.

Virus isolation was attempted from throat swabs of pigs but because of a breakdown in the -70°C deep-freezer in which the specimens were stored, only 3.7% (4/107) yielded an agent which, however, was too low in titre for identification by the HI test.

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MUCOCUTANEOUS LYMPH NODE SYNDROME IN MALAYSIA

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INTRODUCTION

ACUTE febrile mucocutaneous lymph node syndrome (MLNS), a febrile exanthematous illness of young children was first described in Japan by Kawasaki (1967). Since the establishment of diagnostic guidelines by the Japanese Ministry of Health and Welfare (1974), the disease has been recognised with increasing frequency in many different countries including the United States (Melish *et al.*, 1976; Korea (Kim *et al.*, 1975), Hawaii (Melish *et al.*, 1974) and Greece (Valaes, 1975).

We present here a report of three cases of mucocutaneous lymph node syndrome from the University Hospital, Kuala Lumpur, which we believe are the first to be recognised in Malaysia.

REPORT OF CASES

CASE 1: A 5 year old Chinese girl was hospitalised in November 1977 with a 4 day history of cough, anorexia, and fever non-responsive to ampicillin. She had mild jaundice, conjunctival injection, erythema of the mouth, pharynx and tongue and a generalised maculopapular rash with redness of the palms and soles. The cervical nodes were enlarged and the liver was 2 cm palpable below the rib margin; the rest of the clinical examination revealed no abnormalities.

Investigations revealed the following: haemoglobin 10.6 g/dl, white blood cell count 12.4 x 10^9/l, polymorphs 87%, lymphocytes 10%, monocytes 2%, eosinophils 1%, platelet count 230 x 10^9/l, ESR 86 mm/hr, serum total bilirubin 61.6 umol/l, unconjugated bilirubin 27.4 umol/l and conjugated bilirubin 34.2 umol/l, SGOT 23 iu/l; SGPT 56 iu/l, serum alkaline phosphatase 234 iu/l. Serum IgG, IgA, IgM, complement C_3, and C_4 were normal. Other tests with normal or negative results included Monospot test, Widal test, Weil-Felix reaction, antistreptolysin O titre, mantoux test, LE cells, rheumatoid factor, viral cultures of nasopharyngeal washings and stool, urine and blood cultures and chest X-ray.

Four days after admission the child developed acute left heart failure with gallop rhythm and electrocardiogram (ECG) revealed uniformly low voltages, PR interval O.16 sec and depressed ST-T segments in V_3 and V_5. She responded well to digoxin and lasix. The fever settled on the seventh hospital day and on the tenth day she was observed to have desquamation of the finger tips. She was then discharged and has remained well since.

CASE 2: A 4 year old Indian boy was admitted in December 1978 with a 8 day history of fever, conjunctival injection and a mild transient erythematous rash on the trunk. On examination, he was febrile, temperature 38°C and toxic. Ulcers were observed on the lips and buccal mucosa and there was moderate cervical right axillary, and supratrochlear lymphadenopathy. The liver was 1.5 cm palpable below the rib margin. The rest of the clinical examination was normal. Investigations revealed, haemoglobin 12.7 g/dl, total white blood cell count 11.7 x 10^9/l, polymorphs 78%, lymphocytes 17%, monocytes 4%, eosinophils 1%, platelets 250 x 10^9/l, ESR 71 mm/hr, serum total bilirubin 5 umol/l, SGOT 23 iu/l, SGPT 80 iu/l, serum alkaline phosphatase 206 iu/l, serum total proteins 73 g/l, albumin 31g/l and globulin 42 g/l. Chest X-ray was normal. Cultures of throat washings, blood and stools were negative for both bacteria and viruses. Monospot, Widal and Weil-Felix tests were negative. Serology for arboviruses, CMV, herpes, measles rubella and toxoplasma were negative. LE cells and tests for rheumatoid factor were negative. Bone marrow

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examination revealed active granulopoeisis and lymphocytosis suggestive of a viral infection.

Patient became afebrile 6 days after admission and developed desquamation of the finger tips and around mouth. He has remained well since.

CASE 3: A 2 year old Indian boy was admitted in January 1979 with a 6 day history of fever followed by swelling of the feet and the appearance of a macular rash over the face and trunk two days before admission. On examination, temperature was 38°C and the child appeared toxic with conjunctival injection and ulcerations of the lips and buccal mucosa. The cervical nodes were enlarged and discrete. The results of the rest of the clinical examination were negative. Investigations revealed, haemoglobin 9.6 g/dl, total white blood cell count 14.8 x 10^9/1, polymorphs 58%, lymphocytes 38%, eosinophils 2%, monocytes 2%, platelet count 262 x 10^9/1, ESR 96 mm/hr, serum total proteins 91 g/1, serum albumin 30 g/1, serum globulin 61 g/1 and serum total bilirubin 6.8 umol/1. Chest X-ray and electrocordiogram were normal. Other investigations with normal or negative results included. Latex ASL test, ASOT, Monospot test, cultures of blood and urine, serological tests for arbovirus, toxoplasma, herpes, CMV and other related viruses. Left cervical node biopsy revealed prominent germinal centres and a picture of reactive hyperplasia (fig 1). The patient's temperature returned to normal on the fourth hospital day and on the seventh day he was observed to have desquamation of the finger tips (fig 2). He was discharged and has been well since.

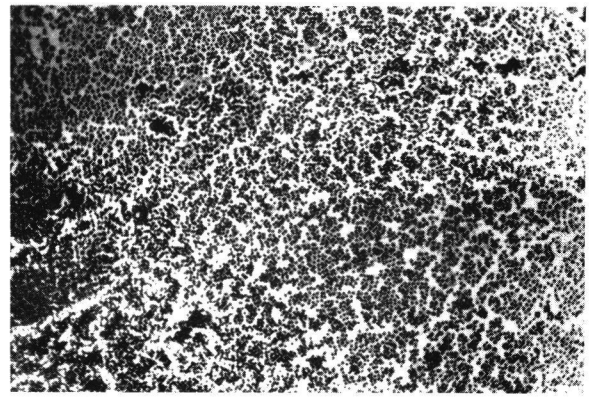

Fig. 1. Left cervical lymph node biopsy revealing reactive hyperplasia

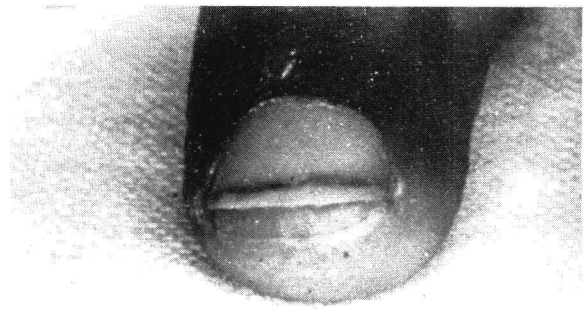

Fig. 2. Desquamation of the finger tip in a case of MLNS

DISCUSSION

The MLNS is an acute febrile mucocutaneous illness which typically begins with high fever lasting one to two weeks unresponsive to antibiotics, conjunctival injection, reddening of the oral cavity, lips, palms and soles, induration and oedema of hands and feet, polymorphous erythematous macular rash involving the trunk, non-suppurative cervical lymphadenitis, desquamation of the finger tips and cardiographic changes (Yamamoto, 1975). Laboratory investigations usually reveal leukocytosis with a shift to the left, mild anaemia, elevated ESR and normal ASOT. Bacterial and viral cultures are unrewarding. The mortality rate is 1.5% (Yanagawa, 1976) and almost all deaths are caused by sudden rupture or thrombosis of aneurysms in the main coronary arteries (Tanaka, 1972). Abnormal electrocardiograms have been recorded in 90% of non-fatal cases (Yanagisawa *et al.*, 1974). There is difficulty in differentiating the underlying thromboarteritis in the MLNS from that seen in infantile periarteritis nodosa making

the distinction between the two disorders unclear (Tanaka *et al.*, 1971). Elevated α_2 globulin and IgE have been reported in some cases (Kusakawa and Heiner, 1976). The aetiology of MLNS is still unknown. The significance of rickettsia-like bodies which have been visualised by electron microscopy in biopsy specimens of skin and lymph nodes is still uncertain (Hamashima *et al.*, 1973). Aspirin therapy is now considered to have a place in therapy of MLNS for its anti-inflammatory effects and its potential in reducing hypercoagulable states.

Table I summarises the findings in our patients as compared with the diagnostic criteria established by the Research Committee on MLNS of the Japanese Ministry of Health and Welfare (1974). The clinical features of our 3 patients are consistent with the established guidelines.

Table I
Criteria for the diagnosis of MLNS based on the definition proposed by The Research Committee on MLNS of the Japanese Ministry of Health and Welfare

Criteria	Case No.		
	1	2	3
1. Fever lasting 5 or more days unresponsive to antibiotics	+	+	+
2. Bilateral conjunctival injection	+	+	+
3. Redness and fissuring of lips, orosphoryngeal mucosa, strawberry tongue	+	+	+
4. Oedema of extremities, reddening of palms and soles, desquamation of finger tips	+	+	+
5. Polymorphous non vesicular	+	+	+
6. Acute non-suppurative lymph adenopathy	+	+	+
* Absence of other well-known aetiologies	+	+	+

Diagnosis based on meeting at least 5 of the above 6 criteria plus * criteria.

SUMMARY

Mucocutaneous lymph node syndrome (MLNS); a newly recognised disease, widely prevalent in Japan has more recently been recognised in USA, Korea, Hawaii and Greece.

We have recently seen three children, 2 to 5 years of age with MLNS in the University Hospital, Kuala Lumpur which we believe are the first to be recognised in Malaysia. All three cases had the principle features characteristic of MLNS, including myocarditis in one case. The detection of these cases over a 2 year period indicates that MLNS affects children in Malaysia as in Japan and other countries. With increasing awareness more cases undoubtedly will be recognised.

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THE PATTERN OF PSYCHOTROPIC DRUG USAGE IN A GENERAL OUT—PATIENT CLINIC

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INTRODUCTION

PSYCHOTROPIC drugs have become important in the management of emotional and psychiatric disorders since their introduction in the mid - 1950s. This group of drugs, conveniently described as psychotropics have expanded over the years and fall into 5 main groups, the sedative - hypnotics, antidepressants, stimulants, antipsychotics and antianxiety or anxiolytics. (The terms antipsychotics and antianxiety have replaced the older terms of major and minor transquillisers respectively).

Psychotropic drugs are mostly prescribed by non-psychiatrists as shown in cross-national studies by Hollister (1977) and Balter and Levine (1969). Even for the antidepressants and antipsychotics, used primarily for mental disorders psychiatrists and neurologists account for only one third of prescriptions written in the United States in the study by Parry *et al.* (1973). From this same study 85% of a patient survey responded that they had never visited a psychiatrist though they had used a psychotropic drug in the preceeding year.

The use of psychotropic drugs can be high in some countries as was shown by Parry *et al.* (1973) in the United States where it was found that one in three adult Americans had occassion to use at least once a psychotherapeutic drug in the preceeding year and the most frequently group of drugs used was the antianxiety drugs.

This present study is to determine in a general hospital out-patient clinic setting the extent and type of psychotropic drugs prescribed in relation to symptomatology or diagnosis.

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METHOD

This study was conducted in the general out-patient of a general hospital in an urban area. The period of study was for 3 days in March 1979. All prescriptions were scrutinised and those containing any transquilliser, hypnotic, antidepressant, stimulant or antianxiety drug were identified. Those excluded were from patients suffering from epilepsy and those below the age of 15 years. Prescriptions from specialised clinics including the psychiatric and drug abuse clinics were not included.

From the prescription, details of duration and drugs prescribed and combination with other drugs were noted. An attempt was made to trace all case notes but only 85 (80%) out of the 106 were traced by the records office. From these case notes, the past frequency and duration of usage and the diagnoses or symptomatology were studied.

The general out-patient clinic dealt with new and follow-up patients and functioned as a screen and referral source to the specialised clinics. Hence the nature of complaints were diverse.

RESULTS

Percentage of out-patients prescribed psychotropic medication

One hundred and six out-patients were prescribed psychotropic medication out of a total of 1502. This was a percentage of 7.1 This is relatively low compared to the 17% reported by Parry *et al.* (1973) in the United States.

Type of drugs

Antianxiety drugs of the benzodiazepine group was the most commonly prescribed comprising 83% of the sample of 106 prescriptions (Table I). Following this was phenobarbitone (the only barbiturate prescribed) comprising 14.1% and one case of a tricylic antidepressant and 2 cases of a hypnotic of the benzodiazepine group. The

total percentage of antianxiety and hypnotic prescriptions was 99%. The phenothiazines, butyrophenones and other psychotropics were not prescribed. In only one case was a combination of psychotropic drugs used i.e. a combination of 2 benzodiazepines. Excluding the one prescription of antidepressant, the incidence of antianxiety and hypnotic prescriptions among the 1502 out-patients was 7%. This percentage was higher than the 3.5% of antianxiety and hypnotic drugs prescribed in 1,000 out-patients of the psychiatric clinic.

Table 1
Psychotropic drugs prescribed in a general out-patient department

Drugs	Number of cases	Percentage of cases
Antianxiety	88	83
Sedative - hypnotic	17	16*
Antidepressant	1	1
Antipsychotic	0	0
Stimulant	0	0
Total	106	100

*Phenobarbitone alone 14.1%

Duration of prescriptions

The duration ranged from 2 days to 1 month. Seventy-six (71.7%) of 106 prescriptions were from 2 days to 7 days. Prescriptions of 1 to 2 weeks comprised 13.2%.

Frequency of usage

Sixty-eight cases (80%) out of 85 cases whose case notes were traceable were either prescribed for the first time ever or the first occasion after an interval of six months. Of the 17 (20%) cases who were repeat users, 2 had been using the drugs for 3 to 5 years, 4 for 1 to 2 years, 2 for 6 to 12 months, 6 for 1 to 6 months and 3 for 2 to 4 weeks. The doctors prescribing for these repeat users were different in all but one case.

Combination with other drugs

One hundred out of 106 cases were prescribed other drugs too. These drugs were analgesics, vitamins, coronary dilators, anti-hypertensives, anti-inflammatory drugs, anti-biotics, carminatives, anti-diabetics, antacids, antitussive, antihistaminics and bronchodilators. Some sample prescriptions were (a) ibu profen and diazepam, (b) gylcerol trinitrate, prenylamine lactate and diazepam, (c) lorazepam and paracetamol, (d) paracetamol, vitamin B complex and diazepam, (e) lorazepam, vitamin C and B complex and chlorpheniramine and (f) diazepam and cough expectorant.

Diagnoses

The diagnoses were not written down in all cases but 85, whose case notes were traceable, were reviewed to determine the symptomatology and diagnoses where possible. In 38 cases pain was mentioned. This description covered symptoms such as "aches", "joint pains", "headache" "bodyache" "muscular pains", "abdominal pain" and "chest pain". Almost all of these cases were also prescribed an analgesic, anti-inflammatory drug or a liniment for external use.

In 6 cases insomnia was given as the symptom. In 2 cases, palpitations were noted, one of these was a thyrotoxic patient. In 3 cases, giddiness was the presenting symptom.

Among organic illnesses which had been fully investigated, 3 cases were noted to be of ischemic heart disease, 10 cases of hypertension, 2 cases of thyrotoxicosis and 2 cases of bronchial asthma. Of the 17 cases (out of 85 cases with traceable cases notes) who were repeat users the diagnoses or symptomatology recorded were hypertension in 5 cases, ischemic heart disease in 3 cases, "cough" and "chest pain" in 2 cases each and one case each for "palpitation", "sternal pain", "abdominal distension and fatulence", and "cries easily". Another patient only requested for medication.

DISCUSSION

The results give some indication of the extent and pattern of psychotropic prescriptions in a general out-patient clinic of a general hospital. The percentage of out-patients receiving psychotropic medication was 7.1% and this was lower than the 17% in an American study by Parry *et*

al. (1975). The prescription of antianxiety drugs and hypnotics in the general out-patient clinic in this study was higher than in the psychiatric clinic of the same hospital. Excluding the one case of antidepressant prescribed, the prescription of antianxiety drugs and hypnotics was 7% of the out-patients. Similiar prescription of these two groups of drugs in the psychiatric clinic in the same hospital was 3.5%. This finding in this study was not surprising. It could be that psychiatrists see more psychotic than neurotic patients, on the other hand psychiatrists use a wider range of non-drug management procedures including psychotherapy and behaviour modification therapy. Having a wider range of management procedures psychotropic medication is viewed as only one of many procedures. It had been also reported by Parry *et al.* (1973) and Hollister (1977) that non-psychiatrists were the sources of more psychotropic medication than psychiatrists.

Of the hosts of psychotropic drugs, only one group was extensively use i.e. the benzodiazepines. Five members of this group were used by the doctors out of 6 which were available to them. Phenobarbitone was the other commonly prescribed drug and in 1 case only was a tricyclic antidepressant prescribed. In the psychiatric clinic no barbiturate was prescribed in the 1,000 cases screened. Conspicous by their absence were drugs associated with anti-psychotic properties such as phenothiazines and butyrophenones. The choice of the benzodiazepines with their anxiolytic properties would indicate that the prescribing doctors perceived the complaints was neurotic or psychosomatic as opposed to psychotic.

Each prescription order ranged from 2 to one month, with the majority (71.7%) from 2 to 7 days. Prescriptions for periods longer than 2 weeks comprised 15% and were mainly for the chronic repeaters. Except for a small group of patients, the doctors did not prescribe for long periods at each visit.

The prescriptions could be separated into two groups. One group had been continuously receiving repeat prescriptions and comprised 20% of the 85 traceable case notes. One of these cases had been on a benzodiazepine for 5 years. Eight (10%) were suffering chronic cardiovascular illnesses of hypertension or ischemic heart disease. The remaining nine had symptoms of vague etiology. Only one of these was likely to have a psychiatric basis as she "cried easily". In 16 cases a benzodiazepine was prescribed and in one case a phenobarbitone. The use of antianxiety drugs in chronic non-psychiatric disorders is not infrequent. Greenblatt *et al.* (1976) reported the use of an antianxiety drug in chronic cardiovascular and gastrointestinal disorders to be between 20% to 40% in the Boston area.

The second group comprising 80% of the 85 traceable case notes revealed that they were prescribed psychotropic drugs for the first time or after an interval of six months. Symptomatology which could be associated with psychoneurotic disorders were mentioned in only 13% of first or fresh prescriptions. These symptoms were giddiness, palpitations and insomnia. Fifty three percent (36 cases) of these first or fresh prescription were for complaints of aches or pains. Invariably an analgesic or anti-inflammatory drug was also prescribed. The use of anxiolytics in musculoskeletal disorders, psychophysiologic disorders and anxiety secondary to other medical problems was reported by Blackwell (1973) to be 70% of prescriptions and the remaining 30% was prescribed for anxiety and insomnia. In this present study 34% of first or fresh prescriptions had other symptoms of a non-psychiatric nature.

Symptoms attributable to psychiatric disorders were recorded in only 12 cases (14.5%) of all the 83 case notes traced. This low figure could be the result of a low recording by doctors of psychiatric complaints in the cards but this would appear unlikely as other physical symptoms were recorded. The remaining 85.5% were prescribed psychotropic medication solely or as adjuncts for non-psychiatric symptoms. In the study by Parry *et al.* (1973) about half of new prescriptions for the antianxiety drugs were prescribed for non-psychiatric conditions.

It would interesting to know the transaction occuring between the prescribing doctor and the patient resulting in the prescription of an anxiolytic or hypnotic when no specific psychiatric complaints were mentioned by the patient. Few patients do actually complain of anxiety or

depression. For these who do not, the criteria for diagnosing anxiety or depression would depend on individual doctors. There is also the need of the doctor to "do something" for those who cannot be convinced that they have no organic illness and where the psychodynamics are unclear. This especially applies to a busy outpatient clinic. The use of anxiolytics is legitimate even where the psychodynamics is unclear as the medication acts as a bridge for further exploration and management. But where there are frequent changes of doctors any accompanying non-drug management would be scant, superficial or intermittant.

SUMMARY

This study shows that within a general hospital out-patient setting, the prescription of psychotropic medication is mainly confined to the antianxiety drugs and secondarily to the hypnotics. There is a conspicious absence of prescription for antipsychotic drugs and negligible use of antidepressants. The use of anti-anxiety drugs and hypnotics was higher in the general out-patient clinic than in the psychiatric out-patient clinic in the same hospital. This finding is in the trend of similiar findings by others that non-psychiatrists prescribe more psychotropic medication including antianxiety and hypnotic medication. In this study the use of psychotropic medication for patient generated psychiatric symptomalogy was only in 14.5% of cases prescribed these medication. The anti-anxiety drugs were prescribed as adjuncts in non-psychiatric conditions as well. Frequent use as adjuncts were in the treatment of muscular tension and in chronic cardiovascular disorders.

There is a core of patients (20%) that had been continuously prescribed medication up to a period of 5 years. Half of these were chronic cardiovascular patients and half presented with no demonstrable systemic organicity. None had been referred to a psychiatrist.

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PERSONNEL EXPOSURE DURING CEREBRAL ANGIOGRAPHY

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INTRODUCTION

THE exposure of radiologists to x-rays depends to a great extent on the type of examinations conducted. In the majority of radiological investigations, the radiologists and other personnel retire out of the x-ray rooms during exposure. By proper planning of x-ray rooms, personnel exposure can be reduced to insignificant levels. In some procedures, however, the radiologists remain inside the x-ray rooms. These procedures are fluoroscopic investigations and special examinations which require that the contrast medium be injected manually.

A large number of factors such as field size, beam orientation, exposure time and kilovoltage, protective devices used, and the position of the radiologist, affect the level of his exposure. For example, studies on personnel exposure during cardiac catheterisation by Wold *et al.* (1971), Malsky *et al.* (1971), Ardran and Fursdon (1973) and Stacey *et al.* (1974) have shown that exposures of the neck and head varies from undetectable levels to over 60 mR per examination. The recommendations that were subsequently made ranged from the necessity to rotate medical personnel and restrict the workload, to just paying careful attention to radiation protection details.

In the Department of Neurosurgery, General Hospital, Kuala Lumpur, most of the radiological examinations are conducted in the x-ray rooms situated in the department itself. There was some concern over the exposure of personnel who remained inside x-ray rooms during special examinations. More than one-third of these examinations were in cerebral angiography and a study was made in July 1978 to determine the exposure of personnel.

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PROCEDURE AND EQUIPMENT

The contrast medium is injected manually and directly by the percutaneous technique. As fluoroscopy is not required, all assisting personnel leave the x-ray room before radiography is commenced. The neurosurgeon (or medical officer) alone remains standing beside the patient and is exposed during serial radiography. Biplane radiographs are taken with separate anterior-posterior and lateral tube-film-changer systems. Normally eight films are exposed for each side examined. The x-ray machine has a 125kVp, 1000 mA generator, using three phase power with full wave rectification. The exposure settings were at 65 - 75 kVp and 64 80 mAs. The total filtration is 2 mm aluminium. The focus film distance is 90 cm, and the focus skin distance is between 60 - 70 cm. The field size at the film is 20 cm x 25 cm. Elema Schonander serial changes are used.

The neurosurgeon wears a lead apron of 0.5 mm lead equivalent in thickness. A lead rubber sheet of 1 m by 1.3 m and 0.5 mm lead equivalent, with a portion cut off to fit over the neck of the patient is lowered vertically from the ceiling just before exposure. This lead sheet reduces exposure to the parts of the body not shielded by the lead apron.

DOSIMETRY

Personnel monitoring films in their badges were used as dosemeters. These films were calibrated by exposing a set of films to x-rays at 80 kVp, 3 mA tube current, 80 cm focus film distance and 3 mm aluminium total filtration. These factors were chosen so that the quality of the x-ray beam matches the side and backscatter from the patient which was harder, as shown by Keane and Spiegler (1951). The calibration films were exposed side by side with the 35 cm^3 ionisation chamber of the 37D Pitman dosemeter which had been compared to a Baldwin Farmer

secondary standard dosemeter. A set of calibration films were developed together with the test films using standard procedures for monitoring films. The value of two milliroentgens was taken as the threshold of detection and all readings were recorded to the nearest milliroentgen.

RESULTS

The films were positioned as follows: on the forehead, on the dorsum of the hand, at the gonadal area under the apron, and on top of one foot. The results are presented in Table I.

Table 1

Radiation exposure of neurosurgeons at various parts of the body during cerebral angiography

		Dr. A	Dr. B	Dr. C	Dr. D	Dr. E
Total number of radiographs monitored		190	146	93	48	37
total dose for one month	forehead	4	12	6	3	2
	dorsum of hand	82	152	77	2	33
	foot	2	6	3	< 2	< 2
	gonads (under apron)	< 2	< 2	< 2	< 2	< 2
dose per exam.	forehead	0.4	0.7	1.2	1	1
	dorsum of hand	7.5	1.3	15.4	0.7	16.5
	foot	0.2	16.8	0.6	<0.7	< 1

The threshold of detection was taken to be 2mR.

Note: < means less than.

DISCUSSION AND CONCLUSION

A comparison with similar investigations by Santen *et al.* (1975) and Riley *et al.* (1972) is given in Table II. The exposures measured are of the same order of magnitude. Slightly lower exposures for the forehead were measured although the neurosurgeon stands nearer the patient's head when the percutaneous technique is used. This lower exposure can be attributed to the lead sheet hung from the ceiling and justifies the extra precaution taken.

Exposure of the gonads were below 2 mR for up to 190 exposures (Dr. A, Table I) although the hands and forehead have received appreciable exposures. Similarly, Riley reported less than 2 mR for 600 exposures in selective cerebral arteriography. These results once again raises the question where the regular personnel monitoring badges should be worn. If they are worn under the lead apron, the dose to the hands will be underestimated by as much as over 70 times and the dose to the eyes by 6 times. The International Committee on Radiation Protection has recommended a Maximum Permissible Dose for the hands of only 15 times that for the gonads.

Taking into consideration that the greatest exposures occur during angiography and over two-thirds of the radiological examinations are in angiography, this study shows that the neurosurgeons at the General Hospital, Kuala Lumpur would be exposed to doses below the Maximum Permissible Doses as recommended by the International Commission on Radiation Protection.

Table II

Radiation exposure of the hand and forehead of Neurosurgeons per cerebral angiographic examination

	This investigation	Santen *et al.*	Riley *et al.*
Dose to hand in mR	0.7 — 16.8	0.7 — 1.3	7.4
Dose to forehead in mR	0.4 — 1.3	0.7 — 4.8	5.8

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GLANZMANN DISEASE (THROMBASTHENIA) — A CASE REPORT

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INTRODUCTION

THE bleeding time is one of the tests of platelet functions. Quantitative or qualitative platelet dysfunction results in prolonged bleeding time. If the latter is normal further tests are not indicated (Cazapek, 1978).

Platelet control haemostasis by forming a plug at the site of injury and by promoting clotting mechanisms. It acts by adhesions, aggregations and release reactions (Arkel, 1976). One classification of the dysfunctions is given Hardisty (1974) which divides it into congenital forms such as thrombasthenia and defects of platelet release and the acquired variety which includes uraemia, paraproteinaemias or disseminated intravascular coagulation. Thrombasthenia (Glanzmann Disease) is restricted to cases with deficient A.D.P. induced platelet aggregations and deficient clot retractions (Hardisty, 1974). About 100 cases have been reported (Wintrobe, 1974). The rarity of this condition merits reporting this case.

CASE REPORT

An 18 year old male, admitted in April, 1978, with recurrent episodes of spontaneous bleeding on the face, forearms, legs, gums and prolonged bleeding after a trivial injury. He did not give any history of epistaxis, malaena or haematuria. All the other members of his family were normal. He did not take any drugs or anticoagulant nor did he suffer from any renal disease.

Examination revealed echymosis around the left eyelid and petechiae on the forearms and left leg. Hess's test was positive. No lymphadenopathy or hepatosplenomegaly was found. Laboratory results were a normal platelet count, a prolonged bleeding and partial thromboplastin time, impared ADP induced aggregations and no clot retraction. Platelet aggregations to collagen and isoprenaline were normal. Other tests of coagulations, renal, liver, disseminated intravascular coagulation were normal. The patient was transfused with fresh blood. The echymosis and petechiae disappeared within a few days.

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DISCUSSION

The patient with recurrent episodes of bleeding, had a prolonged bleeding time, despite a normal platelet count. Investigations indicated lack of ADP induced platelet aggregations but normal to collagen. There was no clot retraction. Impaired aggregations lead to inadequate thrombus formation and deficient platelet factor 3 (PF-3) availability. This results in impaired orientation to fibrin strands leading to deficient clot retraction (Hardisty, 1974).

There was no family history in this case. This disorder is inherited as an autosomal recessive and consanguinity is common in affected relatives (Pitmann, 1964). Spontaneous bleeding, though not disabling in our patient, was severe. Posttraumatic and post-operative haemorrhages may be serious (Wintrobe, 1974).

Contact activation of thrombasthenic patient's blood is subnormal. Tests which depend on contact activation such as partial thromboplastin time will be prolonged as in our patient. As this test measures the intrinsic pathway of blood coagulation, other tests which measure part of this pathway, for example thromboplastin generation test, may follow this test. This may cause a diagnostic error of Factor IX, Factor VIII deficiency (Wintrobe, 1974).

Platelet factor 3 availability was abnormal in the patient. Variable results occur (Cazpek 1978). Deficiency of fibrinogen is not a constant finding (Caen, 1966) and our patient has normal

level of fibrinogen. This condition is distinguished from other disorders of platelet dysfunctions which show a normal clot retraction and a collagen induced aggregation.

Drugs such as aspirin, which a common ingredient in many proprietary preparations, can inhibit platelet aggregations and release reactions. This may not be significant in a normal person. However, in patients with platelet dysfunctions or coexisting coagulopathy it may precipitate haemorrhage (Arkel, 1976).

SUMMARY

An 18 year old male admitted with recurrent episodes of echymosis, petechiae and bleeding gums. Investigations revealed a prolonged bleeding time, a normal platelet count, impaired ADP induced platelet aggregations and poor clot retraction. He was diagnosed as Glanzmann Disease and responded to fresh blood transfusions. This disorder may be mistaken for a disorder of coagulopathy. Surgery is hazardous. Drugs containing aspirin may precipitate haemorrhage.

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REPRODUCTION RESEARCH AND HEALTH * PART II — FETAL HEALTH

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INTRODUCTION

IN the recent decades, in most developed and some developing countries, the frequency of maternal deaths is so low that the fetal death rates, occurring before and immediately after birth, are being regarded as a more satisfactory and sensitive index of the quality and efficiency of the obstetric services of a hospital or country. The technical term, used by obstetricians and health administrators to measure the extent of fetal deaths, occurring in relation to late pregnancy complications and childbirth, is "perinatal mortality". The term perinatal mortality is defined as the total number of "stillbirths" and "newborn deaths occuring in the first week after birth" per 1,000 total births.

The beneficial impact of research on fetal (perinatal) health in the past 25 years can best be exhibited by reviewing the recent advances in the four major areas of perinatal medicine, namely, (1) low birth-weight infants (premature and dysmature infants), (2) intra-uterine fetal hypoxia (oxygen deprivation for the unborn child), (3) fetal birth injuries, and (4) fetal malformations.

Low Birth-Weight Infants

Fetal wastage (perinatal mortality) from pregnancies resulting in the birth of low birth-weight infants is still the major cause of perinatal mortality in some developing and all under-developed countries of the world. Factors that have contributed towards improved fetal salvage in the "Low Birth-Weight Infants" in the recent 25 years are multi-factorial and these are now discussed.

The socio-economic enhancement of the community, in general, and the mother, in particular, which involves not only, the eradication of poverty, but also, health education to correct misconceptions prevailing as a result of ignorance, socio-cultural taboos and unhealthy traditional practices in the areas of nutrition and health care of pregnant and puerperal mothers and newborns, has contributed considerably in this area of fetal salvage.

Improvements in the quality and extent of ante-natal and post-natal services (both outpatient and inpatient) that are being provided to both mothers and newborns have influenced fetal salvage significantly in this field.

Advances in the pharmacological management of pre-term labour have recently contributed in a small way, and this has consisted of the inhibition of premature labour by the use of Beta — Sympathomimetic drugs, and thus allowing the pregnancy to progress to a better stage of fetal viability. The use of antibiotics, before and after birth, has helped to prevent fetal demise from fetal infection.

Fetal monitoring in labour with the liberal practice of "assisted" vaginal delivery, in particular the latter, has helped to prevent fetal demise from asphyxia and birth trauma in the intrapartum period.

There is presently the availability of expert newborn paediatric services in most reputable obstetric units of hospitals. In the University Hospital, University of Malaya, Malaysia, there is provision of Special Care Nursery, built

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***REPRODUCTION RESEARCH AND HEALTH PART II—FETAL HEALTH**

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*Inaugural Lecture (part) that was delivered on the 2nd March 1979 at the Faculty of Medicine, University of Malaya, Pantai Valley, Kuala Lumpur, MALAYSIA, under the Chairmanship of the Royal Professor Ungku A. Aziz, Vice-Chancellor of University of Malaya.

adjacent to the Labour Ward of the Hospital for the speedy and effective care of the low birth-weight infant, which involves the maintenance of respiration, body temperature and nutrition; the prevention and treatment of infection; and the treatment of jaundice of the newborn.

Intra-Uterine Fetal Hypoxia

In all developed countries and in some developing countries of the world, intra-uterine fetal hypoxia, or in a less technical jargon — "oxygen deprivation for the unborn child", has emerged as the major cause of fetal wastage in pregnancy (perinatal mortality). The two common groups of causes of intra-uterine fetal hypoxia are placental insufficiency syndrome and prolonged or difficult labours.

(i) Placental insufficiency syndrome: "This is a clinical syndrome in which there is a state of dysfunction of the placenta, from failure of optimal growth or premature degeneration of the placenta, with resultant reduction in the placental reserve state, or a failure of the placental membrane to function as an efficient semi-permeable membrane, to such an extent as to jeopardise the oxygen, nutrient and excretory requisites of the fetus. The end result can manifest itself by retarded intra-uterine fetal growth, fetal cachexia or by a state of intrapartum fetal anoxia, any one of which may predispose to perinatal mortality and morbidity from asphyxia, intracranial haemorrhage and infection" (Sinnathuray, 1964). The common clinical conditions that can predispose to "placental insufficiency" syndrome are postmaturity (prolonged pregnancy syndrome) (Sinnathuray, 1967 and 1972), toxaemia of pregnancy, chronic hypertensive diseases, elderly primigravida and diabetes mellitus (Sinnathuray, 1964).

(ii) Prolonged or difficult labour: In this arena of obstetric practice there have been progressive changes in the concept of "prolonged labour" in the past 30 years — from an earlier concept of a labour which exceeded 48 hours duration, to one that exceeded 36 hours, 24 hours and even, presently, to a shorter duration. The present-day practice of the use of partograms to chart the progress of labour in modern institutional obstetric practice has led to the need for the active augmentation of sluggish and inefficient labour, at all stages of the process of labour, by the use of oxytocic agents (oxytocin and prostaglandins), epidural anaesthesia and planned assisted vaginal delivery. This practice has ensured that most women attain the delivery of their babies between the physiological labour duration of 6 to 18 hours.

Fetal Birth Injuries

The contributory role of fetal birth injuries to fetal ill-health (perinatal mortality and morbidity) has shown a rapid decline in the past three to four decades, throughout the world. In the developed and most developing countries. presently, fetal birth injuries contribute to a relatively small role towards the total cause of perinatal (fetal) mortality, much less than any one of the other three causes, namely, "low birth-weight infants, intra-uterine fetal hypoxia or fetal malformations.

The two major groups of causes of fetal birth injuries in the past have been (i) prolonged or difficult labours which were due to cephalo-pelvic disproportion, fetal malpresentations or uterine dysfunction; and (ii) difficult manipulative vaginal deliveries, such as high forceps delivery, difficult breech delivery, or internal version/breech extraction. The major advances that have contributed towards the reduction of fetal birth injuries in the past three or four decades have been multi-factorial, and they are improved health and physique of would-be-mothers — a reflection of the socio-economic upliftment of the community (Baird, 1960); the liberal provisions of ante-natal care; the availability of obstetric trained personnel — both doctors and trained nursing staff; proper pre-delivery pelvic capacity assessment (clinical and radiological); hospital delivery for the high risk pregnancies; partograms to evaluate progress of labour; augmented labour for sluggish labour conditions; and the practice of liberal Caesarean section delivery. In this last context, there is need for restraint and the balanced usage of Caesarean sections in modern obstetric practice. Sir Hector McLennan, who was an eminent British obstetrician and President of the Royal College of Obstetricians & Gynaecologists of the United Kingdom in the mid-1960s, summed up the situation most aptly as follows: "Caesarean section has been a boon — let us prevent it

from falling into disrepute and becoming the first resort of the lazy obstetrician, the escape of the timid obstetrician, and the cloak of the incompetent" (McLennan, 1954 and 1959; Caire, 1978 and 1979).

Skilled conduction of vaginal deliveries bv the proper training of obstetric personnel: It must be appreciated that the proper conduction of abnormal vaginal deliveries is both an art and a skill. It calls for the proper training, skill and judgement of the accoucher. This can best be illustrated in the context of the skilled conduction of vaginal breech delivery in obstetric practice. In the management of breech labour, there needs to be a proper balance between the "masterly inactivity" in the early phases of labour, and the "masterly activity", of a decisive and precisive nature, at the time of conduction of the delivery of the baby's trunk and head. Dr. De Lee (1937, as quoted in British Obstetric Practice, p. 649, 2nd Ed. 1959), an eminent American obstetrician who practised in the early part of this century, had summed up the situation in these words: "Let me watch a man conduct a breech case and I will give you his obstetric rating."

Fetal Malformations

The rapid advances in obstetric research and the excellence of obstetric services in most developed countries of the world have currently considerably reduced the perinatal fetal wastage from low birth-weight infants, intra-uterine fetal hypoxia and fetal birth injuries. This has resulted in a relative increase in the contribution of fetal malformations towards the total picture of perinatal fetal wastage in such situations; and it is probably the second major cause of perinatal fetal wastage in most developed countries of the world.

The major causes of fetal malformations can be broadly classified as inherited disorders, which can be sex-chromosome-linked or autosome-linked, inherited as a Mendelian or recessive nature; or environmentally acquired disorders, which can be due to viral infections (German Measles, rubella), bacterial infection (syphilis), parasitic infection (toxoplasmosis), irradiation (x-rays and radioactive materials), and toxic chemicals (cytotoxic drugs, progestogens, thalidomide and certain other chemicals).

The major research advances that have contributed and can contribute towards the reduction of perinatal fetal wastage from fetal malformations are the provision of genetic counselling of parents — based upon the better understanding of human genetics; the health education of public, in general, and parents, in particular; and the health education of medical personnel — undergraduate and continuing medical education. Further advances in this area have been the sequelae of excellent comprehensive modern ante-natal care services providing for the screening for genetically inherited diseases by amniocentesis and fetal cell culture; the screening for neural tube defects of anencephaly and spina bifida by amniocentesis and detection of alpha-feto-proteins; the screening for infective embryopathies, e.g. tests for syphilis, rubella and toxoplasmosis in the blood of pregnant mothers; and the avoidance of exposure of fetus-in-utero to irradiation and noxious chemicals. Definitive reductions in perinatal fetal wastage from infective embryopathies can be achieved by effective immunisation of women in the non-pregnant status against rubella and the early and effective treatment of matenal infections that can afflict the fetus-in-utero, e.g. syphilis, and toxoplasmosis.

Fetoscopy as a sophisticated procedure in fetal medicine is currently emerging as an invaluable investigatory set-up. This has been recently made possible by the present-day technological advances in the areas of fibre optic endoscopic instrumentation and related "cold" light source. With the aid of fetoscopy it is becoming possible, in the early stages of human pregnancy, between the 4th and 6th months (second trimester of pregnancy), to visualise the small fetus for severe external malformations, such as anencephaly, or other fetal monstrosities. More importantly, it is now possible, through fetoscopy, to take micro-samples of fetal blood from the fetal blood vessels that can be visualised on the fetal surface of the placenta. The access to medical scientists of fetal blood, so early in pregnancy, has now made it possible to diagnose lethal or severely disabling fetal conditions by elaborate blood studies for chromosomal, thalassaemic, biochemical and cellular defects. Thus, it is now becoming possible for us to scientifically detect major fetal malformations and fetal thalassaemia major in the early stages of human pregnancy (Walters, personal communication).

Therapeutic abortion service: With the above scientific advances in the reliable early detection of fetal malformations and fetal blood dyscrasias, it is both socio-medically and ethically acceptable, as well as humanely realistic, to offer therapeutic abortion services to mothers in the early stages of their pregnancies, when the investigatory evidences by maternal serology, amniotic fluid studies and fetal blood (by fetoscopy) studies conclusively show that the unborn fetus is afflicted with the major groups of fetal malformations such as German measles fetal afflictions, major fetal chromosomal afflictions, fetal neural tube defects, e.g. anencephaly (fetal monsters without brains) or overt spina bifida, and severe disabling hereditary blood disorders, e.g. fetal thalassaemia major. In all such situations, adequate psycho-social and genetic counselling should be instituted before and after the therapeutic abortion services, so as to alleviate the mental anguishness in the family.

THE FUTURE

Just as was stated in the previous paper (Sinnathuray, Med. J. Malaysia, 1979) on Maternal Health, the future developments in the field of Fetal Health also promise to be exciting. Advances in the field of social obstetrics and gynaecology, particularly in the context of developing countries, will lead to socio-economic upliftment of the pregnant mothers. This will, in turn, lead to improvements of their general health and nutrition, which will subsequently be reflected in their better fetal growth and in the birth of better babies. The quantity and quality of fetal salvage will be considerably enhanced by the improvements to the quality and extent of the obstetric and neonatal paediatric services made available and utilised.

Fetoscopy seems to hold exciting promises for the future. Recently introduced as a fetal diagnostic tool to visualise the fetus-in-utero and withdraw fetal blood samples for diagnostic purposes, it may become an important avenue through which direct access can be made to the unborn fetus and its fetal circulation, to enable us to institute therapy to the fetus in its early stages of intra-uterine life. Thus, fetoscopy points promisingly towards diagnostic and therapeutic fetal medicine. The currently high prevailing rates of fetal loss from fetal abnormalities will be reduced either by better identification of the causes of the fetal malformations and by related preventive measures, or by their earlier detection in the pregnant women and by subsequent safe termination of such afflicted pregnancies.

CONCLUSIONS

In my inaugural address, I have attempted to comprehensively cover the extensive benefits accruing to human health and human welfare from research in human reproduction in this 20th century. The ultimate objectives of research in human reproduction are firstly, to ensure that the society in general, the family as a unit, or the woman as an individual, is assisted in her or its endeavour to successfully have the desired number of children, at the desired pregnancy intervals, and further to ensure that every pregnancy progresses from conception to childbirth, as uneventfully as possible, with the minimal of health hazards to mother and child.

It is, thus, apparent to all of you that those of us, practising in field of obstetrics and gynaecology, are intimately concerned not only with the quantity of life at conception, but also with the quality and quantity of both maternal and fetal life throughout pregnancy, childbirth, and thereafter!

The sum-total message of my inaugural address, entitled Reproduction, Research and Health, is a healthy woman conceiving at the desired times of her reproductive life, and having, on each occasion, a healthy pregnancy status, culminating in a normal childbirth; and the final return to the society of a happy and healthy mother and child.

SUMMARY

The four major areas of fetal (perinatal) medicine, which have been contributing to excessive fetal (perinatal) wastage in recent years, namely low birth weight (premature and dysmature) infants, intra-uterine fetal hypoxia, fetal birth injuries and fetal malformations, have been presented and discussed. The beneficial impact that research and evolution of modern obstetric practice have had on these four major causes of perinatal (fetal) wastage has been reviewed. The manner in which the future trends towards the betterment of fetal health are likely to develop has been briefly stated.

ACKNOWLEDGEMENTS

To the Honourable Vic-Chancellor, Royal Professor Ungku A. Aziz, I wish to extend my very sincere gratitude for having graciously presided at the meeting of my inaugural address, and for having introduced me with such laudable and kind remarks about my department and myself to a large audience, consisting of staff and students of the University of Malaya and University Hospital, the members of the medical profession and the public. I also wish to thank the Honourable Vice-Chancellor for giving me the honour and distinction of delivering the first inaugural address in this Medical Faculty, in its current resumed series, after a long lapse of over 12 years.

My very sincere appreciation and thanks to Mrs. Ivy Phang of my department for her excellent secretarial assistance rendered on the preparations of the manuscript of my inaugural address, for the presentation and the subsequent publications.

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MEASUREMENTS OF ERYTHEMAL ULTRAVIOLET DOSAGE AT PENANG

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INTRODUCTION

AS a result of the recent concern about the ozone layer depletion (Cutchis, 1974; Bauer, 1978; Ilyas, 1979), considerable attention has been directed towards the investigations of the natural erythemal ultraviolet dosage — responsible for sunburn and skin cancer (Green *et al.*, 1976; Cutchis, 1978) — reaching the terrestrial surface. However, much of these investigations have been of theoretical nature involving estimation of the erythemal dosage distribution with latitude and season (Mo and Green, 1974; Johnson *et al.*, 1976; Mattingly, 1976) as well as the relative effect of any ozone decrease on this dosage (Cutchis, 1974; Mo and Green, 1974; Mattingly, 1976); estimates of the former type are primarily for the clear weather conditions although some progress has been made towards including the effect of average weather conditions (Mo and Green, 1974; Johnson *et al.*, 1976). The experimental data is still restricted to a relatively few stations primarily at the mid latitudes, Australia, Western Europe, North America (Robertson, 1972; Urbach *et al.*, 1974). In view of an almost complete lack of such data originating in the equatorial region and its importance, one of the erythemal UV instrument units from the Australian (CSIRO) network was installed at USM (Universiti Sains Malaysia) Campus, Penang, some months ago. The instrument has an spectral response close to the erythemal damage spectrum of the skin (Fig. 1). The unit prints out half-hourly integrated erythemal dosages. Results from a preliminary analysis of the data are the subject of this note.

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RESULTS AND DISCUSSION

(a) Annual Dosage

Over the observational period (September 78 — Jan 79), the daily dosages were obtained by adding the measured half hourly dosages. The daily dosages were then added to obtain an average daily dosage of 4.06×10^3 counts or an annual dosage of 1.48×10^6 counts. Using the absolute energy calibration of the unit, these correspond to a daily dosage of 4.10×10^3 Jm^{-2} and an annual dosage of 1.50×10^6 Jm^{-2}. A better idea of the annual dosage could be had by comparing it with similar dosage for other places. Green *et al.* (1976) have reported measured dosages for several U.S. stations. The instrument used had an spectral response almost identical to the present unit (Barton and Robertson, 1975) but the units differ in their absolute sensitivities. However, this constant can be easily obtained by comparing the average daily dosage at Penang, using the data for cloudless days with similar reported daily dosage estimate at 5°N latitude and cloudless conditions for the U.S. instrument (Green *et al.*, 1976). The comparision indicated that the U.S. unit was 9.98 times more sensitive; the dosage data for Penang, as measured by the present unit, should be multiplied by this factor for comparision with the similar data at the U.S. stations. The so adjusted annual dosage of 14.76 MJm^{-2} for Penang may be directly compared with the reported annual dosages (in brackets) for Minneapolis (6.5), Philadelphia (6.8), Oakland (9.3), Tallahassee (10.2), Albuquerque (11.7), El Paso (13.7) and Mauna Loa (17.0). The comparision clearly shows that Penang indeed receives a very high dosage; the dosage at Mauana Loa is higher than the dosage at Penang primarily because of the former's elevation of about 4000 feet (UV-B is known to increase with elevation at the rate of about 10 - 20% per km - see Ilyas (1979) for a recent summary). The above

dosages (D) may be easily converted into erythemal dosages (D_E) corresponding to the normalized damage spectrum of the skin (Fig. 1) using the empirical relationship developed by Green *et al:* $D = 13.0\ D_E^{0.82}$.

(b) Diurnal and Day to Day Variability

At any given time, the incoming solar ultraviolet radiation reaching the surface depends, primarily, upon the Solar elevation and the absorbing ozone (and aerosol) column above the surface. Over a short period of a day, the surface ultraviolet dosage varies with time due to the fast changing elevation of the sun. The dosage is additionally affected by the prevailing unclear weather conditions, especially the rainy weather (unlike the visible wavelengths, significant ultraviolet dosages may be received at the surface even with an overcast sky). Large fluctuations in the ozone column, thereby affecting UV-B dosage, over short periods of hours are generally infrequent. Diurnal variability of ½ hourly measured erythemal dosages for some of the most clear days is shown in Fig. 2. The curve for Spetember has been included to show the immediate effect of weather in the form of sharp dips (on the basis of this effect, it has been suggested to use UV-B monitoring for inferring clouds conditions). Information on the diurnal variability of UV-B may be (and should be) utilized to plan the outdoor activities outside the high intensity periods so that, damaging and harmfully high UV dosages even over short exposure intervals, may be avoided.

A variability in daily dosage from one day to another results primarily because of differing weather and sky conditions. The effect is particularly important for the equatorial climate of Malaysia and may be clearly seen in the daily dosage data for the earlier wetter months of September and October in Fig. 3. Over longer time periods (months), the daily insolation (hence erythemal dosage) is affected significantly by the seasonal effects of changing position of the sun (declination) and the variability of the ozone column (the two effects are almost opposed to each other at Penang). The daily dosages averaged over a month (Fig. 3) can be seen to vary rather smoothly (and slowly) and indicate an increase in the average daily dosage towards December when the sun is farthest. The effect, in addition to the clear sky conditions, is mainly

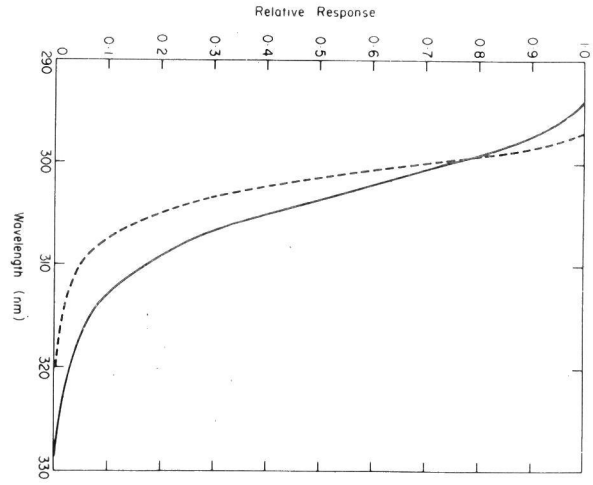

Fig. 1. Spectral response of the detector [solid line] and the erythemal response of human skin.

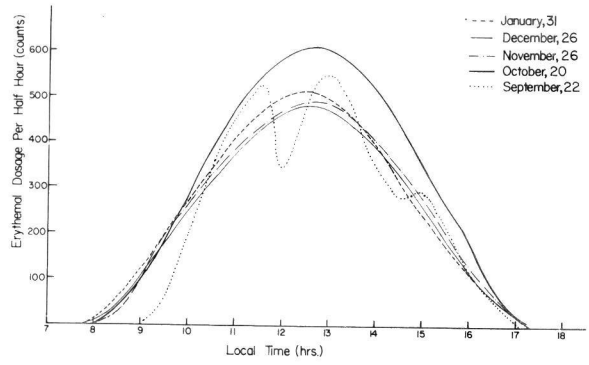

Fig. 2. Diurnal variation of the measured ½ hourly [preceeding the time indicated] erythemal dosage for some of the most clear days during the observation period [Sept. 78-Jan. 79]. The curve for Spetember is included to illustrate the effect of sky [and weather] conditions on the dosage data.

because of the decreased overhead ozone column thus allowing a larger fraction of UV to reach the surface.

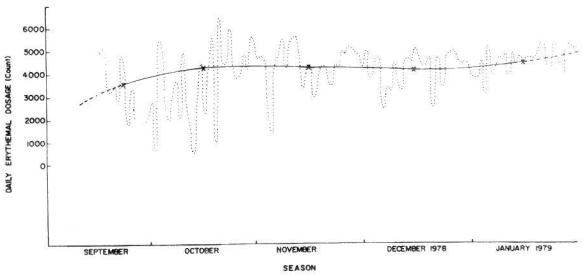

Fig. 3. Seasonal variation of the daily erythemal dosage as measured by the instrument [dotted curve] and the daily dosage averaged over month [solid curve].

CONCLUDING REMARKS

The present results represent first such observational data not only in this region but perhaps over the entire northern equatorial/subtropical latitudes. These data clearly show the erythemal dosages to be relatively higher at Penang (and other equatorial stations) compared to the high latitude stations despite the former experiencing extended periods of cloudy and rainy weather. Further data acquisition would be helpful in developing long term averages but this would very much depend upon the instruments availability, (nevertheless, another UV photometer unit has been acquired by the School of Physics to continue long term monitoring using some intercalibration with the present unit). Of specific interest would be the investigations of the elevation dependence of the erythemal dosage by operating the instrument at some highland stations. The erythemal dosage data together with the ozone data (from another project) should also provide some information on relative UV-B increase as a result of any ozone layer depletions due to activities like SSTs, aerosol spray usage etc. At the same time, erythemal dosage data should be useful to a local dermatologist to correlate the skin cancer and other UV radiational skin damage cases in the local populations as has been done elsewhere (Green *et al.*, 1976; Cutchis, 1978).

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PROGNOSTIC SIGNIFICANCE OF MORPHOLOGICAL AND CYTOCHEMICAL MARKERS IN ADULT ACUTE MYELOGENOUS LEUKAEMIA: CONCEPTS AND OBSERVATIONS

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INTRODUCTION

PRESENT trends of different therapeutic regimens for various acute leukaemias necessitates an accurate definition of the type of blastic proliferation, (Hayhoe *et al.* 1964; Tan *et al.* 1977). Using classic morphological criteria (Bennet *et al.* 1968; Galton and Dacie 1975) cases of adult myelogenous leukaemia were analysed with standard cytochemical markers. These morphological patterns were then related to survival times. Several authors have investigated these relationship with responses to treatment and survival rates. Anner *et al.* (1977) have shown that the subclassification of granulocytic leukaemia according to the presence or absence of Auer rods and percentages of peroxidase positive blasts fail to show significant differences in survival time.

MATERIAL AND METHOD

All the nine patients studied were referred to the General Hospital, Kuala Lumpur, University Kebangsaan division between September 1977 and May 1979 with the presumptive diagnosis of acute leukaemia and had received no prior treatment.

Venous blood was collected in EDTA and analysed on the Coulter S. Prepared smears were stained by Wright's stain and classification of leukaemic blast cell type was performed according to the classic morphologic criteria, (Galton and Dacie 1975; Bennet *et al.* 1968). The cyctochemical stains employed are peroxidase, periodic acid schiff (PAS) reaction, and a non specific esterase stain utilising the substrate Naphthol- AS-D Acetate (NASDA) with and without sodium fluoride as an enzyme inhibitor (NASDA-F). The esterase of monocytes being completely inhibited by NaF in contrast to granulocytes and lymphocytes. All slides were checked for the presence of Auer rods. Examination of bone marrow specimens were obtained by aspiration from the posterior iliac crest or from the sternum, stained by May Grunwald Giemsa, and with standard cytochemical stains. The slides were assessed by two haematologists independantly.

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TREATMENT PROTOCOL

This consisted of daily cytosine arabinoside 100mg/M^2 intravenously with either thioguanine 100mg/M^2 orally or with daunorubicin 1.5mg/kg intravenously on day 1 of each five day treatment schedules.

RESULTS

Nine cases of acute myelogenous leukaemia were diagnosed and their results are summarised in Table I. Their ages ranged from 13 to 42 years: consisting of four males and five female patients. They were further subclassified into four acute myelomonocytic and five myeloblastic leukaemias. No pure acute monocytic leukaemias were included in the study.

The patients with myeloblastic leukaemia with the lowest survival time had a haemoglobin below

5gm/dl; total white cell count greater than $50x10^{9/1}$ and with blasts ranging from 75-85%. The patient with least survival time in this group was Auer rod negative. In either groups patients with ages greater than 35 years had survival times of less than 33 days; the longest survival time being between patients of 20 to 35 years. Shorter survival times were also associated with patients who at onset had a temperature 101°F or greater.

TABLE I : Acute Myelogenous Leukaemia: Common characteristics seen in acute myelomonocytic and myeloblastic leukaemia

	Myelomonocytic	Myeloblastic
Age	13 - 42 years	12 - 40 years
Sex	3 males 1 female	1 male 4 females
Race	3 Malays 1 Chinese	3 Malays 2 Chinese
Hb	less than 10mg/dl range 3.8 - 10	less than 10gm/dl range 2.9 - 7
TWDC	greater than $15x10^{9/1}$ range $15.8\text{-}86x10^{9/1}$	50% greater than $15x10^{9/1}$ range $6.0\text{-}384x10^{9/1}$
Blasts	46 - 80%	50 - 85%
Plat.	less than $60x10^{9/1}$	less than $60x10^{9/1}$
Auer Rods	3 negative	1 negative
	1 positive	4 positive
Survival Time	10 - 46 days	33 - 237 days*

(*Two alive at time of writing of this study)

DISCUSSION

Survival rates for patients with acute myelogenous leukaemia have increased considerably in the last two decades with the introduction of better treatment protocols. Anner (1977) had a median survival of 45.4 weeks in the subgroup without Auer rods; our range being 10 to 33 days.

In our limited study of nine cases, patients with Auer rod negative leukaemia had shorter survival than those who were Auer rod positive. In hospitals in this region most acute leukaemic patients are managed in open medical wards and the nearest measure to protective environment nursing is single room units; air laminar flow and barrier nursing are not currently available to all acute leukaemic patients (Levine 1976).

Prophylactice antibiotic cover consists of broad spectrum antibiotics which included a semi-synthetic penicillin carbenicillin and gentamycin. Non absorbable antibiotics were not used in this protocol. Immunotherapy consists of Bacille Calmette Guerin vacine (BCG) given only to one patient in our series.

In studying prognostic factors in relation with response to chemotherapy in acute myelogenous leukaemia in adults the following should be considered at onset. Age, infection, temperature 101°F or greater, total white and blast cell count, presence or absence of Auer rods, percentage of peroxidase positive blast cells, haemoglobin level and platelet count.

Currently all new cases admitted to the medical unit, University Kebangsaan Malaysia are treated by the regime of Gale and Cline (1977).

The treatment protocol is summarised in Fig. I. Patients are started on allorpurinol 100mg four times daily. Induction therapy consists of cytosine arabinoside (Ara C) 100mg intravenously over 30 minutes, thioguanine $100mg/M^2$ orally every twelve hours for seven days and daunorubicin $60mg/M^2$ intravenously on cycle days five, six and seven. Consolidation therapy consisted of two cycles of Ara-C and thioguanine every twelve hours for five days, followed by a single injection of daunorubicin. Consolidation cycles were given at twenty one day intervals. Prophylactic central nervous system therapy consists of 2400 rads cranial irradiation and five doses of intrathecal Ara-C $100mg/M^2$ during the consolidation phase. The patients were then randomised to receive either monthly five day cycles of Ara C/thioguanine alternating with a single dose of daunorubicin. Immunotherapy consists of weekly injections of BCG.

No cell separator is available at our centre: buffy coats being transfused when available to neutropaenic patients.

Other supportive measures included packed

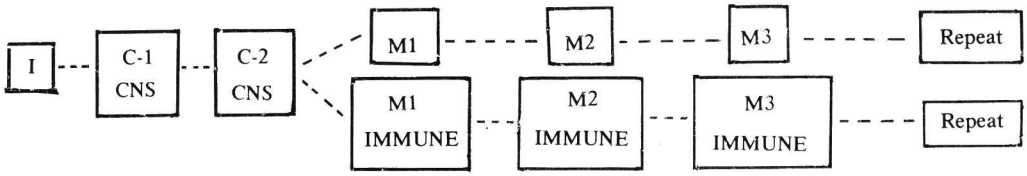

Fig. I - Acute Leukaemia Protocol of Gale and Cline consisting of an induction cycle consolidation and maintenance cycles, central nervous system prophylaxis and immunotherapy

I — induction cycle
C-1, C-2 — consolidation cycles
M-1, M-2, M-3 — maintenance cycles
CNS prophylaxis
immune — immunotherapy

red cell transfusions and platelet concentrates as necessary.

Cytogenetic, immunologic, cultural and cell kinetic studies have prognostic implications (Rowley 1978; Zueller 1977; Alimea 1977; Ross 1977) but these investigations are not within the reach of the average haematologist in this country. Comparative studies within this region are necessary in the wake of changing trends in the treatment of acute leukaemia using prognostic markers that include clinical appraisal, haemogram studies, morphological and cytochemical criteria available at most conventional laboratories.

SUMMARY

Nine adult patients with acute myelogenous leukaemia were studied for assessment of their morphological and cyctochemical characteristics in relation to survival rates with conventional antileukaemic therapy from September 1977 to May 1979. Correlation is limited by the small number of patients. Significant prognostic factors considered are age, temperature, total white cell count, total blast cell count, type of blast cell, presence or absence of Auer rods, haemoglobin and platelet count.

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THE ROLE OF CYCLIC AMP AND CYCLIC GMP IN MITOGEN INDUCED CELL PROLIFERATION IN LEUKOCYTES

GAN SENG CHIEW

INTRODUCTION

ONE of the intriguing questions in immunology today is the understanding of the mechanism by which lymphocytes are activated by mitogenic lectins and antigens (Parker, Snider and Wedner, 1974). Greaves and Bauminger (1972) have shown that lectins can stimulate DNA synthesis without itself entering the cell. This situation is similar to the Two Messenger Hypothesis of hormone action as proposed by Sutherland, Oye and Butcher (1965). It is thus logical to suspect that cyclic nucleotides might similarly be involved.

A report on the possible inhibitory effect of cyclic AMP on cell proliferation was first published by Burk in 1968. Recent evidences confirm a relationship does exist between cyclic AMP and cell proliferation but the precise character of that relationship is far from being clear. Rapidly growing cells have been found to have low cyclic AMP levels and slow growing cells have high cyclic AMP levels (otten, Johnson and Pastan, 1971). There is considerable evidence that indicates cyclic AMP to be involved in certain biochemical events that take the cell through its mitotic cycle.

MITOGEN INDUCED PROLIFERATION

Mature human lymphocytes cultured *in vitro* generally do not synthesize DNA or divide; however, addition of PHA (phytohaemagglutinin; a mitogen) results in a morphological transformation to a lymphoblastoid cell capable of DNA synthesis and eventually mitosis (Nowell, 1960; Robbins, 1964). Lymphocytes are cells whose normal function include quick multiplication upon exposure to antigens. Mitogens or plant lectins mimic the effect of antigen; however unlike antigens they stimulate a large population of predominantly thymus-dependent lymphocytes to divide. Smith, Steiner and Parker (1971) demonstrated that cyclic AMP or agents which stimulates its generation, when introduced before or concomitant with PHA prevents mitogen-induced proliferation. The concentration of cyclic GMP in lymphocytes following PHA-induced mitogenesis was observed to have increased over 10 folds (Hadden *et. al.*, 1972).

YIN—YANG HYPOTHESIS

Goldberg *et. al.* (1973) proposed the "dualism" theory of biological regulation through the opposing actions of cyclic AMP and cyclic GMP. He described the concept of biological regulation through opposing actions of the two cyclic nucleotides by an ancient oriental term, Yin-Yang, which symbolizes a dualism between two opposing natural forces.

MATERIAL AND METHOD

Mature guinea pigs (Central Animal House, Faculty of Medicine, University of Malaya) were sacrificed by injecting 2-3 mls. of Nambutol intravenously. The spleen and appendix were removed aseptically and the organs immersed in RPMI 1640; (Flow Lab., U.K.) with 10% fetal calf serum (Gibco, N.Y.) and 200 units per ml. each of penecillin and streptomycin. Single cell suspension of the organs were prepared and the cell concentration adjusted to $1x10^6$ cells/ml. using a hemocytometer. Cells of 1×10^6 per ml. were cultured in Falcon 16 x 125 mm plastic tubes containing 10% fetal calf serum, mitogen and the modulating agents at various concentrations wherever required, 100 U/ml. of penicillin and 100 ug/ml. of streptomycin, and RPMI 1640 with 1mM glutamine supplemented made up to a total of 2 mls. per culture. The cultures in triplicates were incubated at 37°C in a

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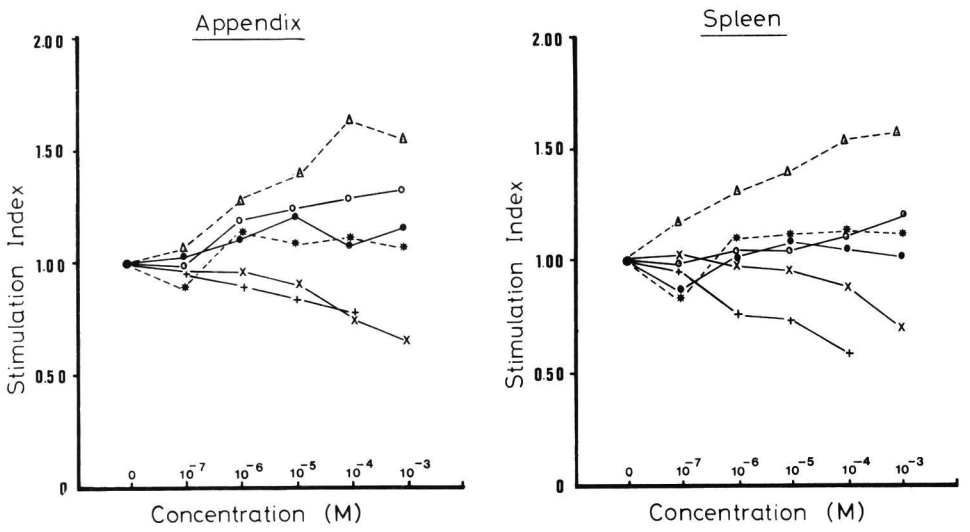

Fig.(1) Control (without any mitogen added)

—•—•— 3' AMP —x—x— c AMP --*----*-- 3' GMP

—o—o— 5' AMP —+—+— DBC --Δ----Δ-- c GMP

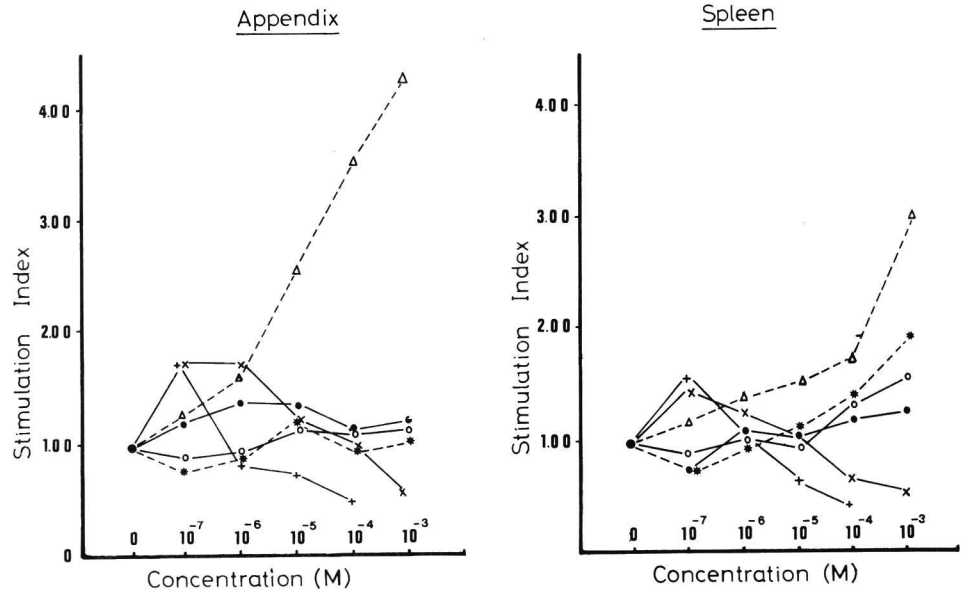

Fig.(2) 10 μg/ml. Phytohemagglutinin (PHA)

—•—•— 3' AMP —x—x— c AMP --*----*-- 3' GMP

—o—o— 5' AMP —+—+— DBC --Δ----Δ-- c GMP

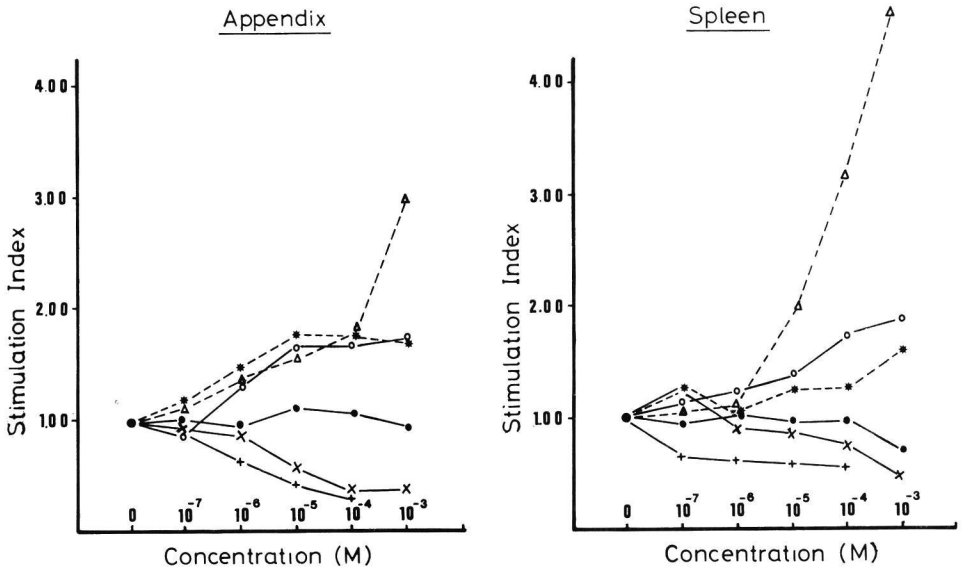

Fig.(3) 5 µg/ml Pokeweed Mitogen (PWM)

—•—•— 3' AMP —x—x— c AMP --*----*-- 3' GMP

—o—o— 5' AMP —+—+— DBC --Δ----Δ-- c GMP

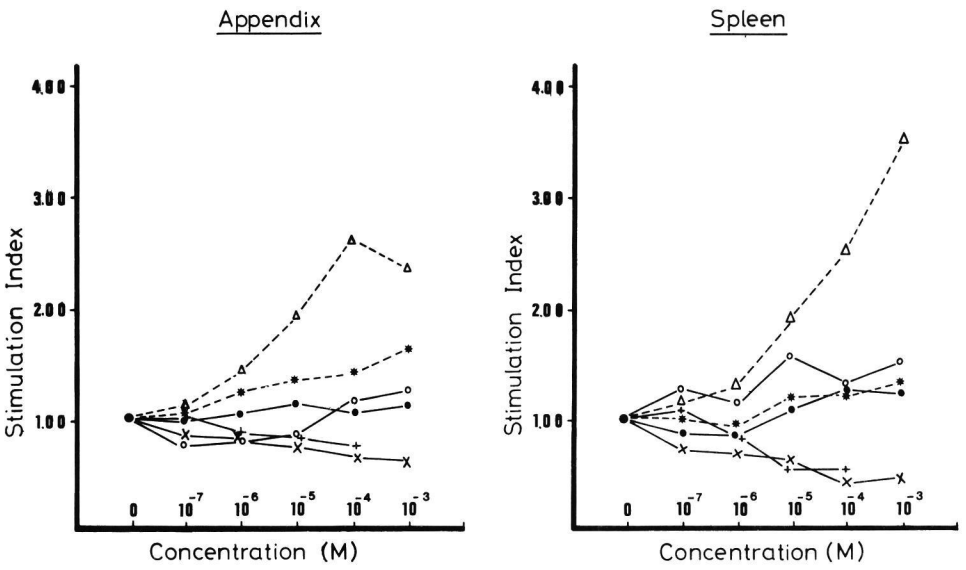

Fig.(4) 7.5 µg./ml. Concanavalin A (Con A)

—•—•— 3' AMP —x—x— c AMP --*----*-- 3' GMP

—o—o— 5 AMP —+—+— DBC --Δ----Δ-- c GMP

humidified atmosphere containing 5% CO_2 (Forma Scientific CO_2 Incubator).

Determination of DNA Synthesis

PHA, Con. A and LPS cultures were terminated on the third day of the experiment, whilst PWM cultures were terminated on the fifth day. 24 hrs. prior to termination to each culture was added 2 uCi of tritiated thymidine (Amersham, England). Harvesting of the cells is by filtration (Bransome and Grower, 1970). The radioactive counts was done by the Beckman LS-100 Liquid Scintillation System. Mean values of triplicate cultures were presented in the results.

Reagents

MITOGEN: Bacto Phytohemagglutinin M (Difco Lab., U.S.A.), Pokeweed mitogen (Gibco, U.S.A.), Concanavalin A and E. coli Lipopolysaccharide (Sigma Chem. Co., U.S.A.).

NUCLEOTIDES AND CYCLIC NUCLEOTIDES: All supplied by Sigma Chem. Co. Adenosine 3'-Monophosphate (A-1377), Adenosine 5'-Monophophate Type IV (A-2002), Guanosine 3'-Monophosphate Grade 1 (G-3628), Adenosine 3':5'-cyclic Monophosphate (A-9501), N^6, $O^{2'}$-Dibutyryl Adenosine 3':5'-cyclic Monophosphate Grade II (D-0627), and Guanosine 3':5'-cyclic Monophosphate (G-6129).

RESULTS

Cyclic AMP, Dibutyryl Cyclic AMP, Cyclic GMP, 3'-AMP, 3'-GMP were added respectively into cell cultures stimulated by the different mitogens. A set of controls was done without any mitogens added to determine whether the nucleotides concerned does affect leukocytes without any mitogenic stimulation. The effect of each nucleotide was observed over a range of concentrations, 10^{-7} to 10^{-3}M.

C.P.M.: Radioactive counts per minute

$$\text{S.I.} : \text{Stimulation Index} = \frac{\text{C.P.M. of Experimental}}{\text{C.P.M. of Control}}$$

DISCUSSION

Lymphocyte populations obtained from various lymphoid tissues differ markedly in their capacity to respond by increased DNA synthesis to T and B cell mitogens (Jacobson and Blomgren, 1974). PHA and Con. A seems to stimulate T-cells almost exclusively, PWM stimulates both B and T cells (Greaves and Roitt, 1968) and lipopolysaccharide triggers non T-cells, predominantly B-cells (Andersson, Moller and Sjoberg, 1972).

A dose-response study was previously done on each of the mitogens used. The optimun concentrations were respectively, PHA at 10 ug/ml., PWM at 5 ug/ml., Con. A at 7.5 ug/ml. and LPS at 10 ug/ml.

The range of effectiveness of each of the nucleotides were obtained. In general there was a notable stimulation by cyclic GMP and inhibition by cyclic AMP at 10^{-4} to 10^{-3}M. 3'-AMP and 3'-GMP showed slight or no stimulation at all, and 5'-AMP showed slight inhibition. A fall in cyclic AMP level is apparently important for the initiation of growth because growth stimulation is prevented if cyclic AMP is maintained at high levels following the addition of growth-promoting agents (Pastan, Johnson and Anderson, 1975). Cyclic AMP and 5'-AMP inhibits the growth of cells apparently by a depletion of pyrimidine precursors for DNA and RNA synthesis (Hilz and Kaukel, 1973). Siefert and Rudland (1974) suggest that cyclic GMP acts as a positive signal in the control of cell functions while cyclic AMP represents a negative signal.

SUMMARY

Goldberg's Ying-Yang Hypothesis of Biological Control through cyclic GMP and cyclic AMP was demonstrated in guinea pig leukocyte proliferation. The results distinctly showed enhancement by cyclic GMP and inhibition by cyclic AMP for all the four mitogens and two cell types used. The pattern of response was similar regardless of the type of mitogens used nor the type of cells. This strongly suggest that the effect of cyclic GMP and cyclic AMP were nonspecific in nature.

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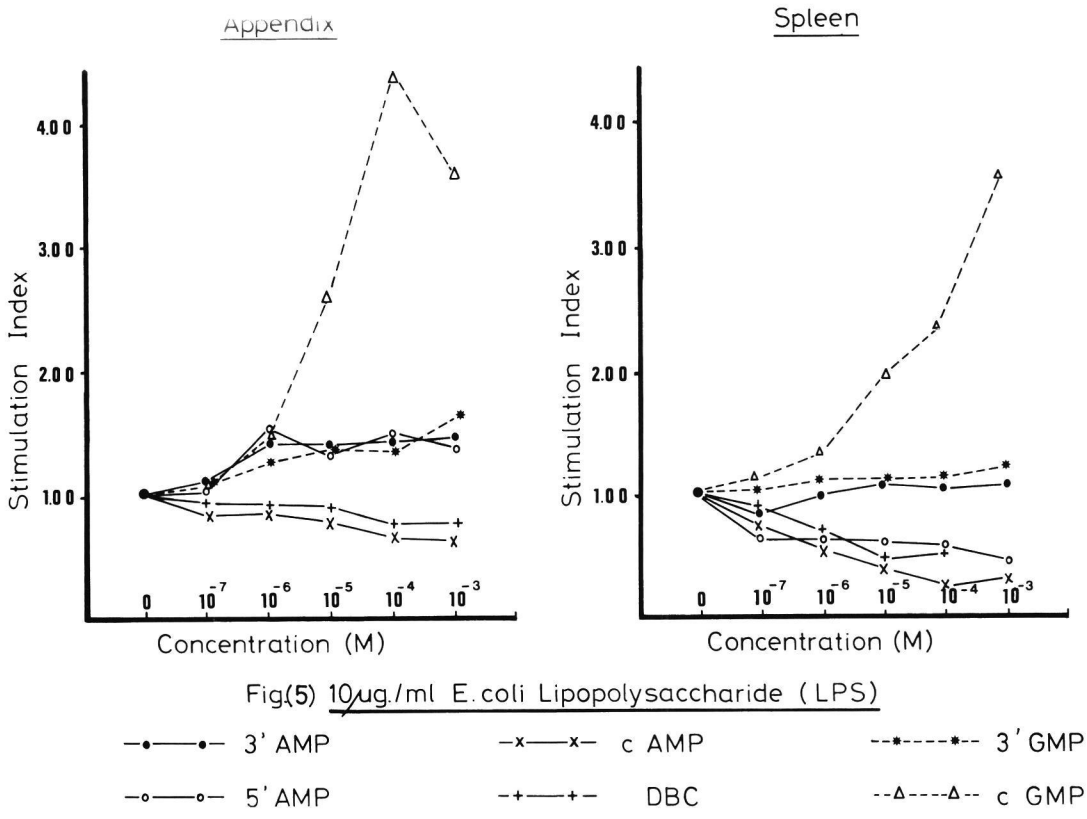

Fig(5) 10µg./ml E.coli Lipopolysaccharide (LPS)

and Dr. K.D. Sukumaran, Head of the Division of Serology & Immunology, Institute for Medical Research; Prof. S.S. Dhaliwal and Assoc. Prof. M. Yadav, Department of Genetics and Cellular Biology, University of Malaya. This piece of work was done in 1976 when I was then with the University of Malaya .

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