韓國農村醫學會誌 第4卷 第1號 1979
Korean J. of Rural Med. Vol. 4, No. 1, 1979

RECENT ADVANCES IN RESEARCH ON TREMATODES OF MAN

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The recent advances on trematode diseases (excluding schistosomiasis) of medical importance based on the most significant world literature published since 1974 (ICOPA Ⅲ) and contributions to the 4th International Congress of Parasitology (ICOPA Ⅳ), Section C have been reviewed in the present paper.

Paragonimus and paragonimiasis

A total 26 species of the genus *Paragonimus* was reported in the literature at present. Among them 7 species were regarded as a cause of human paragonimiasis in Asia, Western Hemisphere and Africa.

In Asia, four species—*P. westermani*, *P. skrjabini*, *P. heterotremus and P. miyazakii*—were found as human parasites. *P. peruvianus* is suspected to cause human paragonimiasis in some countries such as Peru, Ecuador, Panama, Costa Rica. Another two species in Africa are known as human infections; i.e. *P. africanus* in Camercons and *P. uterobilateralis* in Nigeria, Cameroons and Liberia.

P. westermani is widely distributed and is still an important endemic parasitic disease in such areas as Korea, Japan, Taiwan, mainland of China and Philippines. Recently Miyazaki (1978) has made detailed morphological observations on the specimens of *P. westermani* recognising two types—the original (or bisexual) type and the non-spermatozoan (or parthenogenetic) type. The most reliable criterion for separating them is the seminal receptacle. In the former it is occupied with sperm, but in the latter it contains a number of egg cells and/or vitelline cells instead of sperms. Both adults and eggs are evidently smaller in the original type. This type has been hitherto recognized in India, Ceylon, Malaysia, Indonesia (Sumatra), the Philippines, Korea (Cheju Island), China (Northern part), USSR (Southern part), and Japan (Honshu). On the other hand, the parthenogenetic type has been so far proved to exist in Taiwan, Korea (Cheju and Penninsula), and Japan (Kyushu and Shikoku).

Yokogawa *et al.* (1978) stated recently that *P. westermani* in the Philippines seems to be a different species or strain from the Japanese strain, because there is some evidence to show that the size of the larval stages, migrating routes and maturity in rats, and immunoserological tests of *P. westermani* in the Philippines were quite different from those of *P. westermani* in

Japan. Therefore they proposed this *Paragonimus* in the Philippines as a new species *P. philippinensis*(Ito *et al.* 1978).

Miyazaki and Habe (1976) first revealed by experiments that *P. westermani* could not mature in the wild boar and almost all of worms were parasitic in the muscle of the boar. Miyazaki *et al.* (1977) suggested that the occurrence of human paragonimiasis in Kagoshima and Miyazaki Prefectures was due to the customs of eating boars uncooked. Therefore they concluded that the wild boar in Japan is a new source of human infection with this lung fluke. In this connection, Kurochkin and Suchanova (1978) confirmed that some mammals act as paratenic host of *P. westermani*. They have also found the clinical cases infected with immature worms of *Paragonimus sp.* Therefore they proposed a new term of "larval paragonimiasis" in order to differentiate this from the disease occurred by the adult lung fluke in the final hosts.

Since 1974 about a hundred cases of paragonimiasis due to *P. miyazakii* were reported by many workers in the various localities in Japan (Yokogawa *et al.* 1974; Hayashi *et al.* 1974; Minai *et al.* 1975; Matsumoto *et al.* 1976; Nishida and Gyoten, 1976). According to Yokogawa *et al.* (1974, 1978) the clinical symptoms of this infection showed quite different from those of paragonimiasis westermani; such as spontaneous pneumothorax, exudative pleurisy and high eosinophilia. All the cases had consumed raw *Potamon dehaani* which were found to be infected with *P. miyazakii* metacercariae. All these patients had shown positive dermal reaction for intradermal test with both of the antigens prepared from the adult worms of *P. westermani* and *P. miyazakii*. In most of the cases, no *Paragonimus* eggs were present in the sputum and faeces, but sometimes the eggs of *P. miyazakii* were recovered from the pleural effusion. However Nishida and Gyoten (1976) reported the first case diagnosed by the eggs of *P. miyazakii* in sputum. Yokogawa *et al.* (1978) suggested that the complement fixation test, Ouchterlony test and immunoelectrophoresis are useful for the diagnosis of this infection with *P. miyazakii*.

In recent years human paragonimiasis has begun to attract medical attention in some countries of Central and South America such as Mexico, Costa Rica, Panama, Colombia, Ecuador, Peru etc. Miyazaki (1974) suggested that *P. peruvianus* seems to be widely distributed in Central America and northern part of South America, and is proved to be the cause of human paragonimiasis in some countries such as Peru, Ecuador and Costa Rica. In Ecuador Salas *et al.* (1973) found a soft brown mass containing operculated and immature eggs of *Paragonimus sp.* possibly *P. peruvianus* in the paravesicular fat tissue during the operation for the correction of inguinal hernia. Recently in Costa Rica, some cases of paragonimiasis were reported, but the species identification was not determined (Brenes Madrigal *et al.* 1976, a, b).

According to Nwokolo (1974), human paragonimiasis has been recorded in four West African countries but there is clear evidence of endemicity only in certain parts of Nigeria and Cameroons. In Nigeria, the dominant parasite species is *P. uterobilateralis*, while in Cameroons it is *P. africanus*. The fresh water crabs; *Sudanonautes africanus*, *S. pelli* and *S.aubryi* are proved vectors in Nigeria and Cameroons (Voelker and Sachs,

1977). Characteristic syndrome is mild respiratory disease consisting of chronic cough, blood stained sputum, vague chest pains, rarely massive haemoptysis, sacular bronchiectasis, pneumothorax, pleurisy, empyema and extrapulmonary diseases. In 75% of cases definite abnormal radiological shadows are present, usually cotton wool patches, small cysts and hilar lymph-adenopathy (Nwokolo, 1978). In the immunodiagnosis of African paragonimiasis, Oelerich and Volkmer (1976) stated that the haemagglutination test is well suited for seroepidemiological purposes or assessing treatment, but complement fixation is not.

Clonorchiasis and opisthorchiasis

Recently there are many epidemiological surveys of opisthorchiasis in the various areas of USSR (Silorov, 1975; Zavoikin *et al.* 1975; Nepyshnevskaya *et al.* 1975). The highest incidence of *O. felineus* was recorded in the population of the Ob'river basin and its tributaries, in the Tomsk region, USSR. Zavoikin *et al.* (1976) reported that over 95% of the inhabitants of Kazaltsevo, a village of the Ob', were found to be infected. The cyprinid fishes and *Bithynia inflata* were confirmed the intermediate hosts. Dippon and Widmer (1976) reported a cases of *O. felineus* infection in Switzerland. Kammerer *et al.* (1977) made examination of faecal samples from 150 Chinese-born residents of New York City, USA, revealed ova of *C. sinensis* in 26.0%. Most of the infected immigrants were from Kwangtung Province of China, but only one case of 50 American-born Chinese examined was infected with this parasite. Sornmani *et al.* (1974) reported that 46.5% were found to be infected with *O. viverrini* in 2,493 stool samples examined in Vientiane, Laos.

The clinical manifestations of acute early opisthorchiasis were studied by many investigators in USSR. Limakhina (1977) observed 90.4% suffered from intermittent fever and 100% from leucaemoid eosinophilia in 188 patients. Nalobin *et al.* (1974) found atopic bronchial asthma in a patient with an early phase of opisthorchiasis. Mel'nikov *et al.* (1976) observed allergic lesions of the gastrointestinal tract in the early stages of opisthorchiasis. In 81 patients disturbances of the hepato-biliary system were in 56.8% of cases, accompanied and sometimes overshadowed, by non-specific gastrointestinal symptoms rendering diagnosis difficult. These gastrointestinal changes included diffuse inflammation, eosinophilic infiltration, infiltrative and ulcerative changes. Tomilov *et al.* (1977) studied the haemopoietic function of the bone marrow from 23 patients at various stages of opisthorchiasis. Leucaemoid eosinophilia, focal myelopoiesis and granulocytic hyperplasia in all its stages were observed. These changes are regarded as specific to acute opisthorchiasis and to superinvasion during the chronic stage of the infection.

Studies on experimental opisthorchiasis were done by various workers in USSR. The formation of granulomas in the wall of bile ducts around *Opisthorchis* eggs which had penetrated there by lymphogenic pathways was observed by Zubov and Mukanov (1976) at the 20th—25th days of the experiments in the Golden hamsters. Changes in cardiac and vascular tissue of laboratory hamsters experimentally infected with *O. felineus* metacercariae were monitored by Mukanov *et al.* (1977). On the other hand Glumov *et al.* (1977) observed the functional changes of

the livers of guinea-pigs experimentally infected with *Opisthorchis* by radio-isotope screening. In contrast to clinical examination this method of investigation shows that not only the excretory but also the absorptive function of the liver was impaired. Scans taken at intervals after successful anthelmintic treatment showed that functional normalization was slow usually 3.5 to 4 months after cure by Chloxyle treatment.

In recent years there has been an increased interest on the hepatic carcinoma and trematode infections in the bile ducts. Chainuvati *et al.* (1976) reported 4 cases in Thailand with obstructing carcinoma of the cystic duct and with the presence of enlarged and palpable gallbladders but without jaundice. All cases came from areas where opisthorchiasis was endemic and peritoneascopy and surgical examination revealed evidence of *Opisthorchis* infection. Purtilo (1976) has studied well documented Chinese cases involving residents in Hong Kong for 7 to 50 years, and had all suffered from chronic *C. sinensis* infection. He found a close association between cirrhosis and hepatic carcinoma. With regard to cholangiocarcinoma, he stated that these tumors originate at sites where the flukes dwell and provoke hyperplasia and neoplasia, the process of cholangiocarcinogenesis taking longer than that of hepatocellular carcinogenesis. Likewise, Chung and Lee (1976) investigated the relationship of primary liver carcinoma and clonorchiasis in Busan area one of the areas most heavily infected with *C. sinensis* in the southern part of Korea. A series of consecutive 368 cases of primary liver carcinoma were analysed statistically from an epidemiological view point. The relative risk of *C. sinensis* infection in cholangiocarcinoma compared to hepatocellular carcinoma is about 5 times. The prevalence rate of clonorchiasis is much higher in cholangiocarcinoma than in cases without primary liver carcinoma, but it is not so with hepatocellular carcinoma.

Beer (1975) studied the dynamics of the infection rate of *Bithynia inflata* molluscs with larval forms of *O. felineus* in water bodies of the Tomsk region. The infection rate of the snails in water bodies depends upon the population density of molluscs and the degree of remoteness of the water bodies from sources of the invasion. The seasonal dynamic of the extensiveness of invasion of *Bithynia* is characterized by a one-peak curve, the peak being observed in late July. However the spring period presents the greatest epidemiological danger. For the completion of the parthenogenetic cycle of *Opisthorchis* development in molluscs by the middle or late July they must be infected in the middle or late May. Therefore he stressed the necessity of controlling molluscs which is the easiest way of eradicating opisthorchiasis.

A series of epidemiological studies on *C. sinensis* in Kyungpook Province, Korea was conducted by Choi *et al.* (1975, 1976 a, b). They stated that snail host *Parafossarulus manchouricus* exists in limited areas within the rivers under study and the infection of the snail with cercariae of *C. sinensis* is very low (0.8 per thousand of all snails examined). However 21 species of the fish caught in the rivers were examined for the presence of the metacercaria of *C. sinensis*. Of these, 10 species of the fish harboured the encysted larvae. The most frequently infected one was *Pseudorasbora parva* 92.3 per cent, followed by *Pseudogobio esocinus* 90.4 per cent, *Sarcocheilichthys sinensis* 87.7%, *Hemibarbus labeo* 87.2% and *Pungtungia herzi* 60.8%. In the intensity

of infection with the larvae, *Pseudorasbora parva* was most heavily infected and the mean number of metacercaria per ml of flesh was 51.4. Furthermore Choi *et al.* compared the prevalence rate of *C. sinensis* in 1976 with the results of a survey made in 1964. A marked reduction in the prevalence was encountered in the youngest age group, but there was no significant difference in the older age groups. The overall prevalence rate for clonorchiasis was reduced from 27.7% to 19.6% in a period of 10 years. They concluded that health education is thought to have assisted in the general decrease in infection. However recently traditional ways are changing in Korea. Mechanization of farms, the use of chemical fertilizer, pesticides and insecticides may have affected the parasite or its intermediate hosts. At the same time the cultural, dietary and economic changes may have had their effect.

Heterophyiasis and metagonimiasis

Potentially all species of the family heterophyidae may become human intestinal parasites. In Thailand, Kliks and Tantachamrua (1974) recovered a matured adult worm of *Haplorchis taichui* from the ileum of a patient at necropsy. Dovgalev (1974) studied the epidemiology of metagonimiasis and found infection in 17.5% of 1,891 people investigated. *Semisulcospira cancellata* and *S. laevigata* molluscs are intermediate hosts of *M. yokogawai*. *Cyprinus carpio*, *Carassius auratus*, *Leuciscus waleckii* and *Coregonus ussuriensis* are the fish intermediate hosts.

Recently in Japan, Kagei (1974) stated that the wide spread practice of farming the"Ayu" fish(*Plecoglossus altivelis*), caught in Lake Biwa or at the river mouth or in ponds for distribution to market is considered to be responsible to some extent for the wide endemicity of *M. yokogawai*. In this connection, a case of intestinal fluke infection (probably *M. yokogawai*) acquired by a French Professor visiting Japan was reported by Lamy *et al.* (1976).

Hamed and Elias (1975) attempted to use gamma radiation for control of the trematode *Heterophyes sp.* in the flesh of fish caught from brackish waters. 7.5×10^5r killed the larvae in all species of fish.

Fascioliasis

More than 1,300 cases of human infections were reported in the world. It is an increasing important parasite of man in Latin America as well as in France, Algeria and other Mediterranean countries.

Recently in Japan more than 20 cases have been reported up to the present. However it is hardly possible to identify those found in man simply as *Fasciola hepatica*, because the distribution of *F. hepatica* is not as wide as that of *F. gigantica*. Therefore in most case reports they gave the name of *Fasciola sp.* During the last 4 years, some sporadic cases occurred in Slovakia (Giboda and Beno, 1974), USSR(Demidov and Gigitashvili, 1975), Turkey (Kayabali, 1975), Japan (Yoshida *et al.* 1974, 1975; Kaneda *et al.* 1975), England (Beresford, 1976), Korea (Cho *et al.* 1976), Guatemala (Echeverria *et al.* 1976), Cuba (Fabregas Rodriguez *et al.* 1976), France (Hillyer, 1975) and Zambia (Hira, 1976).

The increase in the number of cases is probably related to better study and understanding of the disease, especially in its chronic form as well as to the use of selective methods of diagnosis. The symptoms of

these patients were characterized by the abdominal pain predominantly in the right hypochondrium, spasmodic epigastralgia, irregular fever, high eosinophilia, increase in γ-globulin, some signs of hepatic insufficiency and positive reactions of some immunological tests such as skin test and Ouchterlony double diffusion test. Recently Hillyer and Capron (1975, 1976) have developed a new rapid technique for the detection of active infection of *F. hepatica* by counterelectrophoresis using a crude *F. hepatica* extract as antigen.

Fasciolopsiasis

Fasciolopsis buski, the giant intestinal fluke, is a common parasite of man and pig in Central and South China, Taiwan, Vietnam, Laos, Cambodia, East Pakistan, India, Assam, Thailand and Sumatra, but not in Japan and Korea.

Chandra *et al.* (1974) found a case of *F. buski* infestation in Utter Pradesh, India. After this he carried out a field survey in 6 villages of this area to record the results of clinical and laboratory tests amongst *F. buski* infested cases. 181 (22.4%) of 808 persons were shown to be infected with *F. buski* (Chandra, 1976). Of the 181 with positive faecal examinations, 111 (61.2%) were asymptomatic. Anaemia was more common in infected cases. Almost 85% of the cases showed an eosinophil count of more than 5%.

A pilot survey of the incidence of *F. buski* in two villages near Dacca, Bangladesh have been studied by Muttalib and Islam (1975). Stool examinations of 851 children from 2 villages revealed that 39.2% of 296 and 8.6% of 555 were infected with *F. buski*. The highest incidence was in the village with the poorest sanitation and lowest economic status.

Echinostomiasis

According to Yamashita (1970), 13 species have been testified to cause, or considered likely to cause, parasitism within the human body. Human infections of *Echinostoma revolutum*, *E. cinetorchis*, *E. macrorchis*, *E. lindoensis*, *Echinoparyphium recurvatum*, *Echinochasmus japonicus*, *E. perfoliatus*, *Euparyphium ilocanum*, *E. jassyense*, *E. malayanum* and *E. sufrartyfex* were found in the Southeast Asian countries and Far East. *Echinostoma paraulum* and *Himasthla muehlensi* were found in USSR and Germany respectively. Recently in Japan Tani *et al.* (1974) collected 11 worms with generic characters of the genus *Echinostoma* from a farmer who lived in Chokai village, Akita Prefecture. After this Tani (1976) conducted an epidemiological survey in this area with stool examination. Fifteen cases out of 6,356 people from 3 communities in Akita Prefecture were found infected with *Echinostoma*. All of 12 treated with Kamala were cleared and adult worms, recovered from 2 cases, were identified as *E. hortense*. This is the first report of this species in man. Metacercariae were found in *Misgurnus augillicaudatus* and raw loach is thought to be the source of infection. On the other hand, Arizono *et al.* (1976) confirmed also the human infection of *E. hortense* by the 4 natural and two experimental infections of man living in Osaka or Kobe Prefecture which were diagnosed by the characteristic eggs found by repeated stool examinations. In all of the cases some degree of abdominal pain developed and 3 cases out of four showed high eosinophilia. The infections were perhaps acquired from the consumption of raw loaches except in one case

when two loaches but raw green frogs were eaten. For human experimental infections, the metacercariae were collected from soft tissues adjacent to gills of the loaches, which were obtained from a restaurant where the two cases occurred. Two volunteers were each orally infected with 10 metacercariae, and one puppy with 40 metacercariae. The prepatent period was 16 days in man, and 14 days in the dog. Five adult *E. hortense* were recovered from the puppy 33 days after infection. In the human volunteers, abdominal pain developed 3 or 5 weeks after infection; there was an increase in monocytes and later, eosinophiles which reached maxima of 13 and 19% respectively, 6 weeks after infection. The blood picture returned to normal at 10 weeks.

CONCLUSION

It may be concluded that the incidence of trematode infections in man is normally associated with poor sanitation and low economic and educational status. Some reports suggested that at certain areas cultural, dietary and economic changes together with improved agricultural technology have reduced the incidence of some trematode diseases traditionally occurring at certain endemic areas. With more studies on those factors, educational extension and the considerably improved diagnostic techniques, elimination of most trematode diseases should be possible in the future.

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