기 생 충 학 잡 지 제 18권 제 1 호
The Korean Journal of Parasitology
Vol. 18, No. 1, 37-44, June, 1980

Chemotherapeutic Control of *Enterobius vermicularis* Infection in Orphanages

Sung-Tae Hong, Seung-Yull Cho, Byong-Seol Seo and Chong-Ku Yun
Departments of Parasitology and Paediatrics, Institute of Endemic Diseases, College of Medicine, Seoul National University

INTRODUCTION

Nowadays there are many anthelmintics effective against *Enterobius vermicularis:* Pyrvinium pamoate, pyrantel pamoate, mebendazole, *etc.* However, actual treatment of individual patient or institutionized children frequently gave miserable results when evaluated by prolonged observation up to 40 days (Cho *et al.*, 1977). The anal swab positive rate was rapidly returned to pre-treatment level in 18~27 days after the single chemotherapy.

This phenomenon has long been interpreted as a result of reinfection. The reinfection concept has based on the E.B. Cram's summary (1943) in which the life span of female pinworm was stated as 15~28 days. Thus many workers neglected the possibility that young pinworms, which escaped the anthelmintic action of the drugs, reappeared again after growing up for 18~27 days.

Anyway, frequent failure to cease the harassing perianal appearance of female pinworms after single treatment made many workers to repeat the anthelmintic treatment. Matsen and Turner (1969) treated all family members with pyrvinium pamoate for 3 spaced doses, each in 2-week interval to prevent reinfections. However, reexamination undertaken 4 months after the first treatment showed only a slight reduction in reinfection among families. Lormans *et al.* (1975) tried two weeks interval mebendazole treatment for 3 times, followed by two doses of one month interval therapy. After 6 months, the initial egg positive rate, 63% was dropped to 12% in a mental institute.

In our previous study (Hong *et al.*, 1979), we confirmed the necessity to treat all the people in an orphanage concomitantly to control pinworm infection although 20-day interval treatment was tried for 2 or 3 times. To control satisfactorily the vicious reinfection cycle in institutionized children, it was desired to eliminate all of egg source within the institute and to maintain such state for certain period of time.

This study was designed and undertaken to observe the effect of egg-free state on the endemicity of *Enterobius vermicularis.* The egg-free state was theoretically achieved by chemotherapy which was repeated at 20-day interval.

MATERIALS AND METHODS

1. Rationale of study design

The basic concepts adopted in this design are:

(1) The interval between infection and gravid female migration is in range, 42~49 days; in average, 45 days(Schueffner, 1947; Akagi, 1973)

(2) Anthelmintic drugs remove *E. vermicularis* older than 25 days (Cho *et al.*, 1977)

(3) In highly prevalent institute, continuous reinfection is occurring

(4) After the single treatment, eggs are laid

This study was supported by the grant from the Ministry of Education, Republic of Korea Government(1979).

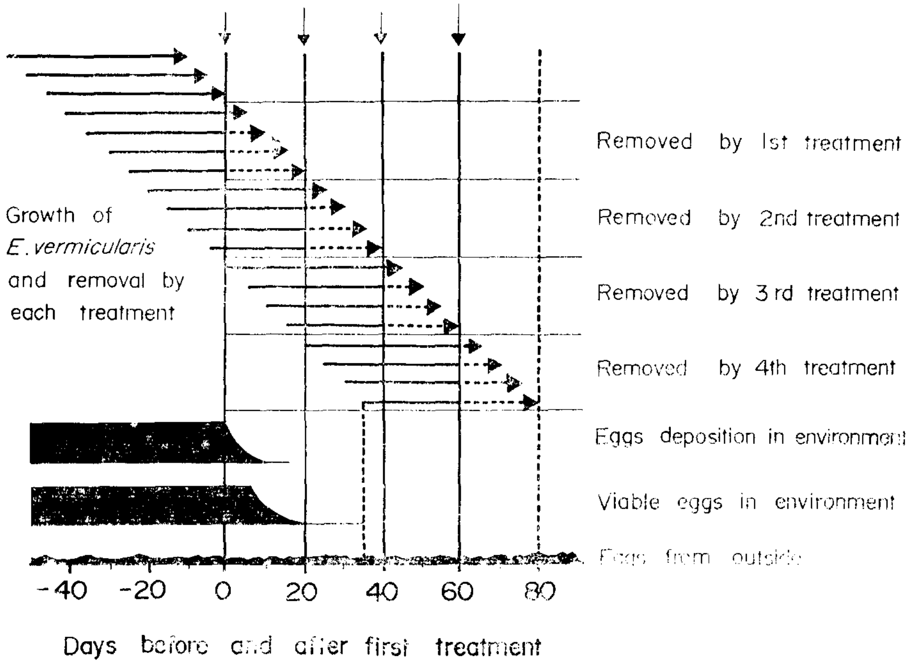

Fig. 1. Basic scheme of this trial. Arrays of transverse arrow mean the growth of female *E. vermicularis* in intestine. The arrowhead means perianal migration. By the successive treatment (vertical arrows on the top of figure), the grown females older than 25 days became susceptible to anthelmintics and removed (interrupted transverse arrows).
By this scheme of treatment, the viable eggs can survive up to 35 days after the first treatment (interrupted vertical line). The reinfection cycle within the orphanage is thus broken.

up to 15 days (Matsen and Turner, 1969; Cho *et al.*, 1977; Hong *et al.*, 1979)

(5) Infective eggs of *E. vermicularis* are retaining their infectivity up to 20 days after the egg laying (Jones and Jacobs, 1941; Schueffner, 1944; Oelkers, 1950).

These are summarized in Fig. 1. Accordingly, to break the reinfection cycle, treatment should be repeated for 4 times.

2. Subjected orphanage

As shown in Table 1, total 280 cases from 4 orphanages were subjected in this study. Among 4 orphanages two (Group I & II) were located in Ejungbu City, where pinworms were highly prevalent among general population and the other two (Group III & IV) were in outskirt of Seoul in which egg positive rate was lower. The sanitary condition of 4 institutes was much similar each other: There were virtually no differences in frequency of underwear changing and bathing, number of children living in a room, total maintenance budget, number of nursing staffs, *etc.* However, Group IV was more closed society than other three, because it took care of mentally retarded children, whereas the remaining three orphanages had many school-children attending nearby elementary school.

There were continual turn-over of children in each orphanage. Total 11 children were discharged from orphanages during the study period. They were excluded from statistics. Newly entered children were 14. They were treated exactly same as other children from the day of entry, but excluded from statistical considera-

Table 1. Treatment scheme for chemotherapeutic control of pinworm infection

Group (Orphanage)	No. of child. treated*	No. of child. examined**	Drug and dosage	No. of treatment	Location of orphanage
I	67	36	Mebendazole 100mg	4	Ejungbu City
II	69	30	Pyrantel pamoate 10mg/kg	4	Ejungbu City
III	70	41	Mebendazole 100mg	4	Seoul
IV***	74	64	Mebendazole 100mg	3	Seoul
Total	280	171	—	3~4	—

* The nursing and managing staffs were included
** Limited to children under 12-year old
*** Mentally retarded children and their nurses

tion.

3. Preliminary anal swabs and treatment

Among 280 cases subjected in this study, children under 12-year old were examined by scotch-tape anal swabs. Only one swab was taken from each child in every examination. Preliminary swabs were secured, each 2-day interval, for 4 times except Group IV (Table 2). The older children, nursing and managing staffs were excluded from examination, but simply subjected to concomitant chemotherapy with all children.

Two anti-pinworm drugs were used; mebendazole and pyrantel pamoate. The basic scheme of treatment by each Group was presented in Table 1. Each treatment was undertaken by 20-day interval.

4. Follow-up examination

Total 171 children were subjected to follow-up swabs. During this treatment period, swabs were taken every 20 day at the same day of next drug administration. Later follow-up swabs were taken with 10~45 days interval, for 9 times in Groups I, II and III up to 145 days after the last treatment. In Group IV, later swabs were taken 8 times with 7~30 day interval for 113 days. The number of children in each follow-up swab was not exactly same with the number subjected. There was 1 or 2 absentee in every examination in each orphanage.

This study was undertaken for 7 months during the period from October 17, 1979 to May 3, 1980.

RESULTS

1. Results of preliminary anal swabs

In Table 2, the preliminary anal swab results were shown. In Groups I & II, the mean rates were higher; 70% in Group I and 55% in Group II, but the cumulative positive rates were same.

Table 2. Results of preliminary anal swab examination

Group	No. of child. followed-up	Egg positive rate (%) 1st	2nd	3rd	4th	Mean posit. rate(%)	Cumulative posit. rate(%)
I	36	72	62	75	72	70	86
II	30	62	45	61	55	55	87
III	41	12	15	21	21	18	39
IV	64	25	36			30	47
Total	171	37	38	51	48	42	60

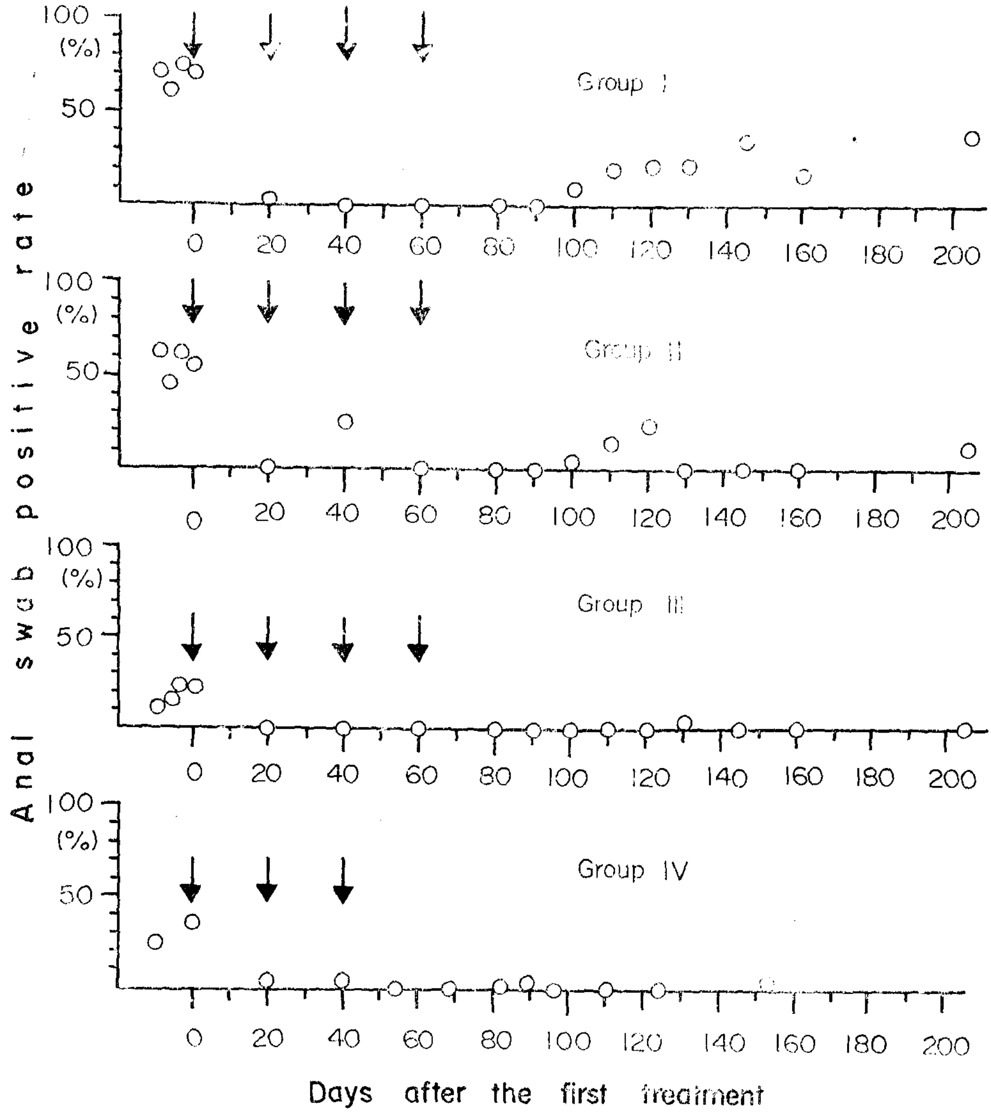

Fig. 2. Egg positive rates before, during and after the treatment. The vertical arrows indicate the day of treatment.

The positive rates in each examination in each Group gave minimal variation, which showed the epidemiological equilibrium state.

In contrast to this, the Group III & IV showed far lower endemicity; mean positive rate being 18% and 30% respectively. As indicated at the former section, the two institutes were located in Seoul where the endemicity of *E. vermicularis* was lower than in rural parts of Korea.

2. Results of follow-up anal swabs

Follow-up results in this study were shown in Fig. 2.

In Group I, positive rate decreased 70% to 3%, 20 days after the first treatment (=the day of second treatment). Egg negative state was maintained for 50 days. On the 100th day (=40 days after the last treatment), the rate began to rise again to 9%, then 19% on 110th day, 21% on 120th, 21% on 130th, 35% on 145th, 17% on 160th and 38% on 205th day. However, during 145 days of follow-up, positive rates never showed as high as pre-treatment level.

The results in Group II were similar with those of Group I. The rate was lowered from 55% to 0% at 20th day after the first treatment, and became 26% at the 40th day. It returned again to 0% until 90th day. Then the rates showed fluctuation; 4% on 100th day, 14% on 110th, 23% on 120th, 0% on 130th, 145th, 160th days and 12% on 205th day.

Mean preliminary positive rate in Group III, 18% was dropped to 0% after the first treatment and remained so throughout the examinations until 205th day after the first treatment. The only exception was one positive case on 130th day, out of 41 examined.

The results of Group IV were almost identical with those of Group III. Throughout follow-up examinations, egg positive rates were 0%. One positive case was found on 89th and 153th day respectively, out of 64 followed.

DISCUSSION

In this study, there were no control groups for comparison. Retrospectively, we should have at least two control groups; one highly endemic and another lowly endemic orphanage treated with placebo. However, in long-term follow-up study like this, setting the control group is practically impossible and socially unacceptable. Control group within the orphanage contradicted with the rationale of this study, because they became the egg source in the study group itself. By the result, the influence of probable seasonal fluctuation and other environmental factors in pinworm infection could not be properly evaluated. To compensate the lack of control group, the basic scheme of treatment was repeated in four separate orphanages.

In designing the basic scheme of this study, the most controversial point is the life span of pinworm. Many workers believe that span is 15∼28 days (Cram, 1943; Matsen and Turner, 1969). Schueffner (1947) and Akagi (1973) agreed that the female worms actually begin to migrate out the anus at 25∼30 days after the experimental infection, as Cram's report. However, they were egg-free females. Only the worms migrated later than 35∼42 days begin to lay eggs in perianal area. Because the egg-free state in an orphanage was a prerequisite in this study, we adopted the latter authors' result. Theoretically, the longer life span rendered the worse condition for removal of infective eggs within the orphanage, because more repeated interval treatment is needed to cover prolonged period of time.

As Cho *et al.* (1977) and Fan *et al.* (1978) reported, egg negative state can be maintained up to 18-27 days by single mebendazole treatment. So, among the rationale of this study design, "the anthelmintic drug removes *E. vermicularis* older than 25 days" was derived from simple calculation; 45 days (=mean life span) minus 20 days (=eggs clearing days after treatment).

Another problem which should be pointed out is the method of follow-up examination. We only depend upon the anal swab to evaluate the effect of treatment. In this connection, the exact meaning of positive result of anal swab is that one or more female pinworms migrated out during past two days (Cho & Kang, 1975). So, ideally it is better to examine every child every other day by anal swab during the whole follow-up period, to figure out the exact pattern of female migration; *i.e.*, treatment failure. However that kind of follow-up was practically impossible. And it was our compromise to examine them for egg positivity in 7- or 10-day interval in the initial stage of follow-up. Through these procedures, we believe, general pattern of endemicity was properly figured out than single remote follow-up swab as did by Matsen and Turner (1969) or Lormans *et al.* (1975).

The results in this study strongly suggest that we can effectively control the pinworm infection when the endemicity is low. However, we must postulate that reinfection was occurring continuously in the highly endemic groups. Theoretically, reinfection cycle within the orphanage must be broken by the scheduled treatment. So we could assume the source of reinfection was not from inside but from outside of the orphanages. Thus success of this scheme of treatment seemed to depend upon the endemicity of outside environment and the nature of the orphanages; closed or opened.

Another possible interpretation for the partial failure in control is that the basic scheme of present study has defects. In fact, in adopting the relevant factors in pinworm epidemiology, we oversimplified some aspect indeed. As Schueffner (1947) and Akagi (1973) stated, the gravid females may migrate out until 72-93 days after experimental infection. However, we postulated simply it was 45 days. And mebendazole or pyrantel treatment frequently failed to stop the female migration within 15 days (Hong *et al.*, 1979). Furthermore, some eggs keep their viability until 60-70 days, although the majority of eggs succumb in a few days, when deposited (Akagi, 1973).

Maybe, both of the above interpretations, defect in the scheme and flux of eggs from outside, contribute to the partial failure in control in highly endemic orphanages. However, it is evident that this scheme brought down the high endemicity to the susceptible range of control, as much as Lormans *et al.* (1975) did.

SUMMARY

To observe the effect of egg-free state in an institute on the endemicity of *Enterobius vermicularis*, the theoretical condition was made by repeated chemotherapy. Mebendazole or pyrantel pamoate were administered to all orphans and their staffs concomitantly for four times, each 20-day interval. In two low endemic orphanages, in which mean egg positive rates were 18% and 39% respectively, the pinworm infection was controlled up to 6~7 months period. And other two highly endemic orphanages, with 70% and 55% of egg positive rates, were controlled up to 90th day after the first treatment. After then up to 7 months, the reinfection occurred, but the endemicity was brought down to about 20% of egg positivity.

REFERENCES

Akagi, K. (1973) *Enterobius vermicularis* and enterobiasis. In *Progress of Medical Parasitology in Japan*, **4**: 229-279, Meguro Parasitological Museum, Tokyo.

Cho, S.Y., Ahn, Y.R., Ryang, Y.S. and Seo, B.S. (1977) Evaluation of anthelmintic treatment on *Enterobius vermicularis* infection in highly endemic population by prolonged observation. *Korean J. Parasit.*, **15**: 100-108.

Cho, S.Y., and Kang, S.Y. (1975) Significance of scotch-tape anal swab technique in diagnosis of *Enterobius vermicularis* infection. *Korean J. Parasit.*, **13**: 102-114.

Cram, E.B. (1943) Studies on oxyuriasis. XXVIII Summary and conclusion. *Am. J. Dis. Child.*, **65**: 46-59.

Fan, P.C., Liu, P.J., Cheung, F.Y., Wang, C.H. and Lee, S.H. (1978) Determination of the minimum effective dose of mebendazole in treatment of *Enterobius vermicularis* infection. *Yonsei Rep. Trop. Med.*, **9**:110, (abstract).

Hong, S.T., Chai, J.Y., Cho, S.Y., Seo, B.S. and

Yun, C.K. (1979) Efficacy of repeated chemotherapy in control of *Enterobius vermicularis* infection. *Seoul J. Med.*, **20**:163-168.

Jones, M.F., and Jacobs, L. (1941) Studies on oxyuriasis. XXIII The survival of eggs of *Enterobius vermicularis* under known condition of temperature and humidity. *Am. J. Hyg.*, **33**:88-102.

Lormans, J.A.C., Wesel, A.J.T., and Vanparijs, O.F. (1975) Mebendazole (R 17635) in enterobiasis. A clinical trial in mental retardates. *Chemotherapy (Basel)*, **21**:255-260.

Matsen, J.M. and Turner, J.A. (1969) Reinfection in enterobiasis (pinworm infection): Simultaneous treatment of family members. *Am. J. Dis. Child.*, **118**:576-581.

Oelkers, H.A. (1950) Untersuchungen an oxyureiern. *Z. Parasitenk.*, **14**:574-581.

Schueffner, W. (1944) Die Bedeutung der Staubinfektion fuer die Oxyuriasis: Richtlinien der Therapie und prophylaxie. *Muenchen. Mediz. Wschr.*, **81**:411-414.

Schueffner, W. (1947) Experimentelle Infektionen mit Staubeiern von *Oxyuris (Enterobius) vermicularis. Zb. Bakteriol.*, 152:67-73.

=국문초록=

반복화학요법에 의한 요충감염증의 집단관리

서울대학교 의과대학 기생충학교실 및 풍토병연구소

洪性台·趙昇烈·徐丙卨

서울대학교 의과대학 소아과학교실

尹 鍾 求

蟯蟲感染症에 대해 구충효과가 우수한 여러가지 약제가 현재 사용되고 있음에도 불구하고 여전히 완전치료를 이루기는 어려운 상태이다. 그원인은 재감염이 계속 일어나고 있기 때문에 단순히 한번만의 투약으로는 재차 감염을 막기 어렵기 때문이다. 더구나 현재 쓰이고 있는 mebendazole, pyrantel, pyrvinium등이 腸內의 어린 요충까지 모두 제거하지는 못한다는 사실과 20일 간격으로 반복 투약하더라도 집단구성원을 모두 대상으로 하지 않으면 재감염을 근절시킬 수 없다는 사실등 때문에 새로운 치료방법의 개발이 요구되고 있다.

이연구는 한 집단에서 요충란 생산이 중지된 상태를 일정기간 유지시킬 경우에 재감염이 관리되는지를 알아 보고자 실시하였다. 요충란 생산이 중지된 상태를 이론적으로 만들기 위하여 첫째 요충의 장내 감염기간은 평균 45일이다, 둘째 구충제는 감염후 25일이상 자란 요충을 제거한다, 셋째 요충란은 외계에서 20일까지 생존할 수 있다는 등의 조건을 전제로 하였다. 이경우 이론적인 無蟲卵상태는 요충치료를 20일 간격으로 4회 반복해야 얻을 수 있다. 따라서 이연구에서는 20일 간격으로 전집단 구성원을 대상으로 4회 반복치료했을 때 요충의 재감염상황이 어떻게 변하는가를 관찰한 것이다.

서울과 의정부시에 있는 4개 보육원에 대하여 각 보육원을 단위로 mebendazole 100mg 또는 pyrantel pamoate 10mg/kg의 용량으로 4회 전구성원에게 투여하였다. 치료전 감염정도와 치료결과의 파악을 위해 280명의 투약대상자중 4~12세의 아동 171명만을 대상으로 치료전에는 2일 간격으로 4회, 치료중에는 20일 간격으로 3~4회, 치료후에는 7~45일 간격으로 115~145일간 항문주위도말검사를 실시하였다.

그결과를 요약하면 다음과 같다.

1. 치료전 4회 검사의 충란양성율이 70%인 제 I 군에는 mebendazole을 20일 간격으로 4회 투여하였다. 네번째 투약일 전후 50일간 충란양성자는 없었고, 마지막 투약후 40일째부터 3명의 양성자가 나타나기 시작하여 그이후 항문주위도말검사 양성율은 17~38%의 범위에 있었다.

2. Pyrantel pamoate를 4회 투여한 제 II 군의 경우도 그결과가 제 I 군과 비슷하였다. 치료전 평균 55%의 양성

율이었던 것이 마지막 투약일로 부터 30일까지는 0%로 되었으나 40일째에 1명의 양성자가 나다나기 시작하였다. 그이후 105일동안 양성율은 0~23%의 범위에 있었다.

3. 치료전 4회의 검사에서 양성율이 18%이었던 제Ⅲ군은 mebendazole을 투여하였다. 네번째 투약후 70일째에 1명의 양성자가 있었을 뿐 추적검사기간인 145일동안 전원 음성이었다.

4. 제Ⅳ군은 치료전 2회 검사의 양성율이 30%였으며 mebendazole 3회 투여후 115일간의 추적검사에서 49일과 115일째에 각 1명의 양성자가 있었을 뿐 전원 음성이었다.

위의 결과로 볼 때 요충구충제를 20일 간격으로 4회 투여했을 경우 요충 재감염의 발생상태는 대상집단의 양성율 정도에 따라 차이를 보이고 있었다. 양성율이 18%와 30%인 群에서는 관찰기간안에서 再感染環이 단절되어 관리가 가능하였다. 그러나 70%와 55%였던 2個群에서는 감염경도가 치료전보다 매우 낮아졌지만 새로운 재감염이 마지막 투약후 40일부터 나다나고 있었다.

재감염 발생의 원인은 주로 관리대상이 아닌 외부환경에서 유래되었을 것으로 생각된다.

★ 원고 작성때의 유의사항 ★

기생충학잡지 이번호(18권 1호)부터 인용 참고문헌의 나열방법을 약간 변경하였읍니다. 이에 대하여 안내해 드리오니 앞으로의 원고 작성때에는 이점을 유의하시기 바랍니다.

달라진 점은 첫째 歐文논문을 나열할때 저자 성명의 ABC순서에 혼란을 적게하기 위하여 姓, 이름의 첫머리자의 순으로 계속 나열하는 방법을 취했읍니다. 이럴 경우 제 2 저자부터 이름의 첫머리자를 姓의 앞에 배열할 경우보다 논문 배열순서가 명확하여 질수 있읍니다. 둘째로 인용논문의 게재잡지를 이태릭체로 바꾸고 권수를 꼬딕체로 하었읍니다. 따라서 앞으로 원고 작성때에는 잡지 이름밑에는 밑줄 ____, 권수밑에는 ____로 표시하여 주시기 바랍니다.

보　기

변경전 : Chi, J.G., H.S. Chi and S.H. Lee (1980). Histopathologic study on human sparganosis. Korean J. Parasit., 18(1):15-23.

변경후 : Chi, J.G., Chi, H.S., and Lee, S.H. (1980) Histopathologic study on human sparganosis. *Korean J. Parasit.*, **18**(1):15-23.

(학술부)