

---

ORIGINAL ARTICLE

---

## Effects of Chloramphenicol on the Titer of Widal in Typhoid Fever

by

HAFNI Z. SOESILO; YATI SOENARTO; SOELISTYOWATI;  
RISTANTO\* and ISMANGOEN.

(From the Department of Child Health and the Department of Microbiology\*,  
Medical School Gadjah Mada University, Yogyakarta).

### Abstract

*A study was carried out on 93 cases of Typhoid fever admitted to the Department of Child Health, Gadjah Mada University Hospital in Yogyakarta.*

*The diagnosis is based on the discovery of Salmonella typhi in the blood.*

*It is stated that Chloramphenicol possesses an immunosuppressive nature, suppressing the titer of antibodies.*

*Chloramphenicol has been administered with a dosage of 75 mg/kg bodyweight/day.*

*Checking on the titer of Widal was done weekly, beginning with the first week (prior to treatment with Chloramphenicol), lasting four weeks (up to approximately one or two weeks after Chloramphenicol administration was stopped).*

*In only 91 of 93 cases follow up was possible : the Widal titer increased in 29 cases (31.9%), decreased in 23 (25.2%) cases and was constant in 39 cases (42.9%).*

---

Presented at the Vth National Indonesian Pediatric Congress, Medan, June 14 — 18, 1981.

Received June 20, 1981.

### Introduction

Typhoid fever has remained endemic in Indonesia and other developing countries.

A low socio-economic level, poor drinking water condition and environmental sanitation have been among the causative factors (Soeharto et al., 1977).

Usually death was caused by intestinal perforation and septic shock.

Earliest possible treatment will give a favorable prognosis, which is difficult to realize since most patients are admitted to the hospital in an advanced condition (Soewandoyo et al., 1979).

Although the use of Chloramphenicol has drawbacks and side effects such as bone marrow depression, toxic crisis and common occurrence of relapse (Hsieh, W.C. and Hsieh, B.S., 1974), Chloramphenicol is still a drug of choice, in addition to proper care and regulated diet (Woodward et al., 1948 and Kaspan et al., 1979). Moreover, Chloramphenicol is relatively a low cost treatment.

There are other remedies said to be safer and more effective, but therapeutic superiority of the latter as a treatment of Typhoid fever (Dawkins and Hornick, 1966) has not yet been proved.

It has been said that Chloramphenicol possesses an immunosuppressive nature (Gan, 1980).

Opinions concerning effects of Chloramphenicol on the titer of antibodies and duration of administration, are still controversial (Tai et al., 1971; Balakrishna et al., 1977).

The aim of this study is to determine the effects of Chloramphenicol on the formation of antibodies by checking the titer of Widal in Typhoid fever cases.

### Material and methods

Ninety three patients suffering from typhoid fever admitted to the Department of Child Health, Gadjah Mada University Hospital (aged from 8 months to 13 years) between October 1979 to October 1980, were studied.

The diagnosis was based on :

1. Clinical symptoms (fever of over seven days, anorexia, constipation, coated tongue etc.).
2. Laboratory findings :
  - blood culture (discovery of *Salmonella typhi* in the blood.)
  - serological test (titer of Widal).

Bacteriological and serological examination were done in the Department of Microbiology, Medical School, Gadjah Mada University.

Treatment and care :

- absolute bedrest until the patients were six days without fever, after which they were allowed to sit up.
- diet of light meals (soft food) until six days without fever, followed by giving more solid food, gradually.
- Chloramphenicol with a dosage of 75 mg/kg bodyweight/day was given until the patients were five days without fever.
- the patients were discharged after nine days without fever (if no complications occur).

Serological examination (the titer of Widal) was done :

- at the time of admission.
- weekly during hospitalization.
- on the day of discharge.
- a month after the patients discharge (on leaving the hospital, patients were given a letter notifying them to return for control a month after discharge).

### Results

Ninety one out of 93 cases of typhoid fever (aged between 8 months — 13 years) consisting of 50 males and 43 females, admitted to the Department of Child Health, Gadjah Mada University Hospital between October 1979 and October 1980 have been studied (table 1).

The patients were admitted during the first, second and third week of fever. Only 91 out of 93 cases could be put under follow up procedures.

Sixty (65.9%) were well nourished and 31 (34.1%) were undernourished.

Chloramphenicol was given during an average of 8.3 days (7-17 days) while fever decreased on the average of 4.9 days (3-5 days after treatment).

The titer of Widal increased in 5 cases, remained constant in 1 of the six patients receiving Chloramphenicol in the first week.

The titer increased in 24, decreased in 21, remained constant in 38 of the 83 patients receiving Chloramphenicol treatment in the second week. Two patients receiving the same treatment in the third week showed a decrease of the titer (table 2).

The titer of Widal increased in 29 (31.9%), decreased in 23 (25.2%), remained constant in 39 (42.9%) of 91 patients.

It turned out, that nutritional status did not have any effect on the titer of Widal (table 3). One patient (1.1%) died due to intestinal perforation, and another one insisted on leaving the hospital prior to total recovery.

### Discussion

Actually no titer of Widal has ever been absolutely proved to possess any certain diagnostic significance.

The determinant most often employed for O agglutinin, has always been based on an agreement, i.e. the immune body is formed whenever there is a contact between an organism and an antigen (Soeharto, 1979).

Approximately two weeks after contact, the immune body was found in the organism's circulation. The amount of immune bodies would reach the optimum between three and four weeks after contact.

Chloramphenicol has remained the drug of choice in addition to proper care and a correct diet although some times there have been drawbacks or side effects (Balakrishna et al., 1977; Hsieh, W.C. and Hsieh, B.S., 1974). Chloramphenicol has a suppressive effect on immunological responses (Gan 1980) so that there is no increase of the titer of antibodies.

Robertson et al. (1968) stated that Chloramphenicol certainly did not influence or disturb the formation of antibodies.

Tai et al. (1971) said that early administration of antibiotics could influence the formation of antibodies, and that whenever the titer of antibodies was found negative prior to this treatment, no increase of titer would take place, but whenever there had already been any increase, previous to this treatment, it would continue to rise afterwards.

Concerning the dosage and duration of treatment, opinions differ :

Nelson (1975) recommended a dosage of 50 mg/kg body weight/day for 10 to 14 days or up to the 5th to 7th day without fever.

Kempe (1976) adopted 14 to 21 days.

Ismail et al. (1976) adopted 14 days with a dosage of 50 mg/kg bodyweight/day.

In this study a dosage of 75 mg/kg bodyweight/day for an average duration of 10 days or up to the 3rd to 5th day without fever has been given.

TABLE 1 : Distribution of age and sex.

Age (years)	Sex				Total
	Male	% age	Female	% age	
0 — 2	1	1.1	2	2.2	3
2 — 5	9	9.7	7	7.5	16
5 — 13	40	43.0	34	36.5	74
Total	50	53.8	43	46.2	93

### Summary

A study was carried out on the effects of Chloramphenicol on the titer of Widal in cases of typhoid fever at the Department of Child Health, Gadjah Mada University Hospital in Yogyakarta from October 1979 through October 1980. There were 93 cases studied (with *Salmonella typhi* discovered in the blood), consisting of 50 males and 43 females, sixty (65.9%) of them were well nourished and 31 (34.1%) undernourished (one patient died due to intestinal perforation, and another one insisted on leaving the hospital prior to total recovery). The ages ranged from 8 months to 13 years.

No effect of Chloramphenicol administration in the first, second or third weeks of treatment on the titer of Widal has been observed in this study.

TABLE 2 : Titer of Widal after Chloramphenicol treatment.

Titer of Widal	Increase		Decrease		Constant		Total
	Number of cases	% age	Number of cases	% age	Number of cases	% age	
1st week	5	5.5	0	0	1	1.1	6
2nd week	24	26.4	21	23.1	38	41.7	83
3rd week	0	0	2	2.2	0	0	2
Total	29	31.9	23	25.3	39	42.8	91

( $p > 0.05$ )

TABLE 3 : Titer of Widal after treatment in relation to nutritional status.

Titer of Widal	Well-nourished		Undernourished		Total	% age
	Number of cases	% age	Number of cases	% age		
Increase	20	22.0	9	9.9	29	31.9
Decrease	13	14.2	10	11.0	23	25.2
Constant	27	29.7	12	13.2	39	42.9
Total	60	65.9	31	34.1	91	100

( $p > 0.05$ )

### REFERENCES

- BALAKRISHNA, S.V.A.; MALAVIYA, A.N.; KUMAR, R.; GHAI, O.P.; BAKHTARY, M.M. : Development of immune response during typhoid fever in man. *Clin. exp. Immunol.* 28 : 35 (1977).
- DAWKINS, A.T. Jr.; HORNICK, R.B. : Evaluation of antibiotics in a typhoid model. *Antimicrobiol. Agents chemother.* 6 : 6 (1966).
- GAN, V.H.S. : Obat immunosupresan. *Farmakologi dan Terapi* 2 : 651-9 (1980).
- GULATI, P.D.; SAKENA, S.M.; GUPTA, P.S. ; CHUTTANI, H.K. : Changing pattern of typhoid fever. *Amer. J. Med* (1968).
- HSIEH, W.C.; HSIEH, B.S. : Influences of Trimethoprim-Sulphamethoxazole and Chloramphenicol on immunoglobulin and

- antibody respons in Typhoid fever. South East Asian J. trop.Med.Pub.Health. 5: 17 (1974).
6. ISMAIL, D.; UTOMO; SUTARYO : Trimethoprim Sulphametoazole and Chloramphenicol in the treatment of typhoid fever in children. Fifth Asia Pacific Congr. Gastroenterol. Singapore 23-24 May (1976).
  7. KASPAN, M. FARIED; S. DWI ATMODOJO; S.B. PARWATI; ISMOEDIYANTO SUGENG, S. : Masalah typhoid fever pada anak. Simp. Peny. Infeksi, Surabaya (1979).
  8. KEMPE, C.H. : Paediatric Diagnosis and Treatment (Lange Med Publ., California, 1976).
  9. NELSON, W.E. : Typhoid Fever. Textbook of Paediatrics, 10th Ed., p. 598-601 (Saunders, Philadelphia, 1975).
  10. ROBERTSON, R.P.; WAHAB, M.F.A.; RAASCH, F.O. : Evaluation of Chloramphenicol and Ampicillin in Salmonella enteric fever. New England J. Med. 278 : 171 (1968).
  11. SOEHARTO, S. : Diagnosis laboratorik pada typhoid fever. Simp. Peny. Infeksi di Surabaya (1979).
  12. SOEHARTO, S. : Salmonella sp.: yang resisten terhadap Chloramphenicol. Maj. Kedok. Indones. 27 : 48 (1977).
  13. SOEWANDOJO, E.; SUHARTO; EF. FENDI CHAERUL; YUWONO, R.; BAMBANG SOEBAGYO : Pengobatan Typhus abdominalis pada penderita dewasa. Simp. Peny. Infeksi di Surabaya (1979).
  14. TAI, F.B.; WANG, H.C.; WANG, W.J. : Current laboratory patterns of typhoid fever. Southeast Asian J. trop.Med.Pub. Health, 2 : 174 (1971).
  15. WOODWARD. T.E.; SIMADEL, J.E.; LEY, H.L.; GREEN, R.; MANKIKAN, D.S. : Preliminary report on beneficial effects of Chloromycetine in the treatment of typhoid fever. Ann. intern. Med. 29 : 131 (1948).