

Seroepidemiological Observation of *Taenia solium* Cysticercosis in Epileptic Patients in Korea

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Prevalence survey of neurocysticercosis was made in a mixed epilepsy patients of Changmi Club in Korea. From February 1987 to July 1990, a total of 2,667 randomly selected patients at 27 local centers was tested for their serum levels of anti-Cysticercus antibody (IgG) by enzyme-linked immunosorbent assay. Positive rate of the antibody was 4.0% in the examined patients. The standardized antibody positive rate by provincial population was 3.1%. The rate was the highest in patients living in Cheju Do (8.4%). The patient age brackets of 0~9 years and over 50-year showed higher positive rates of the antibody. In 750 normal persons who checked up routine physical examination, the antibody positive rate was 2.1% (standardized rate was 1.8%). These seroepidemiological data disclosed for the first time the prevalence of cysticercosis in epileptic patients and in population.

Key Words: *Epidemiology, Neurocysticercosis, Epilepsy*

INTRODUCTION

Neurocysticercosis is not just a simple neurologic disease but an important cause of disabilities in populations living in many developing countries (Mahajan et al., 1982; Woodhouse et al., 1982). In spite of presumed significance of neurocysticercosis, however, it has not been easy to estimate its population based prevalence correctly (Schantz et al., 1989). Difficulty in epidemiologic study has arisen because of the characteristics of the disease itself and problems in the diagnosis. Many neurocysticercosis patients do not develop acute symptoms unless heavily infected. Insidious and intermittent headache, partial/general seizures of long interval, sudden hemiparesis or other neurologic symptoms are the first presenting symptoms long after the equivocal period of infection (Dixon and Lipscomb, 1961). Most patients therefore seek medical service long after the probable period of in-

fection. Subcutaneous nodules are reported to be associated in 50-70% of the patients (Dixon and Lipscomb, 1961). Because the nodules disappear spontaneously about 5 years after the infection, nodules are not found in most chronic neurocysticercosis patients.

In this context, correct diagnosis of neurocysticercosis for epidemiologic purposes is a formidable problem because there are many neurologic diseases which need to be differentiated. Surgical biopsy is definitive diagnosis; however, it is not a practical method of epidemiologic study. Neuroimaging diagnosis as CT or MR is evidently helpful in etiologic differentiation of neurocysticercosis (Nash and Neva, 1984). But imaging diagnosis is only limitedly useful for epidemiologic purpose because it is expensive and not available for large scale studies. The findings may furthermore be ambiguous mainly because of different stages of infection and the presence of racemose form (Chang et al., 1988).

Serologic diagnosis has been regarded as the only available technique for the epidemiologic study of cysticercosis (Flisser and Larralde, 1986; Schantz et al., 1989; Camacho et al., 1989; Dumas et al., 1989). Since the development of sensitive techniques of antibody test such as enzyme-linked immunosorbent assay

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(ELISA), serologic diagnosis is now widely used in both patient diagnosis and epidemiologic studies (Cho et al., 1986; Keilbach et al., 1989; Camacho et al., 1990; Sorvillo et al., 1992). Though the antibody test has its own limitations in the etiologic differentiation of cysticercosis (Chang et al., 1988; Wilson et al., 1991), it is a feasible technique for understanding properly the extent of morbidity in a population.

This study was undertaken to survey the infection status of cysticercosis in both mixed epileptic patients and normal population in Korea. By assaying the anti-*Cysticercus* antibody levels in sera, the extent of cysticercosis morbidity, either manifested or not, was investigated in the Korean population.

MATERIALS AND METHODS

Subjects

1. Epileptic patients

Epileptic patients who registered at the Changmi Club were subjected to the antibody tests. The Changmi Club is a voluntary, civilian, charity activity supported by Protestant churches and volunteer neurologists, neurosurgeons and nurses in Korea (Kang et al., 1979). In addition to the academic activities on epilepsy, periodic physical check-ups, health education on the anticonvulsant therapy together with provision of anticonvulsant drugs have been regularly undertaken. Korean epileptics, who had been ignorant of drug therapy, have been helped by this activity for longer than 20 years since 1968. As of July 1990, the total membership number was 93,121 who registered at 108 local centers of the Changmi Club over the country. The membership number is encouragingly decreasing because the national health insurance has covered a greater proportion of the patients since July 1989.

The subjected patients in this survey were randomized by subjecting all the attending patients to a specific check-up time without prior announcement of the test. The significance, sensitivity, specificity of the antibody test were explained to the attending patients individually; and they were persuaded to participate in the survey. Over 95% of the attending patients agreed voluntarily to participate. This survey was done on February 1987 at a local center in Cheju Do, and from October 1989 to July 1990 at 27 centers in peninsular provinces and cities in Korea. The total number of examined cases is shown in Table 3.

2. Normal population

In order to observe the prevalence of the specific antibody (IgG) to *Taenia solium* metacestodes in the

general population, a total of 750 sera was collected over the country. In March 1987 (Cheju General Hospital) and from July to September 1990, the sera were collected in Chung-Ang University Hospital in Seoul and at provincial branch laboratories of the Korea Association of Health, Inc. These sera were originally collected to do biochemical tests in periodic physical check-ups of university students, employees and workers in firms and factories. The sera tested in this study were serial 50-161 samples collected at random period.

Antibody test

Serum antibody levels, specific to *T. solium* metacestodes, were measured by ELISA (Cho et al., 1986). Cystic fluid was used as antigen. Wells in a polystyrene microtiter plate were coated overnight at 4°C in protein concentration of 2.5 µg/ml in carbonate buffer (pH 9.6). After washing, 1:100 diluted sera in phosphate buffered saline/0.05% Tween 20 (PBS/T, pH 7.4) were reacted for 2 hours at 36°C. After washing, 1:1000 diluted peroxidase-conjugated anti-human IgG (light and heavy-chain specific, Cappel, U.S.A.) in PBS/T was reacted for 2 hours at 36°C. Then substrate (99 ml of distilled water, 1 ml of 1% *o*-phenylene diamine, 10 µl of 30% H₂O₂) was reacted. Absorbance was read at 490 nm using a Microplate Reader (Bio-Rad, M3550, U.S.A.). Each running of ELISA was accompanied with a positive reference (which gives abs. 1.0 ± 0.05) and a negative reference serum. Antibody levels (abs.) were corrected by the abs. in positive reference serum. Cut-off value of positive reaction was set at abs. 0.18 as done by Cho et al. (1986).

RESULTS

1. Geographic distribution of the sample areas

A total of 28 centers of the Changmi Club was surveyed out of 108 centers distributed throughout Korea. As shown in Fig. 1, the surveyed centers distributed in all provinces. Out of 6 major cities in Korea, 3 cities were surveyed. The number of sampled patients was not exactly proportional to the provincial population.

Localities, where normal control sera samples were collected, are shown in Fig. 1 (open circles). The samples were collected in major cities and provincial capital cities.

2. Antibody positive rates in normal population

We collected 750 sera samples at 12 health checking laboratories in 11 provinces and cities. Of them, a total of 16 samples (2.1%) showed positive antibody levels in their sera. By administrative district, Seoul

Table 1. Positive rates of anti-*Cysticercus* antibody (IgG) in sera of normal population (university students, factory workers and employees of firms) in their periodic physical check-ups

Cities Provinces	No. examined	No. positive	Percent (%) positive
Seoul*	124	3	2.2
Inchon	50	1	2.0
Kyonggi	50	0	0
Kangwon	50	1	2.0
Chungbuk	49	1	2.0
Chungnam	50	0	0
Chonbuk	51	3	5.9
Chonnam	50	1	2.0
Kyongbuk	50	1	2.0
Kyongnam	55	1	1.8
Cheju	161	4	2.5
Total	750	16	2.1

* Two sample groups were tested

Table 2. Age and sex distribution of tested cases and number of positive reactors in the normal population

Age (year)	No. antibody positive/No. examined		
	Male	Female	Total
0-9	0	0	0
10-19	1/43	1/87	2/130
20-29	1/85	2/99	3/184
30-39	5/154	1/59	6/213
40-49	1/93	1/26	2/119
50-59	0/50	1/27	1/77
over 60	1/19	1/8	2/27
Total	9/444	7/306	16/750

(2.2%), Chonbuk (5.9%) and Cheju (2.5%) showed positive rates higher than the average (Table 1). When the positive rate of 2.1% is standardized by provincial population in 1990 (Economic Planning, Board 1991) the rate was 1.8%.

In Table 2, age and sex distribution of positive cases in the examined normal population are presented. The antibody positive rates exhibited no differences between sex (male 2.0%; female 2.3%). By age group, group over 60 years showed the highest antibody positive rate (7.4%) and the 30 ~ 39 years group showed the next high rate (2.8%).

3. Antibody positive rates in epileptic patients

1) Positive rates by administrative district

As shown in Table 3, a total of 2,667 epileptic patients at 28 local centers of the Changmi Club was examined for their serum anti-*Cysticercus* antibody levels. The number of sampled patients varied from 3 to 405 by center. The average antibody positive rate was 4.0% out of 2,667 patients. The positive rate varied by local center from 0% to 8.4%. By administrative district, the positive rates were above the average in Cheju Do (8.4%), Kangwon Do (7.5%), Chonbuk (5.9%) and Inchon (5.6%). In other administrative districts, the positive rates were between 1.8 ~ 3.5%. When the antibody positive rate is standardized by provincial population (Economic Planning Board, Republic of Korea Government, 1991), the standardized antibody positive rate was 3.1%. The positive rate was neither standardized in terms of provincial population of epileptic patients

Table 3. Positive rates of anti-*Cysticercus* antibody (IgG) in the Changmi Club epileptic patients shown by province

City/Province	Date of study	No. examined	No. positive	Percent (%) positive
Seoul		204	4	2.0
Chonnong	Apr. 1990	98	4	
Yongdungpo	May, 1990	106	0	
Inchon	Jul. 1990	124	7	5.6
Kyonggi		306	6	2.0
Ansong	Feb. 1990	42	0	
Kangwha	May 1990	14	1	
Kimp'o	May 1990	44	1	
Pochon	Jun. 1990	3	0	
Pyongtaek	Feb. 1990	71	2	
Suwon	Jun. 1990	132	2	
Kangwon		80	6	7.5
Chunchon	Jun. 1990	77	5	
Cholwon	Jun. 1990	3	1	
Taejon	Jul. 1990	101	2	2.0
Chungbuk		89	2	2.2
Chungju	Jul. 1990	42	2	
Eumsong	Jul. 1990	47	0	
Chungnam		312	10	3.2
Hongsong	Feb. 1990	96	1	
Kumsan	Jul. 1990	29	1	
Nonsan	Jul. 1990	86	6	
Chonbuk		171	10	5.9
Iri	Jul. 1990	110	7	
Namwon	Apr. 1990	61	3	
Chonnam		356	12	3.4
Huasun	May 1990	217	8	
Hampyong	May 1990	139	4	
Kyongbuk		276	5	1.8
Andong	Jul. 1990	107	2	
Munhyong	Oct. 1989	97	0	
Sangju	Jul. 1990	41	3	
Yechon	Jul. 1990	31	0	
Kyongnam		344	12	3.5
Kimhae	May 1990	152	3	
Chinyang	May 1990	192	9	
Cheju	Feb. 1987	405	34	8.4
Total		2,667	108	4.0

nor by age/sex.

2) Positive rates by age and sex

The antibody positive rate was analysed by the age and sex of the epileptic patients (Table 4, Figs. 2 & 3). By sex, male epileptic patients (1,474) were slightly more numerous than those of female (1,193). The age bracket of 20 ~ 39 years (1,481) comprised 56% of the

sample population.

The antibody positive rates were higher in male epileptics (4.7%) than in female patients (3.2%). The rates by age showed higher rates in 0 ~ 19 years (5.0% and 6.7%) and older ages of 50 years and over (8.4% and 6.0%). In the age bracket of 20 ~ 49 years (71% of the sample population included), the positive rates were relatively lower at 2.5 ~ 3.4% (Fig. 2). In Fig. 3,

Table 4. Number of epileptic patients and antibody positive cases analysed by age and sex

Age (year)	No. antibody positive/No. examined		
	Male	Female	Total
0-9	3/49	1/31	4/80
10-19	14/187	7/125	21/312
20-29	10/362	10/303	20/665
30-39	11/435	9/381	20/816
40-49	10/214	4/196	14/410
50-59	15/146	6/105	21/251
over 60	7/81	1/52	8/133
Total	70/1474	38/1193	108/2667

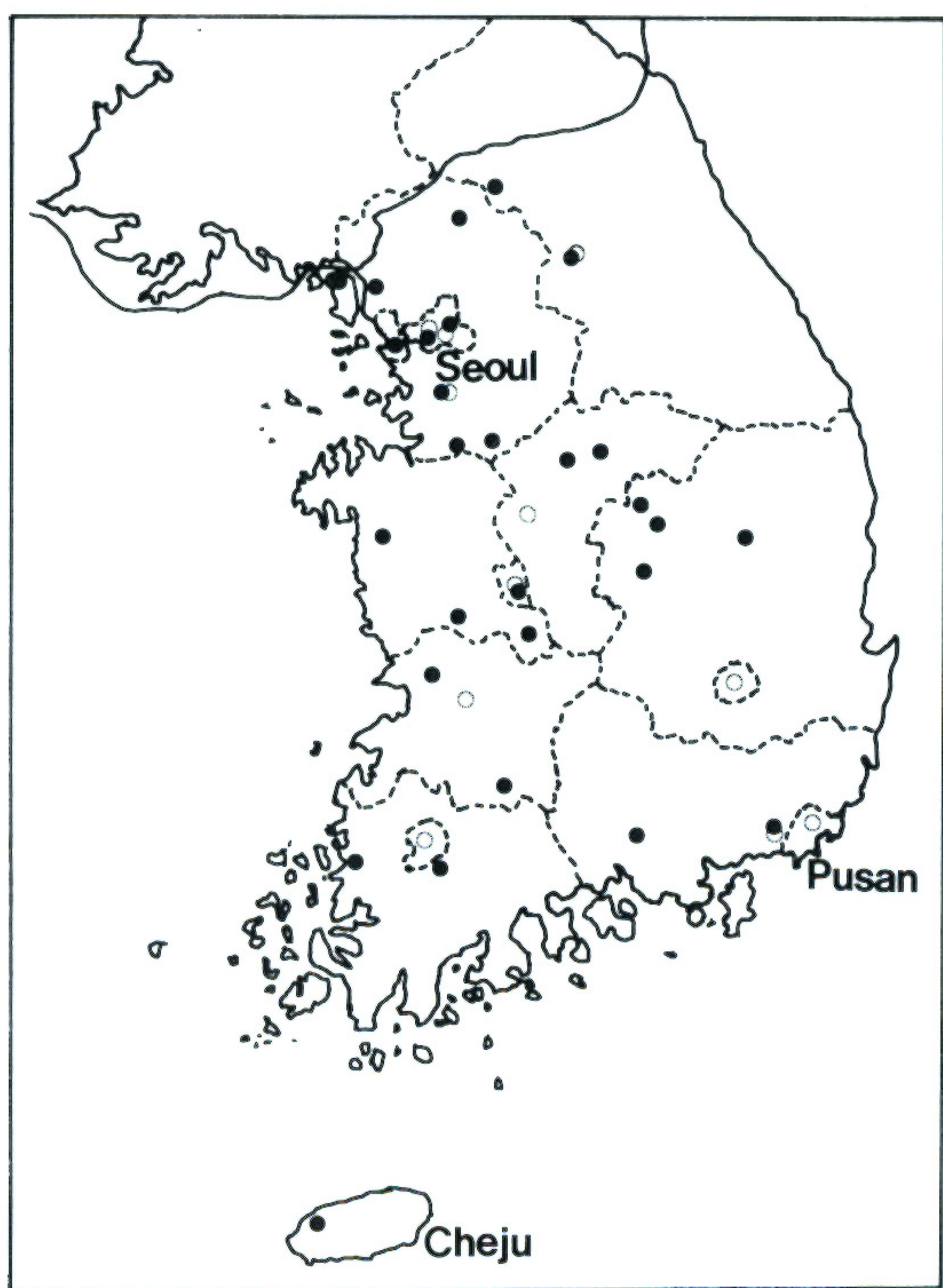


Fig. 1. Localities where sera samples for the antibody test were collected. Closed circles (●) represent the local centers of the Changmi Club for epileptic patients. Open circles (○) show areas where sera of normal population were collected.

the positive rate by age and sex is shown separately in a sample population of Cheju patients. Though sample size is relatively small, the antibody positive rates in the 50 ~ 59 years and over 60 years groups exhibited 13.6% and 30.8% respectively.

3) Distribution of antibody levels in epileptic patients

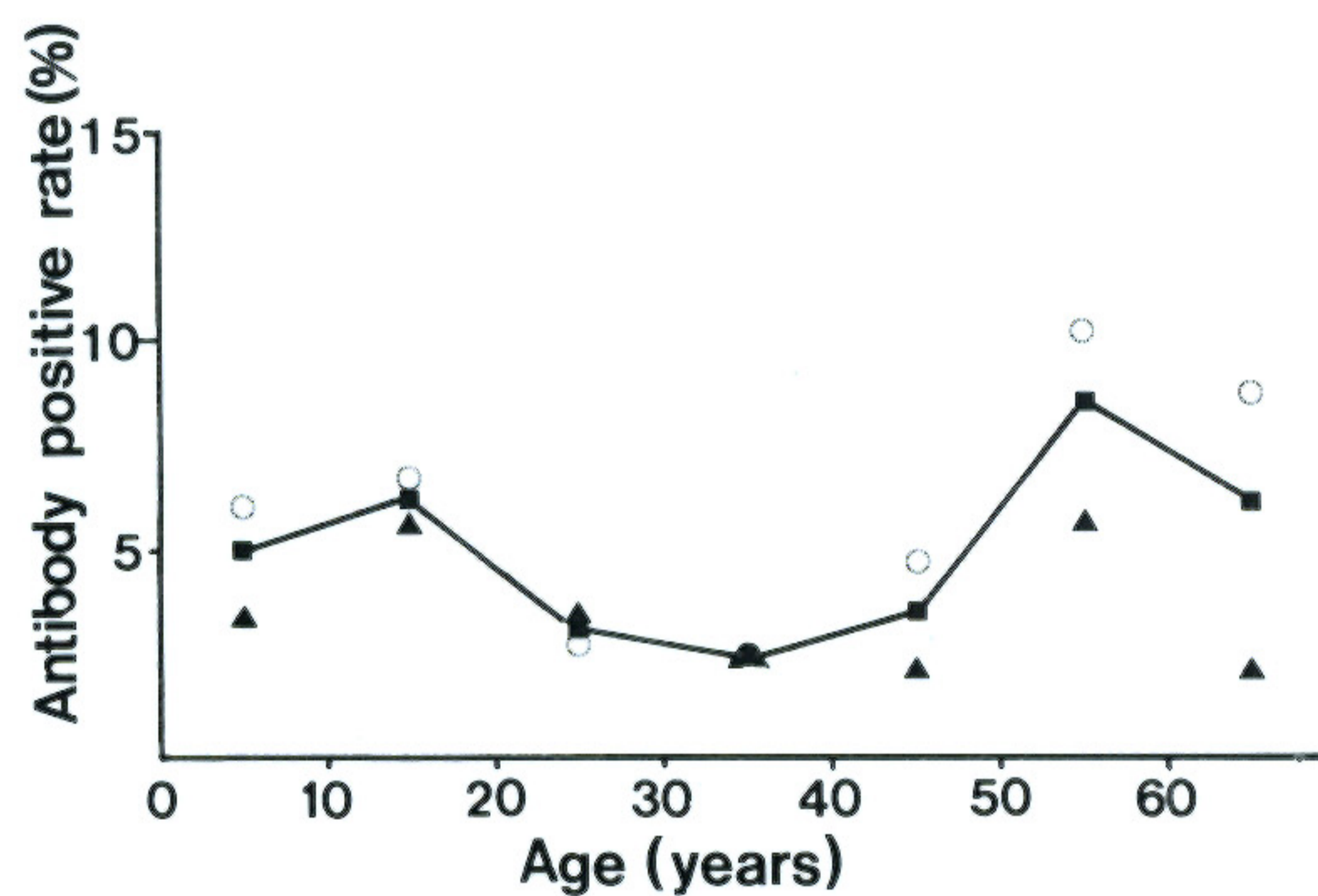


Fig. 2. Anti-*Cysticercus* antibody (IgG) positive rates as shown in the age and sex of the Changmi Club epileptic patients (1987-1990), ●: Male, ▲: Female, ■: Average

and normal population

Distribution patterns of the antibody levels (abs.) in epileptic patients are shown in Fig. 4. The distribution was negatively skewed. The abs. ranges from 0.01 to 1.17. At each abs. in range of 0.01 ~ 0.17 (regarded as antibody negative), there were 10 or more patients. At abs. 0.16 ~ 0.17 the case number was decreased. In the positive antibody ranges of abs. 0.18 ~ 0.25, the case number was 53 (49% of the positive cases). The number of positive patients whose abs. were between 0.26 ~ 0.30, 0.31 ~ 0.35, 0.36 ~ 0.40, 0.41 ~ 0.45, 0.46 ~ 0.50 and over 0.51 was 13, 10, 5, 10, 5 and 35, respectively.

Distribution patterns of abs. in the normal population were almost the same as those in the epileptic patients (Fig. 5). Of 16 positive reactors, abs. in 10 cases was between 0.18 ~ 0.25. In the remaining 6 cases, abs. were 0.28, 0.31, 0.55 and 0.66, respectively.

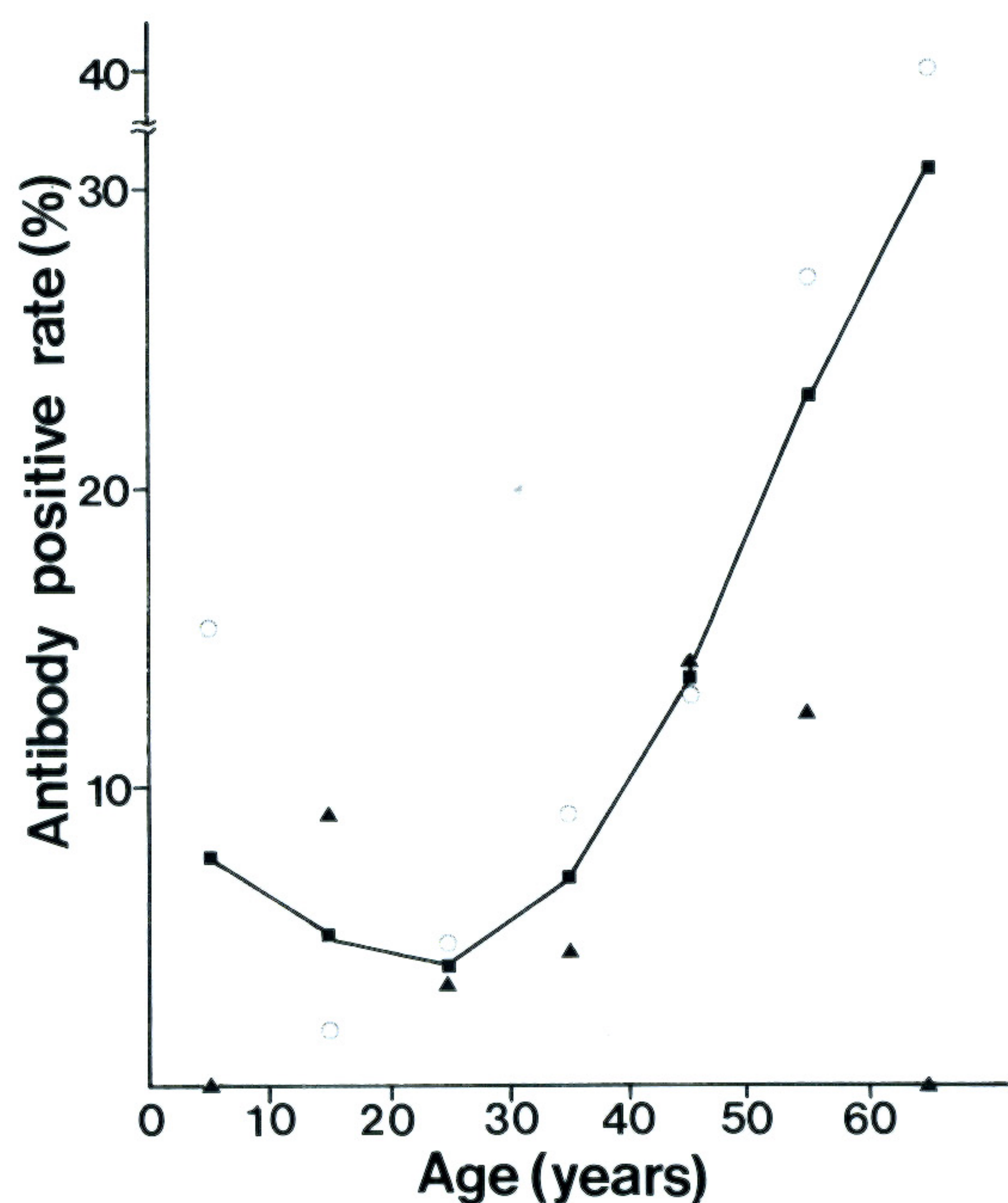


Fig. 3. Positive antibody rates by the age and sex in Cheju Do epileptic patients (1987). Symbols are the same as described in Fig. 2.

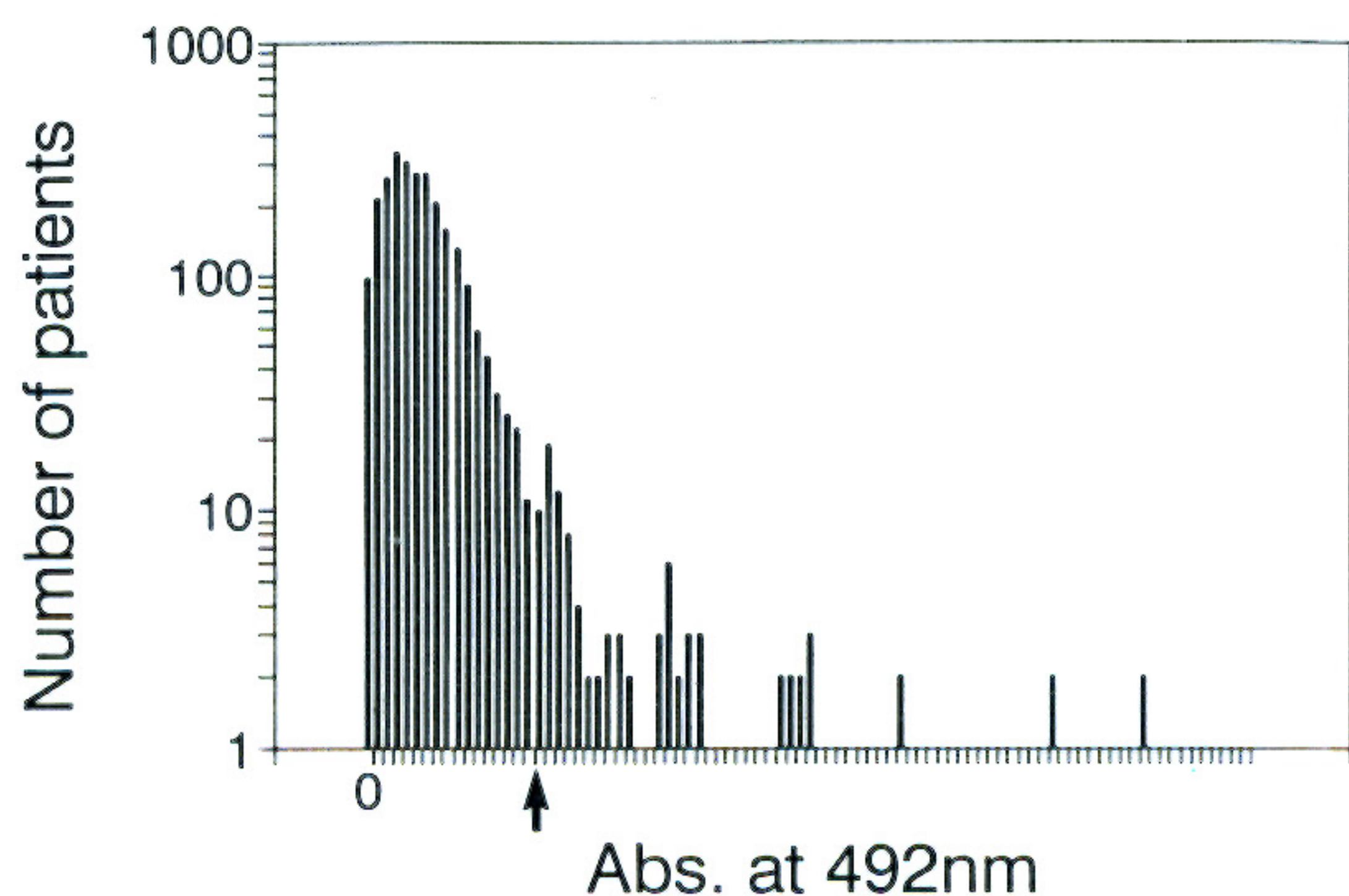


Fig. 4. Case distribution of the epileptic patients by antibody levels in serum. At each abs. the number of cases were shown. Because semi-log paper was used in the presentation, case number in 1-9 was added with 1. Inverted arrow indicates the absorbance of 0.18 (positive criterion).

DISCUSSION

Human cysticercosis has been prevalent in Korea. Rim et al. (1981) summarized the literature on human cysticercosis when they reported the efficacy evalua-

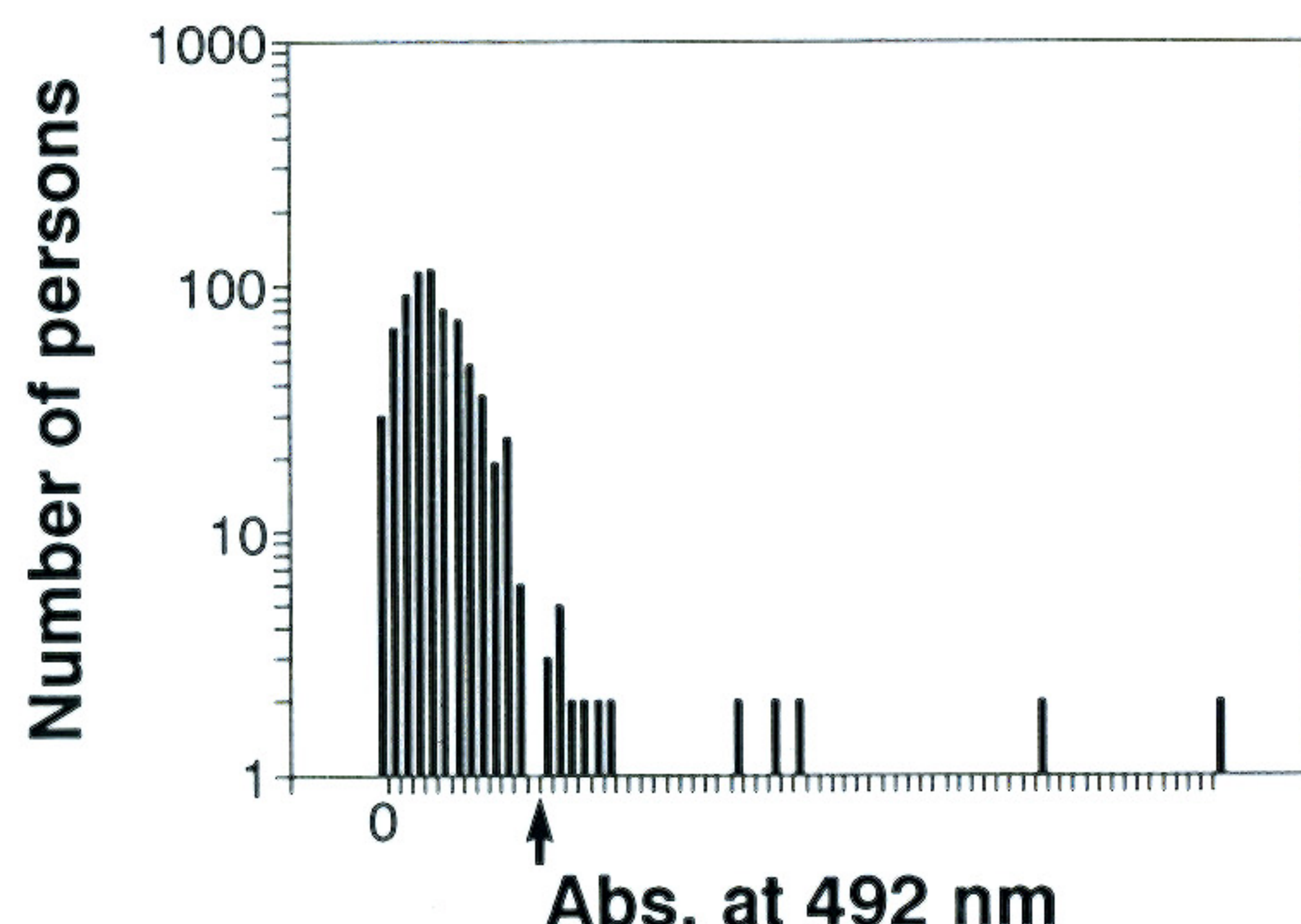


Fig. 5. Distribution of normal population shown by the antibody levels (abs.) in serum. Inverted arrow indicates the absorbance of 0.18 (positive criterion).

tion of praziquantel on the disease. Chi et al. (1988) also summarized the evaluation results of surgical pathology specimens containing parasites in a referral hospital in Seoul. In their reports, 216 of 285 biopsy specimens with parasites (75.8%) in 1968 ~ 1977 and 209 of 296 specimens with parasites (70.6%) in 1978 ~ 1987 were cysticercosis. Human cysticercosis is, without any doubt, the most important tissue invading parasite in this country. The prevalence of human cysticercosis is related closely with the endemicities of human *T. solium* infection and porcine cysticercosis. From numerous local and national surveys, it has been revealed that *Taenia* egg passers have been steadily declining from 1 ~ 2% of population in the 1960s to 0.25% in the mid-1980s. In addition, it has long been recognized that about 1/10 of *Taenia* species infected persons in Korea have *T. solium* infections.

Despite a considerable understanding of the *T. solium* infection states, the morbidity of cysticercosis in Korea could not be figured out in their real states especially on a population base. The reasons are illustrated in the introduction to this paper. In short, there had been no appropriate methods to examine the prevalence of human cysticercosis. In this study, antibody tests by ELISA were applied to the prevalence survey of human cysticercosis. A surprisingly high rate of the antibody, 1.8% was obtained in the normal population. Even if the cross-reactivities of ELISA test for cysticercosis are considered (Cho et al., 1986), the antibody positive rate in the small sample of healthy adult population is embarrassingly high. Repeated larger scale studies are needed to confirm the data preferably including population of children and adolescents. If this data of the positive rate is proved in later sur-

veys, it suggests that there are still unexpectedly large reserves of asymptomatic infections of cysticercosis in the population who will sooner or later pass without any neurologic complication or manifest neurologic diseases. There are only a few available seroepidemiological data on the prevalence of human cysticercosis in the world. Examples are: 2-3% of seropositivity as revealed by hemagglutination test in general population in India (Mahajan et al., 1981); 0.45% in 18,417 sera of Mexican people when observed by less sensitive immunoelectrophoresis (Woodhouse et al., 1981); 2.3% of an endemic rural village people in Mexico (Keilbach et al., 1989); 6.8% (104 of 1527 tested sera) in Togo people (Dumas et al., 1989); 12% of a rural people in Mexico (Camacho et al., 1990).

The relations between the antibody positivity and the etiology of the epilepsy in the subjected patients seem to be very complex. All of the antibody positive epileptic patients may not be caused by the brain infections of *T. solium* metacestodes. This problem of non-specific positive reaction should be less than 10% because the specificity of micro-ELISA has been reported as over 90% (Cho et al., 1986). The incidental extracranial infection of *T. solium* metacestode in epileptic patients of other causes should be about 1.8% as revealed in the serologic tests in the normal population. The definite etiology of epilepsy in the antibody positive cases should be examined in the future by imaging diagnosis such as CT/MR.

Actually the more important problem of seroepidemiological survey for cysticercosis is its low sensitivity. Anti-*Cysticercus* antibody is negative when only a few worms were infected, or when the worms were completely calcified (Chang et al., 1988; Wilson et al., 1991). Therefore in the natural course of uncomplicated cerebral cysticercosis, the positive antibody test seems to return to negative about 10 years after the infection. On the other hand, partial/generalized seizure is still caused and continued by the calcified worm(s). As an etiologic factor study, therefore, the antibody test for cysticercosis can reveal only a part of all the epilepsy caused by the parasite. Therefore it seems quite reasonable at present to presume that at least 3.1% of epilepsy in Korea was caused by *T. solium* metacestodes infections.

In a past report on the etiology of epilepsy in Korea, cysticercosis and other parasites were considered as an etiology only in 0.2% (Kang et al., 1979). The diagnosis of cysticercosis was made when subcutaneous nodules were associated with epilepsy at the period due to lack of serologic tests and imaging diagnosis. The present study results indicate that there are at least 3,100 active CNS cysticercosis patients in

Korea in 1987-1990 when the Changmi Club patients (100,000) only were considered. In a study (Han and Myung, 1986), cysticercosis was etiology in 27% of the late-onset epilepsy in Korea.

It has been generally accepted that epileptics consist 0.5 ~ 1% of the general population (Wilder and Schmidt, 1985; Porter, 1986). Its prevalence in Korea has been reported to be 0.1 ~ 0.2% in many local surveys, undertaken in the 1960s and 1970s (Cho and Kim, 1983). Because the data have included epileptics with generalized seizures, the number would be even higher if patients with focal seizures are added. Nowadays the number of epileptic patients is estimated to be between 200 to 400 thousands in Korea. If the antibody positive rate, obtained in this study, is extrapolated to these figures, the number of cysticercosis would be 6,000 ~ 12,000 in this country. Epileptic seizure is one of the most frequent and important manifestations of cysticercosis. However, only 50-80% of CNS cysticercosis patients manifest epilepsy. There are many patients who present other neurologic deficits such as severe headache, hemiparesis etc. (Powell et al., 1966). This means that the total number of cysticercosis cases manifesting CNS symptoms is even greater than the number presumed above.

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