

ABSTRACTS

PRESENT STATUS OF HEPATITIS B VIRUS INFECTION IN INDIA AND STRATEGIES FOR THE CONTROL

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Viral hepatitis is a major public health problem in many parts of the world. In India, the classical virus hepatitis caused by hepatitis B virus (HBV) has been recognized to occur in towns and cities with high mortality. Current evidence suggests that hepatitis B antigen (HBsAg) is the etiological agent of type B hepatitis.

The rate of chronic carriers of HBsAg has been found to be 0.6-5.85%. The highest carrier rate of 5.85% was detected in the tribal population of north eastern region of India. The use of hepatitis B antigen tests in blood bank laboratories amongst the voluntary and commercial donors revealed that the professional donor group had very significantly higher proportion of individuals with HBsAg as well as with anti-HBs. Among the highest age group (over 41), raised levels of SGPT and SGOT were seen in many persons. It has been confirmed that HBV is not as commonly prevalent in India as in China, Africa and some Southeast Asian countries (ICMR Bull. 13., 1983).

It would, however, appear that in a very high proportion of adults, NANB is the major cause of sporadic cases of viral hepatitis.

In one study on the hospitalized patients, 27 died among 32 affected with hepatic coma. HBsAg was found in 9 cases while the antigens was detected in 62 of 181 adult patients. Thus, the etiology in 23 of 32 coma patient could be attributed to NANB which appeared to be responsible for about 65% of the hospitalized adult patients of viral hepatitis.

The disease is notifiable in most parts of the country. National Institute of Communicable Diseases in a recent seminar on viral hepatitis has strongly recommended the institution of an effective surveillance system in the country involving epidemiological, laboratory and clinical methods. A rigid control and monitoring of blood donors to eliminate the use of HBsAg containing blood have been suggested. It is expected that this alone will drastically reduce the HBV prevalence in the country.

HEPATITIS B PROBLEM IN THE PHILIPPINES

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A study is being undertaken in the Philippines since 1979 to-date to look into the prevalence of Hepatitis B virus in blood

samples obtained from different parts of the country and from different groups of people through the detection of Hepatitis B surface

antigen. The Ministry of Health wanted to know the extent of the problem in order that scientific and realistic plans can be made to tackle the same and also for people to realize why it deserves a priority attention.

Of the serum samples from 70,268 volunteer blood donors of the Philippine National Red Cross, 9,519 (13.5%) were positive for HbsAg. The range of detection was 12.4% to 14.7%. Of the serum samples from 107,564 professional blood donors, 14,743 (13.7%) were positive for HbsAg. The range of detection was 12.9% to 14.6%. Of the serum samples from 4,541 hospitality girls from 18 geographical areas, 401 (8.8%) were positive with a range of detection of 6.07% to 11.6%. Of the serum samples from 3,691 prisoners confined in 5 penal colonies and in Manila, 595 (16.12%) were positive for HbsAg the range of detection was 4.7% to 19.8%.

In a test conducted in 1979-1980 in 675 serum samples from residents of Metro

Manila, 82 (11.8%) were positive and of 426 serum samples from the rural peripheral areas 43 (10.9%) were detected positive. In 1982, of 10,303 samples collected from all over the country about the same time for a diabetic survey, 794 (7.7%) had HbsAg and the range of detection was from 2.5% to 12.1%. Of 399 samples from the residents of the Mountain Provinces in Luzon (minority tribes of Luzon), 8% were found to be positive. Of 175 samples from a minority tribe residing in the mountains of Cotabato, 28 (16%) were positive and one out of the 20 children, 15 years old and below, was positive. From a recent visit to an island province of Marinduque, 50 blood samples were obtained from the inhabitants 14(28%) were positive for HbsAg.

Studies on the relation of hepatitis virus and hepatocellular carcinoma, *Schistosoma japonicum* and perinatal transmission have been done.

COUNTERMEASURES FOR PREVENTION OF HEPATITIS B BY THE KOREAN GOVERNMENT

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Viral hepatitis which shows endemic occurrence is the one of the major communicable disease emerging at the moment, with its prevalence rate of 9 percent. This may be caused by various factors but it is conjectured that it is attributed to population over crowding by industrial development, unhygienic ways of living and lack of public health consciousness.

To improve and upgrade this circumstance to those of developed countries before 1988 Olympic, the government has established a

five-year plan for eradication of hepatitis in 1983. For the first year plan, 2,000 thousand persons accepted vaccination in 1984; for the second year plan, vaccination program expanded to 2,100 thousand persons in 1985 and for the last year, it is planned that 17 millions will be vaccinated up to 1988.

Target population is primarily children under primary school and vulnerable group such as medical personnels, food workers, and public services among adults.

Hepatitis examination equipments have been distributed to county health centers to assign the test function in 1985. The government has provided free hepatitis test to parturient women who are registered at health centers and MCH centers, and free hepatitis vaccination to children of those who are antigen positive in order to prevent vertical transmission. Through this procedure vertical transmission between mother and child

which is known to be the major infection channel can be blocked.

Korea is the third nation that have been successful in hepatitis vaccine production after U.S.A. and France. Since the development of production technique, cost have been drastically reduced and it is hoped that mass distribution of hepatitis diagnostic agent will be possible as well.

HEPATITIS WITH OTHER CAUSES THAN HVA, HVB, NON-A NON-B VIRUS IN THE TEACHING HOSPITALS OF UNIVERSITY OF INDONESIA

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In tropical countries, such as Indonesia, infection is still a major problem since most diseases have an infective basis, or usually are concomittant with infection. The liver and biliary tract is frequently the site of such diseases, and the causative micro-organisms are protozoa, bacteria, fungus, helminth and

viruses. This review presents patterns of diseases of the liver and biliary tract with nonviral causes recorded in the infectious diseases wards of Internal Medicine Department, University of Indonesia, Jakarta in the period of 1979-1984. Some epidemiological and clinical aspects were discussed.

STATISTICS ON HEPATITIS CASES IN INTERNATIONAL CLINIC, SEVERANCE HOSPITAL

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International Clinic in Seoul Severance Hospital is devoted to foreign patients in Korea. These are mostly composed of Americans, Europeans and Australians. There is also a small number of Indonesian, Indian, Japanese, Chinese and African nationals.

Among 4000 charts reviewed up from

January 1981 to July 1985, 45 cases of hepatitis were found, but little information could be collected. This can be easily explained by two facts:

First is that hepatitis markers are of more common use only in the last 2 years. As they are at high cost and without immediate

benefit in the treatment to the patient, their study was not automatically done in our practice and general prophylactic measures were taught to the patient. Research for B hepatitis Ag and the chronic carrier state was done later.

The second fact to consider is the high mobility of the foreign population of Seoul. These foreign patients move frequently to other countries. People stay here often just one or two years and go back home readily in case of some long duration illness. Thus, quite a number of patients in this study went back home before they were cured or did not come to the clinic for long term follow-up.

All these facts explain the special results obtained throughout this study where B hepatitis seems to be more frequent than A type among the foreign population.

37 cases were undocumented or under documented, and 3 cases were documented as having A hepatitis by the anti HAV, IgM positive test.

Five cases were documented as having B hepatitis: at least one positive result, at sufficient levels, among HbsAg, anti Hbs, anti Hbc. There were no cases of documented non A non B hepatitis.

Among the non documented cases, 21 were probably A type hepatitis as they appeared during a small epidemic during the winter 1982-1983.

Among the 5 documented cases of B hepatitis, 2 patients were Japanese.

For none of the 45 cases the contamination source could be found. These cases remained isolated in their direct environment, even in their families, though family members of hepatitis patients are usually advised to receive a standard gamma-globulin shot.

Transaminases levels remained moderately high and do not seem to be related with the type of the hepatitis:

In 8 cases the level was below 1000 units and 2 of these were B hepatitis cases; 15 cases were between 1000 and 2000 units, and 2 patients had B hepatitis; 12 cases were between 2000 and 4000 units, one case was B hepatitis.

Though it is true that very few people could have long term follow-up of transaminases levels, most of the cases had good immediate results. Still 23 cases were followed until transaminases levels returned to normal, which happened most of time after 2-3 months, even among 4 probable cases of A hepatitis who had small repeat elevation of transaminases levels about one month after the onset of symptoms. Only one case was found to have a slight repeat elevation of the transaminases levels one year after illness (SGOT 104, SGPT 144), but so few patients were followed for that long a time that this even cannot be given any real signification.

Bilirubin levels were studied only in 10 cases and remained moderate below 8mg/dl. In two cases they were higher, 12mg in one case of A hepatitis and 14mg in one case of B hepatitis. None of the patients had any blood coagulation impairment or any other complication from the illness.

All together this small and not sufficiently documented study still reflects the usual features of hepatitis among the white population. A hepatitis seems more common even the only A documented cases in our study could be the contrary. B type remain rare among white Caucasian group, even in those living in Asia for one or more years. Hepatitis is an illness of low contagion and has a tendency to heal completely, whatever the type is.

MOLECULAR GENETICS OF THE HEPATITIS B VIRUS, SUBTYPE ADR-K

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The hepatitis B virus (HBV) is a small DNA virus of humans which belongs to hepadna virus group, causes serious liver diseases, hepatitis, and associated with the development of hepatocellular carcinoma. The viral genome is about 3.2kb long and circular of partially single-strand DNA. The long(L) strand has a nick and the short(S) strand is of variable length ranging from 50 to 70% that of the L strand. Four possible open reading frames have been defined in L strand transcript: gene S (codes for HBsAg), gene C (codes for HBcAg and HBeAg), gene P (probably encodes the possible DNA polymerase), and gene B (encodes protein the function of which is undefined). HBV associated proteins experimentally defined are envelope protein (P25, GP29, GP33 and GP36), core protein (P22 and P19), HBeAg (P15.5) and gene B product, P28. The 5' binding protein and proteins which contain polymerase activity and protein kinase activity remain unpurified.

Viral subtypes are well defined for HBsAg, which has a common determinant 'a' plus two pairs of mutually exclusive determinants d-y and w/r. Nine subtypes have now been defined and there are correlations between these subtypes and geographical locations. With these reasons, we have cloned the hepatitis B viral DNA, isolated from the sera of Korean patients, into the Bam HI site of pBR 322. Physical mapping of HBV DNA has been done by using numerous restriction

endonuclease; showing that adr-k subtype contains a single cut site for Bam HI, Xho I, Xba I and Sph I, and lack the cleavage site for Cla I, Eco RI, Hind III, Hpa I, Pst I, Pvu II, and Sal I. It has also two cleavage sites for Ava I, and three sites for Hinc II and Taq I. Xho I divides two genes for surface and core antigens. We have also cloned the genes coding for surface antigen and the region of 'Pre S-S-poly(A) addition site' and transformed into *E. coli*, yeast and animal cells, respectively, for the expression of surface antigen. The nucleotide sequence of core antigen-coding region of the subtype adr-k has been determined by the dideoxy chain termination/M13 phage template. This sequence is about 1.3 kb long and includes the open reading frame for gene B. Our results showed 96% homology to adr, 92% to adw and 91% to ayw subtype compared with corresponding region of reported sequence. The nucleotide sequence we determined showed differences from reported adr subtype DNA by 27 nucleotides addition at the position of 1791-1817, that was also reported in adw and ayw subtype, and differed by one nucleotide(T) addition at the position 1826. The core-antigen coding region appears to be very important, because this region contains unique signal sequences such as direct repeat sequences (TTCACCTCTGC), poly (A) addition site (TATAAA), and RNA polymerase binding site (TACATA). Possible roles of this region were discussed.

CIRCUMSCRIBED HEPATIC NECROSIS DEVELOPING IN THE COURSE OF CHRONIC HEPATITIS B

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Thirty-five sequential biopsy specimens from fourteen adult Korean patients obtained during periods of from 20 days to 11 years were studied and correlated with clinical findings. In eleven, a circumscribed severe alteration of the lobular parenchyma was noted and on three others minor degrees of a similar lesion. The circumscribed hepatic necrosis shows an acinar arrangement of altered hepatocytes surrounded by increased connective tissue, progressing to collapse. The lesion frequently followed histologically documented acute viral hepatitis but was found in the presence of chronic active hepatitis and was also preceded by chronic

lobular hepatitis which differs from the emphasized circumscribed lesion by diffuse lobular development. The lesion was frequently associated with transition to cirrhosis and may be a factor in this process. It is usually accompanied by clinical manifestations of hepatic failure and has been followed by demise of the patient during observation but recovery has also been recorded. The pathogenesis of the lesion, which may be relatively rare in Western countries, requires exploration. The presented observations suggest a major role of parenchymal changes in the evolution of chronic viral hepatitis B.

COMPARISON STUDY ON THREE HBsAg AND ANTI-HBs TEST REAGENTS USING RPHA AND PHA

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In Korea, foreign products are widely used for detecting HBsAg and anti-HBs despite of high running cost. A new domestic product is now available with less expenses. Authors studied the sensitivity and specificity of the product in comparison with two other widely used imported kits.

The results were as follows: As to HBsAg tests, RPHA results were quite close to those

of RIA in both the sensitivity and specificity but as to anti-HBs tests, PHA results were much less sensitive (68-79%) and less specific (86-92%) than that of RIA.

Among the tested three brands of kit, there was no significant difference in both sensitivity and specificity, and it was concluded that domestic products were as good as imported kits.

SERUM HBsAg AND ANTI-HBs OF THE POPULATION AT KOJA UTARA DISTRICT, NORTH JAKARTA, INDONESIA

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Koja Utara district is typical for Jakarta, with dense population and consists of different ethnic groups and socio-economic classes from various parts of Indonesia.

1430 individuals 15 years and older from Koja Utara district were selected by stratified multi-stage random sampling from screening for HBsAg carriers. Of these, 68 individuals (4.76%) were positive. Of 1206 individuals which were also screened for blood HBsAb, 253 individuals (20.99%) were positive.

The prevalences of HBsAg carrier according to sexual grouping were 4.49% for males, and 5.01% for females, while the results for HBsAb carrier were 23.26% and 18.83% for males and females respectively.

There is a tendency of decreasing HBsAg positive rate in the older age group.

In male there is a tendency of decreasing anti-HBs with increasing age.

There is a lower HBsAg and higher anti-HBs in the higher socio-economic group compared to the lower group, 3.2% against 5.1% for HBsAg and 28.6% against 17.3% for anti-HBs.

There is no definite influence of educational status to the HBsAg and anti-HBs status.

The infection rate in males is relatively higher than females, 27.7% and 24.1% respectively.

HEPATITIS B VIRUS DNA DETECTION IN SERUM BY HYBRIDIZATION TECHNIQUE

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The use of ³²P-labelled hepatitis B virus probe in hybridization technique could provide a rapid and sensitive diagnostic tool for the detection of HBV DNA in the liver or serum. For the development of simple and direct diagnostic test kits of hepatitis B virus DNA, this study was designed and carried out.

We constructed the recombinant DNA clone with the hepatitis B virus, and labelled

the cloned DNA with radioisotope by nick translation.

HBV DNA extracted from serum samples were transferred to nitrocellulose filter papers by the Hybri-dot kit. The filters were dried in air and baked at 80°C for 1 hour. Sample DNAs transferred to nitrocellulose filters were hybridized in hybridization solution containing probes. The results were obtained by autoradiography. The results were as follows:

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- (1) Minimum quantity of detectable DNA by ³²P-labelled probes were 0.4 pg.
- (2) HBV DNA in HBsAg negative serum (199) was determined in 31 serum samples (16%), confirming that HBsAg negative serum could be cause of post-transfusion hepatitis.
- (3) From 92 HBeAg-positive serum, HBV DNA were detected in 88 serum samples (88%), confirming that HBeAg is a marker of active viral replication.
- (4) HBV DNA positive serum with

HBsAg and HBeAg was 99% (70/71)

- (5) HBsAg negative serum with anti-HBe could not detect HBV DNA.
- (6) HBsAg positive serum with anti-HBe was detected in 9 serum samples (64%)

These results indicated that the hybridization method by using ³²P-labelled probe not only provide a more sensitive and direct method for detecting HBV DNA in serum or liver, but also provided the serological evolution of patients.

PERINATAL TRANSMISSION OF HEPATITIS B VIRUS AND ITS PREVENTION IN KOREA

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The perinatal transmission of hepatitis B virus means transmission of hepatitis B virus (HBV) from mothers to their infants. Many authors suggested the route of perinatal transmission before, during, or after delivery. The exact mode of transmission of HBV from HBsAg positive mothers to their infants is still uncertain, but the perinatal transmission generally seems to occur at birth and after birth.

The difference of HBV markers between umbilical cord blood and neonates' blood is still unknown. The frequency of the transmission of HBV from asymptomatic carrier mothers to their infants is variable according to races and countries. The efficacy for prevention differs according to various investigators.

This study was designed to detect the frequency of perinatal transmission of hepati-

tis B virus in Korea and to evaluate the effectiveness of HBIG and HB vaccine for prevention. A total of 1,028 cases of pregnant women without history of liver diseases and their babies were studied from 1983 to 1985. HBV markers including HBsAg, anti-HBs, anti-HBc, HBeAg and anti-HBe in 48 pairs (sera of mothers, umbilical cord blood, neonates at birth and infants 6 to 12 months after birth) were tested by radioimmunoassay.

Babies born to HBsAg carrier mothers were divided into HBIG only immunized group (HBIG 100 I.U., at birth) and HBIG with HB vaccine immunized group (HBIG 100 I.U., at birth and one month after birth and HB vaccine 10 µg i.m. one month, two months and seven months after birth). After immunization, follow up test for HBV markers were taken for analyzing the efficacy of immunization.

The results were as follows:

1. In a total of 1,028 cases of pregnant women, 90 were HBsAg positive (8.8%) and 432 were anti-HBs positive (42.1%),
2. Among 48 HBsAg positive mothers, HBeAg was positive in 25(52.1%), anti-HBe was positive in 10 (20.8%) and anti-HBc was positive in 47(97.9%). Among 48 HBsAg positive mothers, HBsAg in umbilical cord blood was positive in 23. The occurrence of HBeAg, anti-HBe and anti-HBc were same as those of mothers. Among 48 neonates born to HBsAg positive mothers, 4 were positive HBsAg in neonates' blood. Thus, the transplacental transmission rate was 8.3%.
3. Neonates' HBV markers were very different from those of cord blood, especially in HBsAg (23 HBsAg positive in cord blood vs 4 HBsAg positive in neonates).
4. HBsAg positivity in cord blood was higher (64.0%) in HBeAg positive mothers than in anti-HBe positive mothers (30.0%).
5. HBsAg was positive only in neonates born to HBeAg positive mothers. Thus, transplacental transmission occurred only in HBeAg positive mothers.
6. Among 8 babies immunized with HBIG only, HBsAg at 6 to 12 months after birth were positive in 5 babies (62.5%), but among 10 babies immunized with HBIG and HB vaccine, there was no HBsAg positive baby and anti-HBs were positive in 8 babies (80.0%).
7. All of HBsAg positive babies were born to HBeAg positive mothers. There was no correlation between positive conversion rate of anti-HBs in infants and HBeAg status of mothers.
8. Negative conversion rate of HBeAg after immunization were 60.0% (3 among 5) in HBIG only immunized group and 100% (4 among 4) in HBIG and HB vaccine immunized group.
9. Negative conversion rate of anti-HBc after immunization was 20.0% (2 among 10) only in HBIG and HB vaccine immunized group.

In conclusion, the most likely route, of perinatal transmission seems to be contamination of the babies' blood with maternal blood at delivery or close contact between mother and baby during the postpartum period rather than transplacental transmission. In this study the transplacental transmission rate was 8.3% and neonates born to anti-HBe positive mother escaped the transplacental infection. There was a significant difference between HBV markers in cord blood and neonates' especially HBsAg. This study also suggested that immunization with HBIG and HB vaccine appeared to be effective, as compared to HBIG only, in preventing neonatal hepatitis B virus infection in all newborn infants born to HBsAg positive mothers regardless of the presence of HBeAg or anti-HBe.

PERITONEOSCOPIC AND PATHOLOGIC FINDINGS OF THE LIVER IN ASYMPTOMATIC HBsAg CARRIERS

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The hepatic status of HBsAg carrier is still controversial. To clarify this issue a prospective study was performed in 41 HBsAg carriers whose liver functions were normal and who had no hepatomegaly on examination and liver scan. All HBsAg carriers underwent peritoneoscopy and liver biopsy using Vim-Silvermann needle.

Viral markers, age and sex distribution, occupations, reasons for HBsAg check, peritoneoscopic findings, pathologic findings, comparison of peritoneoscopic with pathologic findings, and pathologic findings according to HBeAg and anti-HBe status were analyzed in HBsAg carriers.

The results were as follows:

1. HBsAg and anti-HBc were positive and anti-HBs negative in all 41 carriers. HBeAg and anti-HBe were checked in 33 among 41 carriers. HBeAg was positive in 15 cases (45.4%), anti-HBe positive in 16 cases (48.5%), and both negative in 2 cases (6.1%).

2. The 3rd and 4th decades had peak incidence (70.7%) and the male outnumbered the female at a rate of 1.73 to 1.
3. In 46.7% of the carriers, the peritoneoscopic findings were consistent with chronic liver diseases.
4. In 34.1% of the carriers, the pathologic findings were consistent with chronic liver diseases.
5. Of the 15 cases with HBeAg positive, 7 cases (46.7%) had chronic liver diseases, 5 cases (33.3%) nonspecific findings, and 3 cases (20.0%) normal liver. Of the 16 cases with anti-HBe positive, only 3 cases (18.8%) had chronic liver diseases, 11 cases (68.8%) nonspecific findings, and 2 cases (1.4%) normal liver.

In conclusion, a significant number of HBsAg carriers had chronic liver diseases even though their liver functions were normal and they had no hepatomegaly. It is recommended that a liver biopsy be done in every HBsAg carrier although his liver functions are normal and he has no hepatomegaly.

HBV MARKERS IN KOREA, AND PREVENTION OF HBV INFECTION IN THE INFANTS WITH PASSIVE-ACTIVE IMMUNIZATION

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Korea is one of the well known endemic area for HBV infection. The chronic

infection of HBV would play a role in the pathogenesis of chronic active liver diseases

terminating eventually in primary liver cancer. The surveys also found the clustering of HBV infection in the family members of patients with chronic liver disease, compared to the controls in Korea. It was also found that the infants born to mother positive for HBsAg become chronic carriers for HBsAg. The serologic response to HBV increases from the age of 7, indicating that the immunization should begin before this age group. To 147 infants born to HBsAg positive mothers, HB vaccine (5 µg HBsAg protein) and HBIG (200 IU) were given simultaneously within 24 hours after birth, followed by HB vaccine (5µg) 1 and 6 months later as boosters and

they were followed up at least for 15 months from birth. During observation period, HBsAg was positive only in 5 infants including possible transplacental infection and transient antigenemia. Positive rates of anti-HBs were 97.7%, 97.8%, 95.2%, 91.9% and 87.1% at 1, 3, 6, 9 and 15 months of age, respectively, and the titers of anti-HBs did not decline throughout the period of observation. These results suggest that passive-active immunization with a single injection of HBIG and 3 doses of HB vaccine is effective for the prevention of HBV infection from the carrier mothers in the perinatal period.

INFECTIOUS HEPATITIS : A COMPARATIVE STUDY OF THERAPEUTIC METHODS

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A comparative analysis of two methods of treatment of infectious hepatitis was done on two groups of adult patients at the Clinical Division of the Santo Tomas University Hospital. Each group consisted of 35 patients. The groups were as homogeneous as possible with respect to age, sex, and epidemiologic character. The duration of this study was from March 1972 to April, 1973.

Group 1 patients received Methisoprinol plus conventional treatment of fluids, vitamins, diet and bed rest. Group 11 patients did not receive the drug but only the standard anti-hepatitis regimen consisting of fluids, vitamins, diet and bed rest.

Results revealed that patients in Group 1 responded satisfactorily to treatment with rapid relief of symptoms and decline in enzymes activity (SGOT, SGPT) within two

weeks of drug administration. The serum bilirubin, however, declined a little slower. Symptoms of anorexia, malaise, nausea, headache and abdominal pain generally disappeared within 5 to 10 days. Hepatomegaly and icteric sclerae were the signs that lasted beyond the two-week period of treatment. The number of hospitalization lasted 14 days.

Group 11 patients had a much slower decline in the enzymes values compared to Group 1. The serum bilirubin values remained high during the 3 weeks of hospitalization. Symptoms improved on the third week of hospitalization. The number of hospitalization lasted 20 days.

In conclusion therefore, it indicates that Methisoprinol in the course of the treatment of infectious hepatitis stands as a very effective

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tive new therapeutic means which allows a successful treatment of infectious hepatitis, in addition to shortening the average duration

of the disease in comparison with the group of patients treated with the conventional therapy.

CLINICAL TRIAL OF ISOPRINOSINE IN THE TREATMENT OF INFECTIOUS HEPATITIS

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Thirty five cases of infectious hepatitis were treated with isoprinosine, a new wide-spectrum antiviral compound (Para-acetamidobenzoate of dimethylaminoisopropanol inosine) that was obtained from Newport Pharmaceuticals International, Inc., Newport Beach, California, USA.

All the 24 cases of HAA-negative viral (IH) hepatitis responded satisfactorily to treatment with rapid relief of symptoms and decline in enzymes activity (SGOT & SGPT) within two weeks of drug administration. HAA-positive cases of viral hepatitis and Salmonella hepatitis responded poorly to treatment. Symptoms of anorexia, malaise, nausea, headache and abdominal pain generally disappeared within five to ten days of treatment among the HAA-negative viral hepatitis. Hepatomegaly and icteric sclerae were

the signs that lasted beyond the 2 week period of treatment.

No serious adverse or toxic drug reactions were observed, except for nausea and vomiting in two patients. Slight elevation of serum uric acid was also noted during treatment, but generally the values went down to normal level within two weeks after treatment. No attack of gout was observed among patients who showed elevation in serum uric acid. Further clinical trial is necessary to establish the clinical efficacy of isoprinosine in the treatment of infectious hepatitis. A double-blind study should be undertaken to arrive at a more logical conclusion as to the efficacy and safety of isoprinosine in the management of infectious hepatitis among Filipino patients.

POST MARKETING SURVEILLANCE WITH HEPATITIS B VACCINE

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For the preliminary studies, it was decided to conduct a post market survey against

10,000 healthy persons injected with Hepavax-B in 52 hospitals. Questionnaire sheets were

distributed to all participating hospitals in March 1984, which contained the date of the immunization, antecedents, results of pre-immunization surveillance, hepatitis B markers and ALT, previous other vaccination and side effects.

For the primary immunization, one milliliter containing 20µg of HBsAg (10µg for children under 10 years) was injected into the upper arm intramuscularly. The second immunization was done after 1 month and third immunization after 6 months from the primary immunization by the same method.

All the vaccinees stayed in the clinic for 30 minutes after vaccination to monitor whether immediate local or general reactions develop.

An oral temperature was taken over a 5-minute period of time at the end of 30 minutes stay.

Vaccinees were asked to take and record their own temperature every 12 hour during the next 24 hours. Vaccinees were also told to visit the clinic if they wish to have their temperature taken in the clinic.

The summarized results are from 5024 vaccinees who followed guidelines for the post vaccination surveillance.

In the study, it was found that the side reaction rates of the first, second and third injections were almost the same, and that about 17% of the vaccinees showed the local symptoms such as mild pain at injection site, redness and induration swelling; and about

6% showed general symptoms such as transient low grade fever, malaise.

The side reactions by sex indicated that local symptom cases, e.g., pain at injection area, redness, induration swelling, between the male and female were almost similar in number whereas the female fever cases and general symptom cases including malaise were more than the male cases by approximately 1% and 3% respectively.

The side reactions by age group (one group of up to 15, the other of 16 to 70) represented that the children's side reaction rate was slightly higher than that of the adults in local symptoms while the adults showed almost similar results obtained in fever and in general symptoms including malaise with the children.

Fever reaction, the common side reaction problem, was surveyed by sex and age after the first injection, using control (placebo) group, and temperature rise by 1°C or more was considered positive.

The positive reaction was recorded in 1.6% of the male and 1.3% of the placebo group whereas it was 2.5% of the female and 1.6% of the placebo group.

By age, the positive reaction was observed in 2.0% of the children and 1.5% of the placebo group while it developed in 2.0% of the adults and 1.9% of the placebo group, showing the adult's fever rate was similar to that of the children. The placebo was prepared with the same solution but contained no HBsAg.

SCHISTOSOMIASIS IN MAINLAND OF SOUTHEAST ASIA

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Schistosome infection in the mainland of Southeast Asia is caused by two species, *Schistosoma mekongi* and *S. japonicum* complex. The first one is prevalent in southern Laos and Cambodia and *Tricula aperta* is the snail intermediate host. Clinical manifestations, in general, are asymptomatic or mild, however severe portal hypertension is also not uncommon. Diagnosis by stool examination is difficult to differentiate from the classical strains of *S. japonicum*. *S. mekongi* infection respond very well to Praziquantel

treatment.

The other schistosomes in Malaysia and Thailand which at present are considered as species complex of classical strain of *S. japonicum*. *Robertsiella kaporensis* is known to be the intermediate host of Malaysian schistosome but the snail host for Thai schistosome is still obscure. Clinical manifestations of these schistosome infections were mostly asymptomatic and the discovery was usually incidental.

BIOCHEMICAL DIFFERENTIATION OF ASIATIC SCHISTOSOMES

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Four taxa of Asiatic schistosomes (*Schistosoma japonicum*, *S. mekongi*, *S. sinensium*-like from Thailand and the undescribed *S. japonicum*-like schistosome from Peninsular Malaysia) were compared by means of horizontal starch-gel electrophoresis.

Single adult worms were utilized for this study. The gene-enzyme systems studied included glucosephosphate isomerase, phosphoglucomutase, malate dehydrogenase, phosphogluconate dehydrogenase, hexokinase, adenylate kinase, mannose phosphate isomerase, malic enzyme, glucose-6-phos-

phate dehydrogenase, lactate dehydrogenase and superoxide dismutase.

The four taxa could be unequivocally differentiated by a number of gene-enzyme systems. No clearcut intrastain variations were observed. The electrophoretic data provide strong evidence for the species status of the *S. japonicum*-like Malaysian schistosome, being distinct from *S. japonicum* and *S. mekongi*. Of these schistosomes, the Malaysian taxon and *S. mekongi* are closer related than to *S. japonicum*.

LIPID AND BILE ACIDS PATTERN IN PATIENTS WITH OPISTHORCHIASIS

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Lipid and lipoprotein profiles were studied in 67 patients with opisthorchiasis and compared with 118 controls at the Bangkok Hospital for Tropical Diseases. Serum bile acids pattern of 38 controls and 84 patients were also studied.

The results showed that in opisthorchiasis there was a significant increase in the levels of prebeta-lipoprotein, cholesterol and phospholipids, whereas beta and alpha lipoprotein were decreased. The levels of glycocheno-

deoxycholic, taurocholic, taurocheno-deoxycholic and total bile acids were also elevated. There were significant decreases in trihydroxy-dihydroxy ratio and glycine-taurine ratio in patients with opisthorchiasis. The changes of serum bile acid levels and ratios might be due to the disturbance in the enterohepatic cycle of bile acids. Biliary obstruction from worms caused retention of bile acids in the biliary system, thus regurgitation into the porta-systemic circulation.

ENCAPSULATED-EGG-DEPOSITION-PATTERN OF SCHISTOSOMES IN THE ECTOPIC SITE, THE PERITONEAL CAVITY

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Many studies have been reported dealing with egg formation, development, production, passage, distribution and destruction of schistosomes. But very little is known about the encapsulated egg-deposition-pattern in the ectopic location, the peritoneal cavity.

In the present study two series of mice were exposed each to 20-300 cercariae of *Schistosoma japonicum* and/or *S. mansoni* by intraperitoneal and/or percutaneous infections. They were sacrificed and examined 60-116 days post-infection. The peritoneal cavity was carefully washed with normal saline, the worms were perfused by Duvall and De Witt's technique (1976). The washings were carefully examined under stereoscopic

microscope. Both encapsulated eggs and worms were found in the peritoneal cavity after intraperitoneal infection, but only encapsulated eggs were observed in the peritoneal cavity after percutaneous infection. 194 encapsulated eggs of *S. mansoni*, 78 in peritoneal cavity and 116 on the intestinal wall were found after infection by both routes. On the other hand, 109 encapsulated eggs of *S. japonicum*, 62 in the peritoneal cavity and 47 on the intestinal wall were detected after infection by both routes.

The capsulated eggs either in the peritoneal cavity or on this intestinal wall often varied markedly in size, which was not always related to the number of eggs in the encapsules

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However, the bigger capsules usually contained a larger number of eggs. Most of the encapsulated eggs were dead and/or have degenerated. If they were viable, most remained in the 5th stage or mature eggs.

Most interesting finding was that some encapsulated eggs were connected to the intestinal wall by a rather long, thin fiber. Some other even dropped into the peritoneal cavity, but they still had a short, armlike fiber. The length decreased gradually, until it finally disappeared, while the capsule gradually changed to an oval shape. However, some abnormal forms of capsules were also found.

The above phenomenon seems to identify Hoepli's syndrome (1932). The reason is

that a special proteolytic enzyme is constantly secreted from the cephalic glands of the miracidium in the mature eggs. The enzyme can penetrate the minute pore of the egg shell, and dissolve the capillary, submucosa and mucosa. Therefore, the oviposited eggs are easily discharged into the lumen of the bowel and passed into the feces. Similarly, the mature eggs following the proteolytic enzyme, can also readily break through the smooth (circular and longitudinal) muscles and peritoneum, and be finally discharged into the peritoneal cavity.

This study was supported in part by the National Science Council, ROC (No. NSC72-0412-B010-12), and in part by the Veterans General Hospital, Taipei, ROC, FY1983.

A NEW MODULATING MECHANISM FOR GRANULOMA FORMATION IN SCHISTOSOMIASIS JAPONICA

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Recently demonstrated evidence indicate that reduced efficiency of embryonation of *Schistosoma japonicum* eggs in the tissues, i.e. anti-embryonation immunity is a contributory mechanism to modulation of granulomatous hypersensitivity in chronic in-

fection. Fresh uterine eggs of *S. japonicum* mature less efficiently in chronically egg-sensitized mice. Also sera from some chronically infected humans modulate granuloma formation and reduce rate at which eggs mature in liver and intestines of infected mice.

EFFECT OF FOOD ON OLTIPRAZ PHARMACOKINETICS AND ANTISCHISTOSOMAL EFFICACY

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Coadministration of Oltipraz with a fatty diet increased significantly its plasma concentrations. The effect of the fatty diet on Oltipraz pharmacokinetics and efficacy was examined on two age and weight matched groups (A & B) of *S. mansoni* patients. Group A (14 patients with an egg output of 260-1320 egg/g received a single dose of 25g/kg body weight with food. Group B (11 patients, with an egg output of 240-720 egg/g) were dosed similarly but without food. Efficacy was assessed by stool examination

on 3 consecutive days for egg count and hatching. The PPC (mg/l), PPCT (hrs) and AUC were determined. The values were 1.574 ± 0.14 mg/l; 4.0 hrs & 0.8768 for group A & 0.205mg/l; 4.5 hrs & 0.1595 for group B. All patients of group A were cured 6 weeks after therapy. The difference in cure rate in the two groups was significant. In conclusion, coadministration of Oltipraz with fatty food enhanced considerably its blood levels and antischistosomal efficacy.

A REVIEW OF THE CHEMOTHERAPY OF SCHISTOSOMIASIS IN THE FAR EAST

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There are at present two defined species of schistosomes which are known to infect humans in the Far East. These are, *Schistosoma japonicum* consisting of several geographic strains (Peoples Republic of China, Philippine Islands, Japan and Indonesia) and *S. mekongi* (Laos and Cambodia).

S. japonicum infections have for the most part been the more intractable to treatment with currently available drugs than any of the major schistosome species infective to man. This species has for the most part been the most resistant of the species to treatment with

antimony compounds, especially to the compound fuadin.

Since 1962, two of the non antimonial compounds introduced clinically for treatment of schistosomiasis have shown excellent efficacy against *S. japonicum*. Niridazole, introduced clinically in 1964, and used extensively for several years is no longer the drug of choice for treatment of *S. japonicum* due to its severe toxicity. Praziquantel, introduced clinically in 1983, is now the drug of choice for treatment of *S. japonicum* with low levels of toxicity reported.

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Still in the investigational stage is the drug Amoscanate which has shown curative efficacy against *S. japonicum* both experimentally and clinically.

For *S. mekongi*, very little data is available concerning the response of this species to currently available drugs used in the therapy of schistosomiasis. However, the limited data available (experimentally and clinically) indicates that two drugs, praziquantel and amoscanate have excellent activity against

this species. Praziquantel has been used to treat infected persons in America, Canada and Thailand and high levels of efficacy were obtained. Amoscanate has been studied experimentally in mice and monkeys for both prophylactic and curative activity and the results obtained are very promising.

Discussion of the dosages, toxicity and mode of action of the drugs used to treat *S. japonicum* and *S. mekongi* were also presented.

EFFICACY OF DISTOCIDE IN *CLONORCHIS SINENSIS* INFECTION

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Distocide, a brand name of Praziquantel preparation by Shin-Poong Pharm. Co., Seoul, Korea, was administered to 64 (37 males, 27 females) human clonorchiasis cases.

Two different regimens: 75 mg/kg of body weight in a day and for 2 days, were applied. The results were summarized as follows:

To 11 light and 15 moderate infection cases, three doses of Distocide of 25 mg/kg in a day were administered orally. Three weeks after treatment 25 cases were cured. The egg

reduction rate and the cure rate were 98.7% and 96.2% respectively.

To 22 light, 15 moderate and a heavy infection cases, three doses of Distocide of 25 mg/kg in a day were administered orally for 2 days. Three weeks after treatment the egg reduction rate was 100% and the cure rate was 100%.

During the first day of drug administration mild headache and dizziness were complaints from 3 cases as immediate untoward side effects, but were temporary.

PRAZIQUANTEL IN THE TREATMENT OF SEVERE OPISTHORCHIASIS VIVERRINI

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Clinical trial of praziquantel on severe opisthorchiasis viverrini was carried out at the

Bangkok Hospital for Tropical Diseases in July 1982 to June 1984 on 88 adult patients.

Clinical evaluation, laboratory tests including hematology, biochemistry, urinalysis and faecal egg counts were performed before treatment. The patients were treated with praziquantel 25 mg per kg body weight tid for one day. Clinical assessment and laboratory tests were performed weekly during the first month after treatment and once on 2nd, 3rd, 6th, 12th, 18th and 24th month. Percutaneous liver biopsies were done on 10 patients and 12 patients were referred to surgery.

Fifty-one patients came for follow-up. 31.4, 29.4, 13.7 and 7.8% completed the follow up period of one, two, three and six month respectively. Few came back in one and two year period. The results of treatment were : 7.8% complete recovery; 23.5% had good improvement, 41.2% had partial or no improvement. The mortality rate was 11.8%

There were 16 cases associated with adenocarcinoma of the bile duct which were excluded from the evaluation.

CLINICAL FIELD TRIAL OF PRAZIQUANTEL ON OPISTHORCHIASIS IN NONG RANYA VILLAGE, KHON KAEN PROVINCE, THAILAND

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Nong Ranya Village, Amphur Ban Phai, Khon Kaen Province, 450km. northeast of Bangkok had a population of 309 individuals with 94% prevalence rate of opisthorchiasis. Sixty percent of adults and 15 percent of children had mild gastro-intestinal symptoms (many of them harboured intestinal parasites). A mass treatment was carried out using a single dose of praziquantel at 40 mg per kg body weight. Acceptance for treatment was 91%. Follow up stool examination done on days 14 and 60 showed prevalence of opisthorchiasis 20.5% and 22.2% respectively.

Side effects including dizziness, headache, abdominal discomfort, nausea, vomiting, diarrhoea, lassitude, arthralgia, sleepiness, cramps and hot sensation were the complaints from 80% of adults and 40% of children. All these were mild and transient except in one adult female, who had severe diarrhoea, required intravenous fluid replacement.

This study was supported by a grant from the Rockefeller Foundation and Chongkhon-nee Foundation.

CONTROL OF SCHISTOSOMIASIS JAPONICA THROUGHOUT JAPAN

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Efforts to control schistosomiasis japonica in Japan were stimulated by a series of epidemiological surveys carried out by the 406th Medical General Laboratory and Japanese scientists from 1947-1951. This revealed that 93.2% of 18,788 persons who were examined harbored one or more intestinal parasites. Beginning in 1947 the screening of molluscicides was undertaken, followed by a successful cooperative pilot control experiment (1950-51) in Nagatoishi, Kurume, Kyushu resulting in 99.5% control of the snail host (*Oncomelania h. nosophora*) and the reduction of new cases from 30-35 a year to 5 and 0 at the end of the experiment. This encouraged the Japanese Government to use this molluscicide (and later others) in the 5 main endemic areas of schistosomiasis throughout Japan.

In 1973 a committee was appointed by the Ministry of Health and Welfare to run a series of epidemiological surveys in the former endemic areas of schistosomiasis. A total of 18,923 persons were examined and screened by the IDT, COPT and 5 stools on those who were COPT positive; 9.6% of these stools were positive for eggs of *S. japonicum*. In 1978 the same committee examined 9,279 from the prefectures in which persons were still positive in 1973. The same techniques were used and none were positive for eggs. This same group found some snails, rodents and dogs infected in 1973, but none in 1978. Thus it is clear that by 1978 schistosomiasis japonica had been controlled. A follow-up study should be made to be sure that this disease does not break out again.

CHEMOTHERAPY OF OPISTHORCHIASIS AT BANGKOK HOSPITAL FOR TROPICAL DISEASES

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Clinical drug trial on opisthorchiasis has been an ongoing concern of the Bangkok Hospital for Tropical Diseases from 1965 to date. Up to 1977, 220 patients were treated with various drugs.

The drugs which had minimal or no effect

were chloroquine, bithionol, bitoscanate, metronidazole, lucanthone HCl, and niclofolan.

The drug which had moderate effect but produced high side effects (diarrhoea, myalgia, arthralgia, anorexia and lassitude) was dehy-

droemetine 1.5-2.5 mg/kg/day in divided doses for 10 days producing cure rate up to 57%.

Chlorxyle at 100 mg/kg/day for 5 days yielded 81% to 100% egg reduction.

From 1978 to date some 30,000 patients were treated with various dosages of albendazole and praziquantel.

Albendazole:

- (1) 2×400 mg \times 3 days yielded 12% cure rate and 94% egg reduction in 25 patients (geometric mean egg count per gram 15540).
- (2) 2×400 mg \times 7 days yielded 33% cure rate and 95% egg reduction in 27 patients (geometric mean egg count per gram 16326)

Side effects, diarrhoea and headache were mild and transient.

Praziquantel at 60 day follow up

- (1) $3-6 \times 25$ mg/kg in one and two days yielded 100% cure rate. (5 stools examination)
- (2) $1-2 \times 25$ mg/kg in one day yielded 44-88% cure rate (5 stools examination)
- (3) 1×40 mg/kg single dose yielded 90.90% cure rate (5 stool examination).
- (4) 1×50 mg/kg yielded 97-98% cure rate (single stool examination).

Side effects were mild and transient including diarrhoea, abdominal pain, headache, dizziness and sleepiness; they are much less when a single dose was given at bed time. A single dose is relatively safe when concomittent brain lesions of paragonimiasis and cysticercosis were present.

This study was supported in part by Bayer AG, and Smith, Kline and French, Overseas Co.

OPISTHORCHIASIS IN THAILAND : A REVIEW ON CHEMOTHERAPY AND CONTROL IN ENDEMIC AREAS

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Liver fluke infection in Thailand caused by *Opisthorchis viverrini* is regarded as a public health problem in rural communities in Northeast Thailand and in some provinces of North Thailand. Praziquantel is the drug of choice for the treatment of the patients in the hospitals, with dosage of 25 mg/kg body weight 3 times after meals for one day (a total of 75 mg/kg body weight in one day) producing a cure rate of 100%. In mass treatment in a community, praziquantel is administered as 40 mg/kg body weight once at bed time, the cure rate being about 91%. There were some adverse side effects including

nausea and vomiting, giddiness, headache, abdominal discomfort, myalgia and occasional diarrhoea, which were mild and transient.

Recently Albendazole was reported to have some effective results with the dosage of 400 mg (2 tablets) twice daily after meals for 3 days. The cure rate after 60-90 days was 70%, and there were mild side effects including diarrhoea and headache in a few cases.

Mebendazole at the dosage of 30 mg/kg body weight per day in 3 divided doses for 3

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weeks was reported to yield a cure rate of about 94% after 6 months. There were no side effects with this dosage, even though the course of treatment was long and the drug was rather costly.

For the control of opisthorchiasis in Northeast Thailand, the Faculty of Tropical Medicine has launched since 1981 a pilot control project in Khon Kaen province using a combination of annual mass treatment with praziquantel, improvement of environmental sanitation through primary health

care system and health education to prevent reinfection through village volunteers. The results so far were encouraging, and the expansion of the project to cover a larger scale is being carried out.

The Ministry of Public Health of Thailand has launched since 1984 an opisthorchiasis control programme by establishing 3 *Opisthorchis* Treatment Centres in 3 provinces in Northeast Thailand. The work so far has been satisfactory and is carried out in good progress.

CURRENT STATUS OF CLONORCHIASIS IN KOREA

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Clonorchiasis has been endemic in Korea for a long time. The number of clonorchiasis cases in the Republic of Korea was once estimated in 1959 to be 4.5 million, 15% of the then 30 million population. The endemic areas have been distributed mainly in the plains of the major river valleys. Such holoendemicity of clonorchiasis in Korea has been caused by a wide distribution of intermediate hosts of *Clonorchis sinensis* in many waterbodies of the ecosystem, common habitual practice of raw freshwater fish consumption among local people, and the absence of effective chemotherapy for mass treatment before the advent of praziquantel in the 1980s.

It has been observed recently that the prevalence of *Clonorchis* infection has significantly decreased in nature during the past decade particularly in the endemic areas of lower river valleys throughout the country.

Such regressive transition of the prevalence has largely been due to the water pollution

caused by the recent rapid industrialization and urbanization in many of the endemic areas since 1970s. Water pollution has upset the ecosystem in many of the land waters containing the intermediate hosts of *Clonorchis* and also decreased the consumption of freshwater fish from such waterbodies. The pollution has also contributed in some extent to the aim of health education by preventing young generations from getting infection on, habits of raw freshwater fish consumption.

However, raw freshwater fish consuming habits of the local people in many other areas would not seem to change in the near future. In the areas of upper river valleys where water pollution has never occurred, freshwater fish are consumed raw by village people more often among adult males. In another aspect, pisciculture free of *Clonorchis* infection has become popular in some of the reservoirs of upper river valleys.

In contrast to the common knowledge that the clonorchiasis is prevalent in the plains, the endemicity of the infection has recently been found to be extended even to the mountainous upper valleys of the major rivers.

Mass chemotherapy for clonorchiasis has been conducted since 1982. So far, by the Government support, a total of 52,343 cases were treated with praziquantel. In 1982, 2,958 cases out of 28,826 persons examined were treated. In 1984, 17,895 cases (13.3%) out of 168,877 examined were treated. In 1985, 31,490 cases (7.0%) out of 447,237 examined are under treatment. Case finding surveys were conducted along the endemic river valleys throughout the country. This

type of control programme will be extended for successive years. Also, praziquantel has widely been used by clinic and community basis for treatment of clonorchiasis. So far in the past 4 years, some 244,000 packets (600 mg \times 8) were sold locally by the two firms.

In conclusion, the prevalence of *Clonorchis* infection in Korea has been decreasing rapidly largely owing to the natural regressive transition and wide application of chemotherapy with praziquantel. However, it is mandatory that the control campaign of clonorchiasis has to be continued for many years before reaching a negligible level of prevalence of the infection.

AN ATTEMPT TO STUDY THE CASE FATALITY RATE IN *SCHISTOSOMA JAPONICUM* INFECTION IN THE PHILIPPINES

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As a sequence to a cross-sectional study on the clinical gradient of the disease by Pesign et al., a follow-up of the subjects in that study was made after 12 years. Of the 135 untreated cases followed up, 23 (17.04%) died from various causes of which 12 (8.89%) had signs and symptoms attributable to schistosomiasis as the immediate cause or one of the main causes of death. This occurred in 1 to 11 years with an average of 5 years,

which corresponds roughly to 1.78% of the infected cases per year. This is considered a conservative estimate for in the other deaths due to other diseases, schistosomiasis is a contributory cause.

A diminishing severity of the disease was observed among the surviving patients which will imply that some form of immunity has been developed by them.

AMOEBIASIS IN SOUTHEAST ASIA

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The prevalences of intestinal amoebiasis in Southeast Asia are considered moderate: 4-8% in Malaysia; by a single stool examination carried out in 1983, the overall prevalence was 8% (range 6-13%) in Indonesia, highest in Java; and 5% (range 2-8%) in the Philippines. The epidemiological survey using indirect haemagglutination test; the positive rate in Indonesia was 14% (range 4-34%) and for the Philippines 5% (range 1-13%). The seropositive rate was higher for males than females and the rates higher in the older age groups.

In Thailand, the overall incidence is rather low 0.5-3.5% in 1970 in many provinces. At the out patient department of a university medical school, general hospital in Bangkok, it was 10.7% in 1979. However, in an orphanage in Bangkok it was as high as 18%.

At present, acute amoebic dysentery is not common, and severe fulminating, necrotising amoebic colitis is very rare. Complications including haemorrhage, perforation was common in the past.

For extraintestinal amoebiasis, amoebic liver abscess is the most common. During the past 40 years more than 1,000 cases of amoebic liver abscess were admitted to one of the largest hospital in Bangkok. Incidence predominately in adults between 30 to 60 years of age with a higher frequency in males

than females (7:1%). A single cavity was found in 90% especially in the upper part of the right lobe. The pus was bacterologically sterile, blood odour, and anchovy sauce in colour.

The clinical features are fever, pain over the liver region or right lower chest, often referred to the right shoulder. The liver usually enlarged and tender. The right dome of the diaphragm elevated with limitation in movement. Blood picture shows leucocytosis with high percentage of neutrophils and mild anaemia. Scintillography, ultrasonography and computerized axial tomography show space occupying lesion. Serodiagnosis for *E. histolytica* antibodies was positive in 95% of the cases.

Pulmonary amoebiasis, brain abscess, pericarditis secondary to liver abscess have been observed.

On rare occasions amoebiasis of other organs including amoebic cervicitis, vaginitis, cystitis and cutaneous amoebiasis have been reported.

With early diagnosis and potent amoebicides together with better management the prognosis is good; the mortality is less than 5%.

Better sanitation, clean water supply and health education play important roles in the reduction of the prevalence of amoebiasis.

EXPERIMENTAL STUDIES ON THE ESTABLISHMENT OF AMOEBIC LIVER ABSCESS

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This study is to visualize the effect of amoeba on the amoebic abscess formation in the experimental animals which is in the state of impaired hepatic function.

Entamoeba histolytica, strain YS-27 and YS-37, was isolated from the patient with amoebic liver abscess. These amoebae were cultured with concomitant bacteria in the modified diphasic medium. The amoebae were inoculated directly into the hepatic parenchyma of mice, rats, golden hamsters and also intravenously into the superior mesenteric vein of the rabbits. Six to 11 days after the inoculation, the animals were sacrificed and the liver examined.

In healthy control, amoebic abscess was not developed in mice, rats and rabbits except in the golden hamsters.

Vacuolization of the hepatic lobule was seen 3 hours after injection of thioacetamide, and mild fatty degeneration was observed 24 hours after carbon tetrachloride administration. In all the rats pretreated with these two hepatotoxic agents, amoebic abscess developed in the liver.

These findings suggest that liver of impaired function may predispose to the development of hepatic amoebic abscess when challenged with *Entamoeba histolytica*.

MANAGEMENT OF AMOEBIC LIVER ABSCESS

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Amoebic liver abscess is the most common form of extra intestinal amoebiasis. In the early part of this century the mortality was approximately 80 per cent but at present with early diagnosis and proper management the mortality is less than 5 percent.

The primary objective in management of amoebic liver abscess is to eliminate the causative organism by using potent amoebicidal drug and aspiration of pus.

Any of the imidazole derivatives (metronidazole, ornidazole and tinidazole) at a dosage

of 1.2-2.4 gram single or divided doses in 24 hours together with aspiration of pus at intervals will give complete cure. The fever, pain and tenderness disappear within a week but it takes some weeks for the cavity to close depending on the size of the cavity, nutritional status of the patient and the duration of illness.

The alternative amoebicide when imidazole is not available or oral administration is inapplicable is emetine or dehydroemetine hydrochloride at a dosage of 1 and 1.5 mg/kg/day respectively for 10 days.

ABSTRACTS

Evacuation of pus is essential if there is more than 100 ml of pus or the diameter of the cavity is more than 6 cm. Needle aspiration is recommended, as it is easy to perform, the healing is quick and there are less complications.

The site and size of the abscess cavity can be visualised in the x-ray film by instillation of air and descending iodized oil into the cavity and by taking x-ray at intervals, the rate of

healing of the abscess can be monitored. The cavity of the abscess is filled by regeneration of hepatocytes from the central towards the peripheral part of the liver.

Symptomatic and supportive measures are valuable for convalescence. The prognosis is good. Relapses are rare. Cirrhotic or malignant changes following amoebic liver abscess has never been observed.

DIAGNOSIS AND TREATMENT OF AMOEBIC LIVER ABSCESS AT CIPTO MANGUNKUSOMO HOSPITAL.

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At the Department of Internal Medicine, Faculty of Medicine, University of Indonesia/ Cipto Mangunkusumo Hospital within 3 years, 25 cases of amoebic liver abscess, were diagnosed.

The diagnosis is certified by clinical, serologic test and USG. Aspiration of

abscess was carried out on 5 cases and the result was positive in 2 cases.

Five cases were found positive with cysts and trophozoites by stool examination. Treatment with metronidazole 4×500 mg gave satisfactory result in variation ± 15 - 30 days. In 5 cases metronidazole was given with chloroquine 3×200 mg.

HEPATITIS B VIRUS INFECTION STATUS AND HEPATOCELLULAR CARCINOMA IN INDONESIA

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The average carrier rate of HBV is 5.5%, but there is variation in percentage from

place to place in Indonesia, and even from sample to sample.

There is a tendency of decreasing carrier rate in the older age group. The carrier rate among hospital personnel is the same as for the normal population. In younger age group of female hospital personnel the anti-HBs was greater than female normal population of the same age group.

The HBsAg carrier rate was significantly higher among lower socio-economic group while there was no clear correlation with education status.

The carrier rate among hospital personnel working in the dialysis ward was not different from the normal population but the anti-HBs rate was higher. This is not related to their work.

The positive e-Ag among carriers in younger pregnant woman must be considered as a special epidemiologic problem.

In a rural area with a high carrier rate, the household contact was also frequent and

this was also seen among family members of patients with HBsAg positive liver diseases.

About 10% - 20% of liver diseases admitted to hospitals in the big cities in Indonesia was hepatocellular carcinoma. Male to female ratio was 3:1 and the highest frequency was found in a 40-50 years age group.

Enlarged hard nodular liver was found in almost every patient. In 50% - 75% there was associations with cirrhosis hepatitis.

Increased alkaline-phosphatase is still used as a laboratory finding to support the diagnosis. The associations with HVB infection is around 50-70%.

Aflatoxin still played a potential role in hepatocellular carcinoma cases.

Although the hospital mortality was 10%-30%, all of the cases were in the advanced stage.

THE RELATIONSHIP BETWEEN *CLONORCHIS SINENSIS* INFECTION AND CHOLANGIOCARCINOMA

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A retrospective epidemiological study was conducted with 348 subjects who were recorded as primary liver carcinoma cases by histopathologic examination during a 5 year period of 1978-1982 in the high endemic and the low endemic areas of clonorchiasis in Korea to elucidate the evidence whether any relationship exists between *Clonorchis sinensis* infection and cholangiocarcinoma.

Besides the epidemiological study, mice were infected with the metacercariae of

Clonorchis sinensis to examine the histopathological changes of the bile ducts. Human cases having cholangiocarcinoma in association with *Clonorchis* infection were studied to identify the histopathologic characteristics.

The epidemiological review showed that occurrence of cholangiocarcinoma associated with clonorchiasis in the high endemic area was not significantly different in comparison with the low endemic area, while difference between occurrences of cholangiocarcinomas

ABSTRACTS

in association with clonorchiasis and cholangiocarcinoma alone in each area was revealed to be highly significant ($p < 0.005$). The animal experiment demonstrated chronological sequences of the histopathological changes in the bile ducts, although no neoplastic transformation was demonstrable at any stage. All tumors found in human cases having *Clonorchis* infection were con-

firmed as mucin-producing cholangiocarcinomas which have arisen from the metaplastic adenomatous tissue lining the second-order bile ducts.

With those findings clonorchiasis appears to act as a basically important predisposing factor in the carcinogenesis of bile duct epithelial cells.

LIVER FLUKE : RELATIONSHIP OF CHOLANGIOCARCINOMA, DIETARY HABIT AND FOOD CONTAMINANTS

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Concerning the carcinogenesis of cholangiocarcinoma in liver fluke infection many factors have to be considered, namely food habits, food contaminant due to chemical carcinogens and alterations of bile acid levels. The obstruction of the worms which irritated the tissue mechanically might not be only involved in metabolic synthesis but also might cause the retention of regurgitated bile acids from portal to systemic circulation.

In northeastern Thailand raw fish (Goi-pla) and uncooked fermented fish (Pla ra) is commonly consumed in combination with vegetables which are also a source of nitrate. The preparation of *Pla ra* is carried out under primitive village conditions without any particular concern for modern standards of hygiene. Nitrate, nitrite and N-nitroso compounds were detected in many locally Thai preserved protein foods including *Pla ra*. It is interesting to note that nitrate and nitrite were also found in rock salt, which is commonly used in the northeast, and also in water supplied both from the

northeast and from Bangkok including tap water.

Serum bile acid pattern were studied in 38 controls and 84 patients with opisthorchiasis. Total bile acid, glycochenodeoxycholic acid, taurocholic acid, taurochenodeoxycholic acid in patients were significantly higher than those of the control while glycine/taurine ratio and trihydroxy/dihydroxy ratio were found to be significantly decreased.

During the processing and preparation of *Pla ra* which is sometimes stored for several months, secondary and tertiary amines are probably formed. These amines may react with nitrates and nitrites that are present as contaminant in salt or water to form nitrosamines. The interaction between *O. viverrini* infection, N-nitroso compound and the high level of bile acid which may react as promotor for carcinogenesis of cholangiocarcinoma were also discussed. These factors may play an important role in causing a high incidence of cholangiocarcinoma in humans in the northeast of Thailand.

ORIENTAL INFESTATIONAL CHOLANGITIS

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One hundred forty-one patients with non-neoplastic cholangitis in Southwest Korea were analyzed for etiologic factors, pathologic changes, and clinical management in an effort to understand the clinico-pathologic course of this disease. The study supports the concept of infestational cholangitis. A

staging system for this disease process has been proposed. The limited value of choledocholithotomy and choledochostomy in the more advanced stages of the disease process has been documented, suggesting the need for more effective internal biliary drainage when irreversible changes have occurred.

HEPATOCELLULAR CARCINOMA AND CHOLANGIOCELLULAR CARCINOMA, COMPARATIVE ANGIOGRAPHIC STUDY OF 127 PATIENTS

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The angiographic findings in 127 patients with primary carcinoma of the liver were analysed in an attempt to find points of differentiation between hepatocellular carcinoma (HCC, 93 patients) and cholangiocellular carcinoma (CCC, 34 patients). Altogether 123 aortographies, 91 coeliac and 24 superior mesenteric angiographies were performed. Vascularity was the most significant feature, with HCC being more vascular than CCC. Diagnostic accuracy rate was 91.4% for HCC and 70.4% for CCC. Tumor vessel and stain and areas of avascularity were visualised

more often in HCC. Arterio-venous shunt, hypervascularity, encirclement of the tumor by arteries, invasion of hepatic artery and its branches by the tumor and vascular stasis were significantly more common in HCC. The intrahepatic arterial intercommunication and the capability to draw blood demonstrated by enlargement of the collateral arteries and development of new arteries were found in HCC only. According to the aforementioned finding, HCC is quite distinctive in angiographic appearance. Intern. Med, 1985; 1 : 16-20.

CLINICAL TRIAL OF 5-DEOXY-5-FLUORURIDINE (DOXIFLURIDINE) IN THE TREATMENT OF PRIMARY HEPATOCELLULAR CARCINOMA

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Doxifluridine is a new chemotherapeutic agent belonging to the fluorinated pyrimidine group. It is a prodrug of 5-Fluorouracil and seems to be significantly more potent than the latter. After oral or intravenous administration doxifluridine accumulates in the tumour tissues at a higher level than normal. It has been used in the treatment of some solid tumours with favourable results.

In view of these results doxifluridine was used in unresectable primary hepatocellular carcinoma, a tumour for which there is no adequate treatment.

Between June 1983 and December 1984 in Veterans General Hospital, Taiwan, an open pilot study was conducted on 17 patients suffering from hepatoma and treated with doxifluridine. Age ranged from 51 to 65. All patients had been histologically or cytologically proved to have hepatocellular carcinoma. Sixteen patients were positive to HBsAg and one patient positive to anti-HBs. The serum bilirubin was below 2mg%, leukocyte count over 4000/c.mm, platelet count over 120000/c.mm and Karnofsky index above 40% before treatment.

Doxifluridine was given intravenously with dosage of 2g/m²/day for 5 consecutive days,

every 3 weeks. Blood tests and chemistry, alpha-feto protein, CT scan were performed regularly to evaluate the effect of the drug and monitor its eventual side-effects. Three patients changed to Chinese traditional medicine and were lost for follow-up.

In 13 out of 14 patients the tumour progressed in spite of the treatment and the patients died after a mean survival per year of 4.2 months. In one single patient the size of the tumour decreased more than 50% after 4 courses of doxifluridine but the patient died one month later from progressive hepatic failure. Partial response in this study was 7% (1/14). In three patients, including the partial response patient, HBsAg disappeared after treatment. Side-effects included dizziness (7), nausea (2), dry mouth (6), anorexia (6), hair loss (5), skin eruption (1), pruritus (1), pigmentation of skin (1), diarrhoea (2), stomatitis (1), rectal ulcers with bleeding (1), jaundice (1), and leukopenia (1).

In conclusion, doxifluridine given intravenously to patients presenting with unresectable primary hepatocellular carcinoma does not alter the fatal evolution of the disease. It remains to be seen whether the administration of this compound by hepatic pump system would give better results.

RECOMBINANT LEUKOCYTE A INTERFERON VS ADRIAMYCIN IN HEPATOCELLULAR CARCINOMA: A RANDOMISED TRIAL

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The median survival of untreated hepatocellular carcinoma (HCC) in Hong Kong is 3.5 wks (1 day - 70 wks).

55 patients with inoperable HCC and with Karnovsky scale of > 70%, were randomised to receive (A) adriamycin 60-75 mg/m² IVI every 3 wks, (B) recombinant leukocyte A interferon (IFL-rA) (Roche) 20 × 10⁶ U/m² IMI daily or (C) IFL-rA 50 × 10⁶ U/m² IMI thrice weekly. Patients not responding after

a complete course of one drug were switched to the other drug. The 3 treatment groups were comparable in clinical and biochemical status. Response to treatment was assessed in patients surviving over 4 weeks, using (1) liver span (2) ultrasonography, (3) α -fetoprotein/ferritin levels and (4) tumour size at diagnosis and at autopsy. The tumours were defined as regressing if 2 or more of the above 4 criteria decreased by > 25%.

The results were as follows:- Five patients had switching of drug therapy.

	Adriamycin	Daily	IFL-rA 3 × wkly	Total
No. of patients	20	18	17	35
Median survival (Range)	5wk (1-25.5)	11wk (1-62)	7wk (1.5-54)	10wk (1-62)
Dead within 4 wks	7	5	6	11
Tumour size assessment				
Progressive	8*	1	2	3*
Non-progressive	3	7	2	9
Regressing	0**	4	5	9**
Fatal drug complications				
Cardiotoxicity	3	0	0	0
Septicaemia	3	0	0	0
Hyperkalaemia	0	1	0	1
Total No. of patients	6***	1	0	1***

* p = 0.0018 **p = 0.0103 ***p = 0.0103 (Fisher's Exact Test)

In the treatment of HCC, IFL-rA, when compared with adriamycin: (a) shows similar patient survival, (b) causes less fatal complications and (c) induces more tumour regression in those patients who survived over 4 weeks.

FINE NEEDLE ASPIRATION IN SUSPECTED LIVER CANCER

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This study was carried out to assess the value of fine needle aspiration (FNA) in suspected liver cancer.

During a period of 20 months (October 1, 1983 to May 31, 1985) FNA under ultrasonic guidance was performed on 77 consecutive patients with suspected of having liver cancer. A real time linear scanning with an ordinary or a puncture transducer were used for this purpose. The aspirated sample was stained according to papanicolaou technique for cytological examination. In most patients final diagnosis was confirmed by a follow-up study.

Correct diagnosis of FNA was found in 71 of 77 patients (92.2%); 66 with liver cancer and 5 with benign lesion. False negative diagnosis was obtained in two patients (2.6%) with primary liver cancer. Inconclusive diagnosis was found in four patients (5.2%); one patient proved to have secondary liver cancer on liver biopsy and the other three patients refused to undergo further investigations. Complications were not noticed in this study.

Ultrasonically guided fine needle aspiration gives a high diagnostic value in suspected liver cancer.

RELATIVE RESISTANCE TO *SCHISTOSOMA MANSONI* IN A STRAIN OF *BIOMPHALARIA STRAMINEA* INTRODUCED TO HONG KONG

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A strain of *Biomphalaria straminea* which was introduced into Hong Kong before 1974 was tested as intermediate host of *Schistosoma mansoni* (Belo Horizonte strain, BHSM).

Observations of 1 snail and 1 miracidium reveal that penetration lasts much longer than in *Biomphalaria glabrata*. This may indicate that *Biomphalaria straminea* is a less adequate host snail for the schistosome strain used in this experiment. 13 days post exposure no mother sporocysts were found. 35 days post exposure none of the snails shed cercariae

but mortality during prepatency seems to be high.

Sectioning of *Biomphalaria straminea* after mass exposures suggests that miracidia of *S. mansoni* were destroyed by host cells even short after penetration. *B. straminea* should be tested for its suitability as decoy snails in long channel experiments. Furthermore hemolymph of *B. straminea* and *B. glabrata* were compared in miracidial immobilizing tests.

A MALACOLOGICAL STUDY ON *PARAFOSSARULUS*
MANCHOURICUS, AN INTERMEDIATE HOST
OF *CLONORCHIS SINENSIS*

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The most medically important snail species of Korea is *Parafossarulus manchouricus*, a member of the freshwater prosobranch family Bithyniidae. The parasite that this snail transmits to humans is *Clonorchis sinensis*, the Chinese liver fluke. This trematode worm is one of the main snail-borne parasites of the Orient, where it infects hundreds of thousands of people in China, Japan, Korea, Vietnam and presumably parts of India.

A second bithyniid species occurs in Korea, *Gabbia misella*. This species also has been suggested as an intermediate host of *C. sinensis*.

However, critical information on *P. manchouricus* and *G. misella*, as well as the whole family to which they belong, is very limited.

The local populations of *P. manchouricus* and *Gabbia misella* were compared in regard to various biological characteristics in this study.

These snails are interoparous and lay eggs once a year. *P. manchouricus* grew to adult size in about 54 days after hatching and laid eggs 150-156 days after hatching.

The bithyniid protoconch is nearly smooth, except for small, low spiral wrinkles, a sculpture which is quite different from that of the Hydrobiidae, a family in which the bithyniids are sometimes placed.

Two different chromosome numbers were observed in the two bithyniid species: $n = 17$ in *P. manchouricus* and $n = 18$ in *G. misella*. There were also morphological differences in the karyotypes of the two species, as might be expected.

Allozyme variations between the local populations of *P. manchouricus* and *G. misella* were observed in glutamate-oxaloacetate transaminase. The banding patterns were population-specific in the Chongpyang (Korea) strain of *P. manchouricus*. The variability may be related to genetics of susceptibility to *Clonorchis* infection.

Laboratory-bred *P. manchouricus* (Human population) were susceptible to *Clonorchis sinensis*, with an overall infection rate of 15%, while Chongpyung population were not entirely susceptible. *Gabbia misella* was refractory to infection with *C. sinensis*, and therefore do not need to be emphasized in snail surveys for clonorchiasis.

LEPTOSPIROSIS IN THAILAND: AN EPIDEMIOLOGICAL PATTERN

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Serological tests for human leptospirosis in Thailand using the agglutination (lysis) test for *Leptospira* on dried blood filter papers were performed in the Leptospirosis Reference Laboratories of the Faculty of Tropical Medicine, Bangkok during 1975-1984. The total 10 year specimens of 8,573 dried blood filter papers included 5,288 specimens from Bangkok hospitals (61.7%) and 3,285 from hospitals in provincial areas (38.3%). The positive agglutination reactions for serotypes of *Leptospira* were found to be 7.9% for those from the Bangkok hospitals, while those from the provincial hospitals were 9.2%, an average of 8.4%.

The serotypes of *Leptospira* found in Bangkok were *L. bataviae* (81.1%), *L. canicola* (3.3%), *L. javanica* (3.0%), *L. autumnalis* (2.5%), *L. hebdomadis* (1.9%), *L. australis* (1.6%), *L. grippityphosa* (1.6%), *L. icterohemorrhagiae* (1.6%), *L. wolffii* (1.3%), *L. hyos* (1.1%), and *L. pyrogenes* (0.8%), while those in provincial areas were *L. autumnalis* (33.6%), *L. bataviae* (18.8%), *L. icterohemorrhagiae* (8.3%), *L. wolffii* (7.6%), *L. canicola* (6.8%), *L. javanica* (6.8%), *L. hebdomadis* (5.4%), *L. australis* (4.7%), *L. grippityphosa* (4.7%) and *L. pyrogenes* (3.3%).

The seasonal prevalence and highest incidence of leptospirosis cases in the hospitals were during the late rainy season i.e. in September-October-November (13.7%-25.8

%), and in early cool season, i.e. December (17.5%). About 65-70% of cases were farmers and labourers whose occupations were liable to expose themselves to contaminated with *Leptospira*.

A clinical investigation on 37 leptospirosis cases in a Bangkok hospital during 1969-1983 revealed that most cases were admitted during November. There were 30 males and 7 females aged between 16 and 74 years with the main symptoms of high fever (92%) and myalgia in lower extremities (93%), nausea and vomiting (90%), mild diarrhea (57%), and with signs of jaundice (73%), injected eyes (68%), muscular tenderness (64%), slight and moderate liver enlargement (61%), lymphadenitis of some lymph nodes (38%) and some petechia hemorrhages on the body (27%). Most cases were caused by *L. bataviae* (76.9%), some by *L. javanica* (15.4%) and *L. canicola* (7.7%).

The field studies on animal hosts for leptospirosis in Bangkok and in provincial areas revealed that rats and dogs were the main reservoirs. Rats usually harboured *L. javanica*, *L. bataviae*, *L. hebdomadis* (*L. saxkoeburg*), *L. grippityphosa*, *L. akiyami A*, *L. pyrogenes*, *L. hyos*, *L. icterohemorrhagiae*, *L. wolffii*, *L. pomona*, *L. hebdomadis*, and *L. rachmat*, while dogs generally had *L. bataviae*, *L. javanica*, *L. canicola*, *L. icterihemorrhagiae*, *L. rachmat*, *L. pyrogenes*, *L. hebdomadis*, and *L. ballico*. Pigs were also found to harbour *L. pomona*.

LEPTOSPIROSIS IN THE PHILIPPINES

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Leptospirosis was first isolated in the Philippines from one of the human cases of Weil's Disease in 1932 and from then up to 1970 a total of 65 cases were studied sporadically. From 1971 up to 1973 a total of 390 cases were studied out of which 82 (21.02%) were found positive by isolation and serological examination.

In 1976 an outbreak of a disease in a penal colony in Mindoro was reported and investigated. The patients had the presenting signs and symptoms of fever, muscular pains, chills, body weakness and in some vomiting, abdominal pains, jaundice and hematuria.

At the time of this outbreak, of the 101 sera from patients with complaints within the month, 31% were positive to one or more leptospirosis antigen pools. Forty percent of reactors reacted to only 1 pool. Of 517 sera from residents without complaints, 1% reacted to one or more pools and 89% were non-

reactors. Three and half years later (1980) the sera of 551 from prisoners of the same area were looked into, 10% reacted to one or more pools and 90% were non-reactors. In 1983, 423 sera from prisoners of the same colony were looked into, 6 or 1.4% were reactors to single pools, 4 to pool 3 (*L. autumnalis*), one each to pool 2 (*L. pyrogenes*) and pool 1 (*L. icterohaemorrhagiae*). The rest were non-reactors.

In 1982, 100 serum samples each were tested from agricultural areas in Cebu, Tacloban, Davao and Cotabato. No reactivity whatsoever was detected with any of the leptospira antigen pools utilizing the micro-agglutination slide test. Of 251 samples tested from patients confined in hospitals from 1980 to July 1985, 30 or 11.9% were reactive mostly to pool 2 and pool 3 with specific reactivity to *L. autumnalis* and *L. icterohaemorrhagiae*.

AN ANALYTIC EPIDEMIOLOGICAL STUDY TO TEST THE HYPOTHESIS; LEPTOSPIROSIS AS THE CAUSE OF THE EPIDEMIC PULMONARY HEMORRHAGIC FEVER IN KOREA

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This is a summarized report on the results of the epidemiological investigations carried out mainly by government epidemiology team and in part by other groups.

These epidemiological investigations were carried out to test the causal hypothesis, leptospirosis, on the epidemic pulmonary hemorrhagic fever of which an outbreak

occurred from the middle of September 1984 in Korea.

The outbreak occurred right after group work of farmers all over the country to tie the fallen rice plants following floods just like the one that had occurred in 1975.

This particular syndrome complex characterized by fever, chill, headache, malaise and nausea-vomiting in the beginning of the onset and severe myalgia, chest pain, hemoptysis and dyspnoea had been reported frequently since 1975 as a new disease of unknown etiology. The syndrome complex that has been called by many names like hemorrhagic pneumonia, pneumonia-like disease, epidemic pulmonary hemorrhagic fever has been occurring predominantly among farmers during the fruit bearing season, particularly among those who worked in wet and muddy rice paddies without protection for abraided skin injuries.

The fatality rate reported by researchers varied widely ranging from 6% to 52%, the direct cause of death being asphyxia due to the massive pulmonary hemorrhage.

Despite the continuous effort of researchers the etiology of the syndrome complex had remained unknown.

The objective of the investigation was to test the specific hypothesis, leptospiral infection, which was derived from the literature review. The clinical, pathological and epidemiological features of the syndrome complex was similar to leptospirosis among others.

The principal method for the field investigation was case-control study for human subjects and spot survey of rice paddies in endemic area for environmental study. Field rodents were trapped in two endemic areas and examined for the agent.

The patients who were admitted or has been admitted to Won Ju Presbyterian Hospital

with diagnosis of epidemic pulmonary hemorrhagic fever were matched with their healthy family members, and villagers having worked in the same environment. Also some of villagers who reported to have croup-like symptoms were studied. The military service men in Kwangju area were matched with their healthy fellow soldiers exposed to the same environment.

The patients who were either admitted or visited Hong Chun Clinic were studied without control however.

Human subjects were interviewed with a structured questionnaire, and paired blood and urine specimens were collected except the patients of Hong Chun Clinic. In order to increase the test validity one batch of the specimen was sent to KNIH laboratory and the other to the microbiology department of Yonsei Medical School blindly for the laboratory work.

Environmental study was carried out on rice paddies located at mountainous sites in endemic area where the water source for cultivation is subterranean water that emerged as springs. There were innumerable rodent holes along the paddy banks with massively accumulated ears of rice plant. From these five sites of rice paddies surveyed, about five liters of water were collected for isolation of the agent.

These specimens collected were primarily inoculated to laboratory animals and then cultured in media.

Results obtained from the study were as follows :

- (1) Leptospiral organisms were isolated from seven patients of typical epidemic pulmonary hemorrhagic fever and two villagers with croup-like syndrome, from seven field rodents, and one paddy water specimen concentrated, all of which made

the Koch's postulate satisfactory in laboratory animal model and had characteristics of *Leptospira interrogans*.

- (2) The incidence rate among military service men, the only study group with defined population and date on exposure to the specific environment, was 2.3 per 1,000 person day exposed.
- (3) The incubation period estimated from the same group ranged from 3 to 11 days

and the mean incubation period estimated by a mathematical model from the epidemic curve was 8 days.

- (4) From the results of the study presented it was concluded that the cause of epidemic pulmonary hemorrhagic fever was leptospiral infection.

The study was the first report on leptospirosis epidemic identified bacteriologically in Korea.

LEPTOSPIRA INTERROGANS "KOREA" ISOLATED FROM PATIENTS WITH EPIDEMIC PULMONARY HEMORRHAGIC FEVER

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Eight strains of *Leptospira* were isolated from patients with epidemic pulmonary hemorrhagic fever and natural rice field water samples.

Sera from 23 out of 35 patients strongly reacted with the isolated bacteria by slide agglutination test, immunofluorescent test and ELISA. The major reacting immunoglobulins were IgM and IgG in the sera.

All of the strains were equally pathogenic for guinea pig and mice, which were confirmed by pathology, immunopathology and bacterial analysis of the sacrificed and dead animals with febrile symptom following the bacterial inoculation.

The representative pathologic feature was massive hemorrhage due to diapedesis in the lung and intracellular existence of the bacterial antigens in liver and kidney, which were

equally fluorescent positive for IgM, IgA, IgG and C3.

The characteristics of the bacteria examined by pathogenicity, morphology and some of cultural behavior in artificial media were matched with *Leptospira interrogans*. Three strains (electron microscope) and the bacteria were found to be tightly coiled and the helix handedness was counter clockwise (left). It is generally accepted that pathogenic spiral bacteria reported up to date are coiled clockwise (right).

Therefore, it was concluded that the bacteria isolated from the patients via animal inoculation were the responsible agent for the human infection. They can be characterized as *Leptospira interrogans* according to pathogenicity, cultural behavior except the fact that they are left handed coil. Thus, the bacteria were tentatively named as *Leptospira* "Korea".

DIAGNOSIS AND TREATMENT OF LEPTOSPIROSIS IN JAKARTA

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The leptospirosis cases to day is rare in Indonesia. At the Department of Internal Medicine, Faculty of Medicine, University of Indonesia/Cipto Mangunkusumo Hospital only 10 cases were diagnosed within 5 years.

The outstanding clinical symptoms are

fever, myalgia, icterus conjunctiva, bleeding, hepatomegaly and hematuria. Culture for this organism is difficult and serological test supported the diagnosis. Penicillin procaine still gives satisfactory results in the treatment of leptospirosis. Case reports were discussed in detail.

ASSESSMENT OF THE ECONOMIC BENEFITS RESULTING FROM THE TREATMENT OF SCHISTOSOMIASIS JAPONICA IN LEYTE

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A total of 801 patients were initially examined and subsequently treated. Six hundred thirty (630) were followed-up one year after. It was observed that severe anaemia was significantly reduced from 7.9% to 3.5%; hepatomegaly from 12.9% to 6.0% and the splenomegaly from 1.7% to 0.9%. Among the new cases, a significant reduction in splenomegaly was observed compared to the untreated group of 1983. Based on these clinical findings, it is quite apparent that one of the impact of chemotherapy is the reduction in the morbidity and severity of the disease.

Among those followed-up one year after treatment, 86 or 13.7% were still positive in their stools. These were separated from the negative ones and the latter serve as a control group which gave a relatively good picture of the man-days lost arising from schistosomiasis alone.

Since for the first year of study, this "control group" is not yet available, this was roughly used to eliminate the effect of other diseases or infections for the first year prior to treatment. However, in the second year, this control group can be used with a degree of accuracy for computing the man-days lost for the new cases of 1984, since both groups were examined in the same year. Subtracting the man-days lost from these negative or control group for the untreated cases in 1983 and the new untreated cases for 1984, it would provide the net effect arising from schistosomiasis alone for these 2 years. This was computed to be 41.6 (45.4 - 3.8) and 22.4 (26.2 - 3.8) for the second year or a net gain of 19.2 man-days per infected person per year.

For the treated cases, the benefit of biltricide therapy was much higher. From the baseline of 45.4 man-days lost, this went down to 4 man-days or a reduction of 91.2%.

In terms of manpower, therefore, aside

from the almost total elimination of disability of the treated group, we can expect an additional 19.2 man-days per year of active labor

force. If this is multiplied by the total number of cases, then, the total man-days gained as a result of treatment could be obtained.

COMPARISON OF PIVAMPICILLIN AND AMOXYCILLIN IN EXACERBATIONS OF CHRONIC BRONCHITIS

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The principal bacterial pathogens in exacerbations of bronchitis are opportunists, which are usually commensals in the upper respiratory tract in particular *Haemophilus influenzae* and *Streptococcus pneumoniae*. Other organisms, such as *Staphylococcus aureus* and the coliforms, are rare and tend to arise only after prolonged chemotherapy or in post-influenzal bronchopneumonia. On most occasions their isolations from sputum merely indicates upper respiratory tract colonization.

Chemotherapy for exacerbations of chronic bronchitis must, therefore, be aimed at *Haemophilus influenzae* and *Streptococcus pneumoniae* primarily.

The most commonly used antibiotic regimens in this indication are tetracycline, co-trimoxazole, and ampicillin or derivatives of ampicillin. Some authors have advocated use of oral cephalosporins, but many strains of *Haemophilus influenzae* are either resistant or relatively insensitive to standard doses of the currently available oral preparations of cephalosporins. Although clindamycin and chloramphenicol exhibit a high degree of activity against the mentioned pathogens combined with a good tissue penetration, these antibiotics should be reserved for severe infections due to their toxicity potential.

Respiratory strains of *Haemophilus influenzae* resistant to ampicillin have been reported, but they are still rare in the Far East. Amoxycillin and the ampicillin esters with improved ampicillin absorption after oral administration are generally considered the most effective and safe antibiotics in the treatment of exacerbations of chronic bronchitis.

In order for antimicrobial therapy of acute exacerbations of chronic bronchitis to be successful, the concentration of drug in the bronchial mucous membrane must at least equal the MIC of the drug for the infecting strain and preferably be 2 or 3 times this value. The absorption of ampicillin from the gastrointestinal tract is only moderate and the availability of pivampicillin, which yields 2-3 times higher serum and tissue concentrations of ampicillin after oral intake, is therefore a valuable improvement of ampicillin therapy and substitutes parenteral treatment.

Amoxycillin is slightly less active *in vitro* against *Haemophilus influenzae*, but is also better absorbed than ampicillin and achieves better serum and sputum concentrations than ampicillin.

Any limitation in antibiotic drug consumption is considered a goal worthwhile pursuing for reasons of patient compliance and drug cost. Therefore, a randomized comparative

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study was undertaken on the efficacy of pivampicillin in a twice-a-day dosage schedule versus amoxycillin in a three times-a-day dosage schedule. The latter regimen in

previous studies has been found effective whereas pivampicillin so far only has been recommended in a three times-a-day dosage schedule.

TYPHOID MYOCARDITIS IN JAKARTA, INDONESIA

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Better and more sophisticated diagnostic facilities as well as more attentive approach toward typhoid fever give rise to a more complete understanding of the disease. Among organ system involvement, septic shock, disseminated intravascular coagulation, hepatitis, neuropsychiatric disturbance and myocarditis are considered as "new" issues.

The incidence of typhoid myocarditis found in the Infectious and Tropical diseases ward, Department of Medicine, Faculty of Medicine, University of Indonesia, Jakarta (42.3%) was more or less similar to those found by other investigators.

ECG abnormalities found in this series was as follows : prolonged Q - Tc interval was found in 86.4 of cases, while T waves changes

prolonged P-R interval, incomplete RBBB were found in 36.4 %, 9.2 % and 9.1 % respectively. S-T segment changes was found in 4.5 % and ventricular extrasystole also in 4.5 % of cases. Second degree A.V. block was also found ; Wenkebach type with bradycardia in 4.54 % of cases. In general, conduction disturbances were more prominent.

The clinical course of the disease was benign, all patients recovered uneventfully. Only in 1 case specific treatment was given other than the general treatment for typhoid fever.

It was concluded that the heart involvement in typhoid fever is primarily caused by the typhoid fever itself. The heart involvement is more likely to be carditis rather than myocarditis.

FILARIA *BRUGIA MALAYI* CAUSING LYMPH VESSEL AND NODE WALL DAMAGES, DETECTED IN TROPICAL EOSINOPHILIA

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Lymphography has been carried out on 17 patients with elephantiasis and positive microfilaraemia *Brugia malayi* and for comparison

10 patients with Tropical eosinophilia. Many typical changes of the lymph pattern were detected due to occlusions and damages of

the lymph vessel and node wall. The same changes were also found in patients with Tropical eosinophilia. This disease is caused by an infection of human or animal microfilariae and can be termed Occult filariasis,

due to the absence of microfilaraemia and elephantiasis is also unknown. Many differences were detected compared to the *Wuchereria bancrofti* type.

CHEMOTHERAPY OF VIRAL INFECTIONS

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Isoprinosine was tested on 180 adult patients with suspected acute viral infections viz. influenza (80); herpes zoster (30); and epidemic parotitis (30). All patients were seen at the Hospital Ng Maynila (City General Hospital), Santo Tomas University Hospital and included private patients.

The diagnosis was made on the basis of the following: clinical history, signs and symptoms, epidemiology and a negative bacteriological blood, sputum, urine and throat

swab culture, obtained before the start of therapy.

Isoprinosine was administered at a dose of two tablets q.i.d. for 4 days. In this study, the therapy was started on the 2nd or 3rd day of illness. Very satisfactory results were found clinically in cases of influenza and herpes zoster. In cases of varicella and epidemic parotitis, some of the responses were poor due perhaps to the development of secondary infections.

SOME PARASITES USUALLY NOT FOUND IN THE LIVER

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Although the liver of humans is a favorite location of a significant number of animal parasites, there are, on occasion, erratic, spurious or unusual parasites reportedly found in the organ. *Ascaris lumbricoides* is an intestinal parasite, but occasionally the adult worms or eggs are seen in bile ducts and liver tissue. Larvae of *Toxocara* sp. are also reported from liver parenchyma. *Capillaria hepatica* has been reported in less than 100 humans, but *C. philippinensis* has been found

in liver tissue once. A granuloma containing *Enterobius vermicularis* has also been reported, as has *Strongyloides stercoralis*, both commonly found in the intestines. *Angiostrongylus costaricensis*, usually in the mesenteric blood vessels, is also reported in liver parenchymal tissue. Gnathostomes may also be found wandering through the liver. A variety of trematodes invade the liver and bile ducts but it is only on rare occasions that *Paragonimus* and *Alaria* spp. are reported. Except for

Echinococcus granulosus, cestode infections are rare in the liver. Protozoan infections such as *Plasmodium* sp., *Leishmania donovani* and *Entamoeba histolytica* are not unusual liver parasites, but it is only on rare occasions that *Toxoplasma gondii* is found. Arthropod

invasion of the liver is occasionally reported. Pentastomids have been found in some populations as well as fly larvae. A brief review of some unusual parasites found in the liver, was presented.

THE PROSPECT OF DEVELOPING A HUMAN HOOKWORM VACCINE BY IRRADIATION OF *NECATOR AMERICANUS* INFECTIVE LARVAE

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It is well documented that in many areas of the world man is constantly exposed and reexposed to severe infections from his heavily contaminated environment, yet in these circumstances, he survives and continues to carry worms for many years if not all his life (Ball and Bartlet, 1969).

This paper reports the behaviour of the infective *N. americanus* larvae attenuated by exposure to ionizing radiation (gamma rays from Cobalt 60). Two groups of neonatal hamsters of 1 to 2 days old were each infected with 300-650 irradiated or normal larvae according to the methods described by Sen (1972). The number of adult worms recovered from hamsters at autopsy following infection with irradiated larvae was less than

that of controls. The infectivity of larvae was directly related to the dose of radiation as determined by worm counts. Haematological changes except plasma protein were more marked in hamsters infected with normal larvae. Male larvae were more sensitive to the effects of irradiation as very few or none were recovered at autopsy done several weeks later while surviving female worms although few were invariably sterile.

Whether a single exposure of hamsters to 40 Kr. irradiated larvae confers immunity to challenge infection has not been clearly established as hamsters develop a strong age immunity to this parasite at the time of challenge. The results of this study were discussed.

DIAGNOSIS OF ENTERIC FEVER

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The evaluation of enteric fever within 1 year at the Department of Internal Medicine,

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was carried out. A total of 79 cases were diagnosed as enteric fever, with the standard titer of 1/40,

33 cases clinical (+) : widal (+) culture (+);
9 cases clinical (+), widal (+) culture (-);
13 cases clinical, widal (+) culture (+); 24
clinical cases: widal (-) culture (-)

The evaluation of coagglutination test in

typhoid when compared, to the culture evaluation is the same. If standard widal 1/200, is used the positive widal would be less. Greater titer standardization of widal or positive cases will be useful. The evaluation of methods in the diagnosis of enteric fever, clinical, widal, culture and serologic coagglutination will be discussed and the liver function tests in typhoid fever.

ASCARIASIS AMONG CHILDREN IN MALAYSIA

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The prevalence of ascariasis was surveyed among 11,874 Malay, Chinese and Indian children, from birth to 15 years of age, from 4 types of communities in Malaysia. These included urban slums, rubber estates in the rural areas, semi-rural settlements and urban flats. The overall prevalence of ascariasis among children from these communities was 19.3%, with the highest prevalence among children in the city slums (45.6%) and the lowest prevalence among children in the flats (7.9%). Indian and Malay children also tend to have higher prevalence of ascariasis, with moderate to heavy worm loads. Chinese children were least frequently infected and generally had low to moderate worm loads, except for Chinese children in the semi-rural settlements who had the highest intensity of infection compared to Indian and Malay

children in the same community. In general, ascariasis was also more prevalent among children from the ages of 4-15 years from all types of communities. Only 3.7% of all infants examined were infected with *Ascaris* whereas about 50% of children from the ages of 4-15 years in the urban slums were infected. There was no marked difference in the distribution of ascariasis among boys and girls from the 4 communities surveyed. The commonest type of *Ascaris* infection among these children was double infections which accounted for more than half to two-thirds of all *Ascaris* infections reported. Almost all the double infections reported among these children was *Ascaris* mixed with *Trichuris* which was the commonest type of helminthic infection found in Malaysia.

THE NON-VIRAL INFECTIOUS DISEASES OF THE LIVER AND BILIARY TRACT IN PERSAHABATAN HOSPITAL, EAST JAKARTA

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In tropical countries, such as Indonesia, most diseases have an infective basis. The liver and biliary tract is frequently the site of such disease, and the causative microorganism in infection of the liver were protozoa, bacteria, fungal, helminth and viruses.

This paper presents the data concerning infectious diseases of the liver and biliary tract of non-viral agent, in Persahabatan Hospital, East Jakarta.

This retrospective study was carried out among in patients with liver diseases in

Internal Medicine wards at Persahabatan Hospital, during six years (1979-1984).

In this study 45 patients were found suffering from infection due to a non-viral agent. Amoebic liver abscess was the commonest infection(36), followed by typhoid hepatitis and leptospirosis respectively in three patients; pyogenic liver abscess in two patients and obstructive jaundice caused by helminth in one patient. There was no mortality in this study. Some epidemiological and clinical aspects were discussed.

MALARIA IN PERSAHABATAN HOSPITAL, JAKARTA

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Between January 1982 and June 1985, 8 cases malaria had been admitted to the Hospital, 4 with malaria tertiana and 4 with malaria tropica, one with delayed R I resistance.

For an Infectious Disease Hospital like Persahabatan Hospital 8 cases of malaria during 3 $\frac{1}{2}$ years is quite a small percentage.

Several factors regarded to be responsible for this were discussed.

Clinical manifestations of both malaria including the RI delayed resistance were presented. Some patients were with jaundice and increase in transaminases (SGOT and SGPT).

POTENTIAL IMMUNOPATHOLOGICAL CONSEQUENCES OF IMMUNIZATION AGAINST INFECTIOUS AGENTS

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Host immune responses to Hepatitis B virus, *Trypanosoma cruzi*, and species of schistosomes are reviewed and related to the pathological consequences of each of the infections. Toxic products, parasite-specific immune reactions, and autoimmunity appear

to contribute to the pathology. Since similar responses may develop as a result of immunization, some procedures are described to eliminate and evaluate undesirable reactions to candidate vaccine antigens.

HOST FACTORS FOR PATHOGENICITY OF *ENTAMOEBIA HISTOLYTICA*

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Factors which may relate with the pathogenicity was studied. The items were hormones, stresses, association of bacteria and nutrition. As experimental animal, rats were mainly utilized.

Testosterone: A "T-strong injection" (Ankuck Pharmaceutical Co.) containing 50mg "testosterone propionate" per ml was used. Experimental rats were injected intramuscularly with 1/8ml of T-strong, a total of 4 times every other day before and after inoculation with 150,000 organisms. The largest number of animals with more than 10 ulcers were observed in the testosterone group (4 among 13 rats). The castration control group followed the next. The average number of ulcerations per rat was 9 in the testosterone group, 4 in the castrated group, but none in the normal control group. Ulcers above 2mm in diameter were predominantly found in the experimental animals (45.5%).

Ergosterone : An Estradiol injection (Sam-Woo Pharmaceutical Co.) containing 2mg estradiol benzoate per ml. was used. The oophorectomized and estradiol injected rats and the normal control group were injected intramuscularly with 1/8ml of Estradiol, a total of 4 times every other day before and after inoculation with 200,000 organisms. The number of animals with less than 10 ulcers was similar in each group. Although rats in the control group had ulcers more than 1mm in diameter (10%), others were below 1mm.

All of the animals except a normal control group were given shaking stress before their inoculation with amoebae. They were put into a cage on the shaking machine (Arthur H. Thomas Co.) and stressed for 4 hours daily for a week.

The exposed ceca of the laporectomized rats were compressed to the same degree by

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surgical forces. A group among the stimulated rats and normal control rats were inoculated intracecally with 300,000 parasites. The rats subjected to shaking stress and physical stimulation showed more pathological findings than the control.

The effect of a previous infection of *Shigella dysenteriae* was more severe than in the non-*Shigella dysenteriae* group, showing an average of 9 ulcerations per rat. Seven were shown in the stressed control group, and 3 were shown in the normal control group.

On nutrition: 40-day-old rats were infected with YS-9 strain of *E. histolytica*. Before infection, the specially designed diets were fed for period of 15 to 17 days:

Group D: Depleted protein diet (rice powder 85% and no casein)

Group L: Low protein diet (rice powder 80%, casein 5%)

Group M: Moderate protein diet (rice powder 70%, casein 15%)

Group H: High protein diet (rice powder 60%, casein 25%)

Olive oil (4%), inorganic salt mixture (4%), cod liver oil (2%) and yeast (5%) were added to each diet at the same rate. (The salt mixture was made using the prescription of H.M. Wakeman, 1937).

The growth of the depleted protein diet group (D) was more poor compared to the other groups from the 3rd day of diet control. The amount of ingested diet in the various groups did not show any difference statistically. To examine the detection rate, all the rats were sacrificed on the 14th day after the inoculation with *E. histolytica*. Amoebae found in the contents of the ileocecal area of the rats were 100% in group D; 85.7% in group L; 73.6% in group M; and 44.4% in group H. Generally the γ -globulin level increased in all the groups after the inoculation with amoebae, especially in the hyperprotein diet group. The value of total serum protein in Group D (6.87 gm %) was the lowest in any group.

Rats fed with depleted or lower protein diets had a higher positive of *E. histolytica* in ileocecal contents.

The cecal ulceration rate and the infectivity of *E. histolytica* increased in rats on a low protein diet as compared to rats fed a high protein diet.

Although the globulin level in the sera of all the rats increased after the inoculation with *E. histolytica*, the level was markedly elevated in the rats with the high protein diet.

The results suggest that lower protein diet retards the growth of the host and decreases the resistance to amoebic infection.

HEPATOCELLULAR CARINOMA IN THAILAND: CURRENT MANAGEMENT AND TREATMENT

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In Thailand, primary hepatocellular carcinoma cases were usually hospitalized in mo-

derate advanced stage, and thus progressed with 100% mortality within 1-4 months.

Most of the patients received supportive as well as symptomatic treatment.

The supportive treatment included (i) adequate diet with high protein and calorie intake, (ii) high doses of vitamins and minerals, (iii) intravenous fluid and electrolytes when necessary, and (iv) steroid treatment. The symptomatic treatment included using potent analgesics for relief of cancer pain, and various means for jaundice, ascitis and intraperitoneal hemorrhage from spontaneous rupture of the liver.

Palliative management was also given to certain patients in order to prolong their lives, even though many chemotherapeutic cytotoxic drugs were also tried to find possible effective drugs.

The palliative treatment included hepatic devascularization using hepatic artery ligation, resulting in decrease in the pain and temporary remission, and in some cases prolonged survival time. Hepatic trans-arterial embolization using gelfoam plus mitomycin-C or with ivalon has been recently performed on some inoperable hepatoma with good immediate results. Surgical resection including partial hepatectomy was performed in some cases with stage I or II hepatic carcinoma with operative mortality rate of 33% and recurrent rate of more than 50%. Unfortunately, subclinical primary liver carcinoma with small localized lesion has never been detected in our series.

Radiotherapy was tried on groups of patients with some responses on the relief of pain and decrease in size of the liver, but no effect on the survival time and mortality rate of the patients.

Immunotherapy using Levamisole for stimulation of T-lymphocyte to increase cell-mediated immunity, and BCG as non-specific immuno-stimulant was also tried in combination with hepatic artery ligation on hepatic cancer patients. The results showed some extension of remission and survival time of the patients. More clinical trials are suggested.

Recently some chemotherapeutic anticancer agents including adriamycin and 5-FU combination, nitrogen mustard, and a combined 5-fluorouridine (FURD), galactosamine and 6-azamidine have been tried on selected patients. The results showed partly effectiveness by alleviation of cancer pain, decrease in size and hardness of the liver with slight extension of survival period of the patients.

It was suggested that detection for early subclinical hepatocellular carcinoma is extremely necessary for increasing the cure rate of the patients, and in moderate advanced cases further clinical trials in palliative treatment by new various means should be conducted in order to find better effective ways in the treatment of the patients.

OBSERVATIONS ON HEPATITIS B CARRIER STATE AMONG VOLUNTARY BLOOD DONORS IN TAIWAN

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This report concerns the status of HBsAg and SGPT reactions observed in some

770,000 voluntary blood donors seen at the three Blood Donation Centers in Taiwan

during 1978-1983. The eligible donors were limited to those between 18 to 60 years of age and who had satisfactorily passed the routine physical examinations and laboratory tests. Portions of the withdrawn blood were tested for HBsAg, SGPT, VDRL, blood grouping, blood cell counts, and hemoglobin before being accepted for human use. Outstanding epidemiological features relating to Hepatitis B infection and liver function are summarized as follows :

- (1) There was a peak average of HBsAb positive rate from 14-16% for male donors and 7-9% for females in the age group 18-20 years old. These rates receded to 7-9% (males) and 3-5% (females) in age group 31-40 years old, and to 2 to 5% in age group 51-60 (both sexes). Thus age and sex differences in the chronic HBsAg carrier state was evident and remarkable.
- (2) Abnormal SGPT rates varied greatly from age-groups, locality and year to year. The general rates of abnormal increment among males (Taipei, 1978) was 2.3% in age group 18-20 and maintained at this level until after age 41 it dropped to about 1%; whereas among the HBsAg positive males, the increment rate was much higher, being 8% for age group 18-20 and maintained until after 41 years old, it had further increased to 16%. The female donors had a generally lower abnormality of GPT rate of less than 1% at age 18-20 group and decreased to about 0.12% after age 41; the abnormality rate among the HBsAg positive female donors was similar, from 1.8%. Apparently the increase of SGPT among different age group was in a reverse order as against the pattern shown with the case of HBsAg positivity.
- (3) The distribution in the incidences of HBsAg positives among the 4 blood groups is essentially the same as normal frequencies of distribution of all blood donors, namely, for group O was 44.44%, group A 27.07%, group B 24.5% and group AB 5.93%.
- (4) Observations on the prevalences of HBsA in the 6 years duration did not show a definite change in the positive rates.
- (5) In comparing the HBsAg carrier rates among blood donors seen at different centers, it appeared the rate was higher in the south Center (KaoHsiung) than the centrally located Center(Taichung) while the northern Center (Taipei) was the lowest.
- (6) A special was made to ascertain persistence of HBsAg in an individual. In a randomly chosen 602 (sero-positive for HBsAg) donors, it was found that 434 (72%) of them were positive for the first time but there were 94(15.6%) individuals who were negative reactors before. Furthermore, 54(9%) of them had reversal of negative to positive to negative and 11(1.8%) reversal from positive to negative to positive. The significance of as becoming positive may suggest remission of a latent infection or new infection through routes other than from mother-newborn or through blood transfusion. Further studies on this aspect are in progress.