

The **Malaysian** Society of Pathologists: 12th Annual General and Scientific Meeting.

The 12th Annual General and Scientific Meeting was held at the Awana Golf and Country Club, Genting Highlands on 7-9 August 1987.

Abstracts of the scientific communications follow:

PAPER PRESENTATIONS:

1. HEPATITIS DELTA VIRUS (HDV) INFECTION IN MALAYSIA

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2. OCCUPATIONAL RISKS OF HEPATITIS B VIRUS INFECTION AMONG HEALTH CARE PERSONNEL IN HIGH-PREVALENCE AREAS: A COHORT STUDY

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Studies were conducted in 1985 and 1986/87 to ascertain the prevalence of HDV infection in Malaysia. It was found that coinfection with HDV in patients with acute HBV (anti-HBc IgM positive) was 18.2% (4/22). Delta antigen was detected in 3 of the patients and delta antibody in one. One of the patients had been infected as early as 1982.

The prevalence of superinfection with HDV in 204 chronic HBsAg carriers were:

- |                                    |                |
|------------------------------------|----------------|
| (a) I.V. drug abusers              | - 20.0% (7/35) |
| (b) prostitutes                    | - 16.7% (1/6)  |
| (c) male homosexuals               | - 12.5% (2/16) |
| (d) blood donors                   | - 0.8% (1/125) |
| (e) "healthy" HBs carriers         | - (0/13)       |
| (f) chronic liver disease patients | - (0/9)        |

The total prevalence of superinfection was 5.4% (11/204).

The overall HDV infection (coinfection and superinfection) was 6.6% (15/226). Although the samples in some groups were small it was obvious that the highest rate of HDV infection was among intravenous drug abusers. It is important to continue monitoring delta infection because once it gains access into the general population, the consequences can be serious. The only way to prevent this is by immunization which should be performed as early as possible and should cover I.V. drug abusers as well as other high risk groups.

Occupational exposure to hepatitis B virus infection (HBV) is well documented in Western countries (Maynard, 1978). In the United Kingdom, laboratory workers are now required to be vaccinated against HBV. In countries such as Malaysia, where there is a high rate of HBV infection it might be expected that this occupational risk would be particularly acute. This study examines whether such risks exist amongst health care personnel in endemic areas.

Blood from 940 hospital workers consisting of doctors, nurses, attendants and laboratory technologists from two large hospitals in Penang and Kubang Kerian, Kelantan were screened for HBs, anti HBs and anti HBc (IgG) using Abott ELISA Kits to determine the prevalence of past exposure to HBV in these groups of people. A second sample of blood was collected from the people whose sera were negative for HBV markers after a period of one year and the blood was tested for these markers to determine the rate of sero conversion. The results were compared with those of a control population comprising first year medical students and University employees. Multivariate analysis of the data was done using the SAS programme (computer software).

Preliminary data indicate that the prevalence of past exposure to HBV is marginally less in the hospital workers (25%) than in the control group (29%). Among the hospital population, prevalence of past exposure to HBV was significantly higher in workers in the

labour room, particularly midwives (38%). Cohort study revealed a sero conversion rate of 12% and 10% in the labour room and the operation theatre respectively, and 50% among the midwives. Details of the results and the significance of the study will be discussed.

### 3. DEMONSTRATION OF *CAMPYLOBACTER PYLORIDIS* IN THE EPITHELIAL MUCUS IN GASTRIC BIOPSIES

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The isolation of *Campylobacter pyloridis* as a separate entity was achieved as late as 1984 by Warren and Marshall. The spectrum of disorders caused by these organisms are slowly coming to light. Previously, the presence of these organisms was taken as a marker of chronic gastritis. But now a host of other conditions are also associated with it, namely, gastric ulceration, non-ulcer dyspepsia and duodenal ulcers.

A study was started in order to isolate, characterise and culture these organisms. The findings presented in this paper are the results of the initial few months of the study. Tissue identification by the Warthin-Starry technique has proved to be convenient and cost-effective and urea-broth cultures give rapid results. However, the aim of the study is to link up the spectrum of clinical manifestations, the presence of *Carnpylobacter pyloridis* and methods in management of the disorder.

### 4. LIPID PEROXIDATION IN PATHOLOGY

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The association of free radical-induced lipid peroxidation with pathological changes is reported in numerous genetic and acquired diseases. The role of membrane lipid peroxidation in the pathogenesis of muscular dystrophy with particular emphasis on Duchenne muscular dystrophy (DMD) is the aim of this study. An increase in the concentration of the intermediate products of lipid peroxidation was found in DMD patients (n = 9) compared with age- and sex-matched groups of healthy male controls (n = 10).

Trichloroacetic acid-precipitable tribarbituric acid-reactive substances (TBARS) were increased by 35% ( $P < 0.01$ ), conjugated dienes by 77% ( $P < 0.02$ ), and lipofuscin-like pigments (fluorescence pigments/FP) by 70% ( $P < 0.001$ ).

The free radical scavenger, alpha-tocopherol, was significantly decreased by 50%, in DMD compared with healthy subjects ( $P < 0.002$ ). In conjugation with the findings of others of a deficiency in DMD of the plasma lipoproteins which normally transport vitamin E to the tissues, this may contribute to the increased lipid peroxidation seen in the disease especially if muscle damage also liberates free Ferrous (Fe).

The protective antioxidant enzyme in plasma, namely, caeruloplasmin was significantly increased ( $P < 0.001$ ) by 25 – 30% in DMD patients compared with male controls. In DMD patients alone, this increase is correlated with the concentration of TBARS and FP suggesting that increased lipid peroxidation may be a trigger for caeruloplasmin synthesis.

This finding may offer further evidence to support the previously reported elevation of glutathione peroxidase (GSHPx) and catalase (CAT) in human muscle (2–4) and of superoxide dismutase (SOD) and CAT in erythrocyte in DMD. This data, more importantly, has strengthened the key role of lipid peroxidation in the pathogenesis of the disease. It is important to examine these same parameters in other myopathies, and particularly the other muscular dystrophies, to determine whether this role of lipid peroxidation is specific for DMD alone or a common denominator in the pathology of several myopathies.

### 5. THE USE OF AN IMAGE SCANNER FOR DIGITISATION OF MICROGRAPHS

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Computerized microscopic image analysis techniques have been used to study important features in histology and morphology. This paper describes the use of an image scanner to digitize micrographs. The image scanner (Microtek MS-200 Intelligent Scanner) utilizes a stationary Charged-Couple Device (CCD) sensor array to digitize micrographs at a very high resolution of 200 dots per inch (dpi).

It is then output to a microcomputer for processing. The present software allows some elementary processing to be carried out such as contrast setting, data compression and zooming an area of interest for details.

The potential of this technique can be realized by incorporating software to process the digitized image for subsequent quantitative analysis. Lastly, the limitations of this technique will be discussed.

#### 6. FROZEN SECTION OF BONE MARROW TREPHINE BIOPSY – A TECHNICAL STUDY

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Bone marrow trephine biopsy specimens are traditionally fixed, decalcified and paraffin-embedded before being processed for staining. This method creates artifacts and the cytological quality of the sections is far from satisfactory. It is also unsuitable for histochemical study. Since cryostat is available in most pathology laboratories, we have examined the technique of frozen section on undecalcified bone marrow specimens. Preliminary results show that it is rapid and gives satisfactory cytological quality with haematoxylin and eosin stains. We have also successfully implemented peroxidase, acid-phosphatase, dual esterases and Leder-Giemsa stains on the undecalcified bone marrow sections.

#### 7. PAROXYSMAL NOCTURNAL HAEMOGLOBINURIA – A STUDY OF SEVEN CASES FROM THE UNIVERSITY HOSPITAL, KUALA LUMPUR

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Seven new patients with Paroxysmal Nocturnal Haemoglobinuria (PNH) seen in the University Hospital, Kuala Lumpur between 1980 and 1986 are analysed. The clinical presentations, laboratory findings including peripheral blood and bone marrow findings are presented. All patients presented with iron deficiency anaemia. Six patients had haemosiderinuria at presentation but none had haemoglobinuria. Five out of six patients had jaundice at

presentation. Bone marrow aspiration was done in six patients out of which five had hypercellular marrow while one had normocellular marrow fragments. One patient developed myelodysplastic syndrome during follow-up.

#### 8. THE PATHOLOGY OF BONE TUMOURS: A STUDY OF 209 CASES IN THE UNIVERSITY HOSPITAL, KUALA LUMPUR

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From 1980 to 1986, 237 biopsies of tumour and tumour-like lesions of bone were received by the Department of Pathology, University Hospital, Kuala Lumpur. These biopsies were obtained from 209 patients. Secondary bone tumours constituted 25.4% of the cases. Tumour-like lesions accounted for 10.0% while the remaining 64.6% were primary bone tumours.

The commonest primary tumour was osteogenic sarcoma (35 cases). The youngest patient was a 6-year old boy. The femur was the most frequent site of involvement followed by the tibia. Osteoclastoma (28 cases) formed the second most common primary bone tumour with osteochondroma (27 cases) as a close third. Other primary malignant lesions of bone, namely, Ewing's sarcoma (9 cases) and chondrosarcoma (6 cases) were relatively rare.

A male preponderance was seen in most of the tumours with the exception of the osteoclastoma group where an almost equal sex distribution was demonstrated.

#### 9. RECTAL SUCTION BIOPSY IN HIRSCHSPRUNGS DISEASE – PROBLEMS FACING THE PATHOLOGIST

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The technique of rectal suction biopsy has gained wide popularity because of its simplicity, safety and accuracy in the diagnosis of Hirschsprung's disease. In a 4-year period between 1983 and 1986, 95 cases of rectal suction biopsies were performed to diagnose Hirschsprung's disease. This technique, based on that described by Noblett in 1969, is easy to perform. No bowel preparation or

anaesthesia is required and it can be carried out in a ward. It is safe and no complication of bleeding or pelvic sepsis occurred in any of the 95 patients. There were 3 false positives and one false negative giving an acceptable accuracy rate of 96%.

This technique, with its many advantages, has made it easier for the surgeon and patient. However, it has made it more difficult for the pathologist and a number of problems are evident from the study: (1) the small size of the specimen containing mucosa and submucosa only (2) the problem of inadequate biopsy (3) the large number of serial sections to be reviewed (4) the problem of identifying ganglion cells in small specimens (5) the importance of hypertrophied nerve bundles in diagnosing Hirschsprung's disease. All these have created more difficulties for the pathologist. Greater skill and experience are essential to overcome these problems.

## 10. HYDRONEPHROSIS SECONDARY TO URETERIC TUMOUR

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A patient presented with pain in the right loin and low grade fever for one month. A mass was felt in the right hypochondrium together with an enlarged spleen. The differential diagnoses ranged from hepatoma, enlarged gall bladder to cancer of the pancreas.

**Findings:** Enlarged lobulated right kidney and a firm mass in the upper end of the ureter. The ureter was studded with multiple cysts.

**Histology:** a) The kidney showed evidence of acute pyelonephritis and hydronephrosis.

b) Ureter:

- (1) had a papillary transitional cell carcinoma.
- (2) Ureteritis cystica.

## POSTER PRESENTATIONS:

### P1. ANTIMICROBIAL SUSCEPTIBILITY OF AEROMONAS SPECIES

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The anti-microbial susceptibility of aeromonas species to the earlier B-lactams and other

antimicrobials such as tetracycline, trimethoprim-sulphamethoxazole, chloramphenicol and aminoglycosides have been widely described. However, their susceptibility to the newer B-lactams and quinolones have not been well documented.

96 strains of aeromonas species isolated at the University Hospital, Kuala Lumpur, were tested for their antimicrobial susceptibility by the agar dilution method, using a multipoint inoculator. The inoculum size was about 104 per "spot" and an *E. coli* control strain (NCTC 10418) was included in all individual runs.

A high degree of *in-vitro* activity was seen amongst the quinolones, norfloxacin and pefloxacin (MIC90s 0.03 and 0.06 mg/L respectively) and the cephalosporins, ceftazidime, cefotaxime, ceftriaxone, cefoperazone and cefuroxime (MIC90s of 0.25, 0.5, 1.0, 2.0 and 4.0 mg/L respectively). Aztreonam, a monobactam, also showed a high degree of activity (MIC90 0.03 mg/L). Antimicrobials such as chloramphenicol, gentamicin, tetracycline and trimethoprim-sulphamethoxazole, whilst showing good *in-vitro* activity, were not as active as the newer B-lactams and quinolones. Ampicillin and carbenicillin had no *in-vitro* activity against the aeromonas strains.

Thus the newer B-lactams and quinolones may be considered in the therapy of life threatening infections with aeromonas species.

### P2. BIOCHEMICAL CHANGES FOLLOWING SURGICAL TRAUMA

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The metabolic response to trauma is varied, resulting in many biochemical alterations. This communication reports on some of the biochemical changes following surgical management of orthopaedic problems in 13 adults. The following biochemical constituents were analysed using standard laboratory procedures, pre-operatively as well as post-operatively a) Urine: non-protein nitrogen (hydroxyproline, creatinine and urea); calcium and phosphate; electrolytes (sodium and potassium) and cortisol. b) Blood: thyroid function tests.

Following surgery there was increased loss of urea, hydroxyproline, creatinine, calcium, phosphate and cortisol in urine, peak levels

being reached between the 2nd and 8th post-operative days. There was an initial decline in the amount of sodium and potassium soon after surgery, which was sustained for a few days indicative of conservation of electrolytes during the post-operative period. There was a fall in serum T4 level soon after surgery, which subsequently returned to normal levels. These changes reflect the catabolic response as well as the stress of surgery. There was a return to normal levels after the 8th – 14th post-operative days, suggestive of recovery and reversion to normal metabolism.

Body homeostasis is disturbed following trauma, in which both neural as well as hormonal mechanisms are involved. The metabolic response is determined by the nature of the trauma, the physiological status of the individual, complications of surgery if any, therapy and nutrition.

### P3. ANTIOXIDANT ENZYMES IN MUSCULAR DYSTROPHY

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A sarcolemmal membrane damage appears to be an early event in the pathogenesis of Duchenne muscular dystrophy (DMD). The exact mechanism involved in the lesion still remains unclear. This report is concerned with the role of lipid peroxidation as a candidate for the peroxidative damage to the membrane. Alteration in the activity of the protective enzymes against lipid peroxidation are found in DMD red blood cells (RBC). Catalase (CAT) activity was increased by 35% ( $P < 0.05$ ), superoxide dismutase (SOD) by 68% ( $P < 0.05$ ), and glutathione peroxidase (GSPHx) was decreased by 20% ( $P < 0.05$ ) in DMD RBC compared with healthy male controls. Thiobarbituric acid-reactive products were also increased by 54% ( $P < 0.05$ ) in DMD compared with the normal subjects. The clinical importance of these findings and the method that had been used (i.e. a combination estimation of antioxidant enzymes and the peroxidation product) in RBC has clearly shown the role of radicals derived from molecular oxygen in the pathogenesis of muscular dystrophy, in this case DMD. It may be important for diagnostic purposes. Furthermore, it may also serve to promote new therapeutic possibilities.

### P4. A RANGE OF AMYLOIDOSIS IN A MALAYSIAN PATIENT POPULATION

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In order to assess the types of amyloidosis encountered in a Malaysian patient population, biopsies received by the Department of Pathology, University Hospital, Kuala Lumpur over a 5.5 year period were screened with Congo red for the presence of amyloid deposits. 27,052 biopsies (obtained from 22,827 patients) were thus screened. These constituted 65% of all biopsies received during the period of screening. Excluded from screening were endometrial curettages and products of conception, which together formed 35% of all specimens received.

Amyloid deposits were detected in biopsies from 186 patients, indicating an overall prevalence of 0.8% (186/22,827). The range of amyloidosis was notably wide. 17 (9.1%) cases were generalized amyloidosis, i.e. showing multisystemic involvement. Both AL (11) and AA (6) types were encountered. Localized amyloidosis was by far the larger group and consisted of: isolated atrial 26 (14.0%), primary localized cutaneous 14 (7.5%), localized tumefactive deposits 6 (3.2%), localized intratumour 107 (57.5%) and dystrophic 16 (8.6%) amyloidosis.

Systemic AL amyloidosis had an association with immunocyte abnormalities of which multiple myeloma was the most severe. Tuberculosis and leprosy were the commonest underlying diseases in systemic AA amyloidosis. Isolated atrial amyloidosis appeared to have an association with chronic rheumatic heart disease. It was also noteworthy that intratumour amyloidosis was encountered in 13% of nasopharyngeal carcinomas and 56% of basal cell carcinomas. Other tumours demonstrated to contain amyloid included islet cell tumour, medullary carcinoma of thyroid and isolated instances of follicular thyroid tumours, basal cell papilloma of the skin and carcinoma of the cervix.

Some characteristics of these various types of amyloidosis will be considered.

**P5. NON-ULCER DYSPEPSIA AND  
CAMPYLOBACTER PYLORIDIS  
INFECTION**

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The aim of this study is to define the prevalence of *Campylobacter pyloridis* infection in patients with non-ulcer dyspepsia in our local population.

Forty-three successive patients with non-ulcer dyspepsia had upper-gastrointestinal endoscopic examinations. In each of these patients, 3 to 4 biopsies were taken from the gastric antrum and subjected to **histopathological** examination. Sections were stained with H & E and studied for the presence of curved spiral organisms of *Campylobacter* as well as for evidence of gastritis.

Fifteen (34.9%) patients were found to have *Campylobacter*. All their biopsies show gastritis on histological examination. 14 (32.6%) patients had evidence of gastritis but *Campylobacter* was absent. The remaining 14 patients had normal gastric mucosal histology and no evidence of *Campylobacter* infection. 15 (52%) of the 29 patients with gastritis had evidence of *Campylobacter* infection.

The preliminary findings from this study are comparable with those obtained elsewhere. Though the aetiological role of *C. pyloridis* remains to be clarified, this study suggests a strong correlation between gastritis and *Campylobacter* infection in our non-ulcer dyspepsia patients.

**P6. SERUM AND TISSUE ALPHA-FETOPROTEIN IN PATIENTS WITH HEPATOCELLULAR CARCINOMA**

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To examine the frequency and degree of elevation of alphafetoprotein (AFP) in patients with hepatocellular carcinoma (HCC), serum AFP levels were measured in 40 patients with biopsy proven HCC. Simultaneously the presence of tissue AFP was looked for using the peroxidase-antiperoxidase technique. In 21 (52.5%) patients, the serum AFP level was markedly elevated, the majority having levels of more than 10,000 iu/ml. Thirteen (32.5%) patients did not show an increase in AFP levels and the rest had mild elevations (< 500 iu/ml).

In sharp contrast, only 4 out of 22 patients with liver cirrhosis had elevated AFP: mildly elevated in 3 and significantly in the fourth case (4800 iu/ml). Similar results were obtained with metastatic neoplastic disease of the liver.

Tissue AFP was detected in 37% of the biopsies examined. In all cases, the corresponding serum AFP was markedly elevated.

About 75% of the subjects tested positive for hepatitis B surface antigen (HBsAg): 90% in the group of patients with markedly elevated AFP and 62% in patients with normal or mildly elevated AFP.