TOXOPLASMOSIS IN PREGNANCY AND ITS TRANSMISSION TO THE FETUS*

GEORGES DESMONTS, M.D.

Chef de Laboratoire
Hôpital Saint Vincent de Paul

JACQUES COUVREUR, M.D.

Medecin Assistant
Hôpitaux de Paris
Paris, France

HUMAN toxoplasmosis has long been most widely recognized as a severe congenital disease in infants born to asymptomatic mothers. It is generally accepted that the parasite is transmitted transplacentally to the fetus from a pregnant woman whose infection was recently acquired. Two arguments support this hypothesis:

1) A high antibody titer, suggestive of recent infection, is present steadily in sera taken from mothers who have just delivered a diseased child. A titer of 1:1,000 (or 300 I.U./ml.) is the minimum usually observed in this laboratory.

2) As a rule, a mother does not give birth to more than one child with congenital toxoplasmosis. This has been established since the earliest reports and is confirmed by experience. More than 800 cases of congenital toxoplasmosis have been studied seriologically in our laboratory. With the exception of 14 pairs of twins, there are no siblings in this series. It would seem that there should have been, were chronic maternal infection responsible for congenital disease.

In most cases maternal infection is subclinical. Thus, it is not usually recognized during pregnancy, and its relation to neonatal toxoplasmosis has been studied, for the most part, retrospectively. Only prospective studies of the offspring of women whose *Toxoplasma* infections are acquired can provide the information necessary for the definition of risk and the anticipated fetal lesions. Surveys for identify-

*Presented as part of a *Symposium on Toxoplasmosis* sponsored by the Tropical Disease Center, Lenox Hill Hospital, New York, N. Y., and The Merck Company Foundation, Rahway, N. J., held at the Center May 5, 1973.

TABLE I. ASYMPTOMATIC MATERNAL TOXOPLASMOSIS FOLLOWED BY SEVERE CONGENITAL INFECTION

Subject	*Stage or age*	*Clinical manifestation*	*Dye test titer (1:)*	Toxoplasma *isolated**
Mother	2½ mos.	None	5	Not done
	8th mo.	Premature delivery	Not done	"
	8 days postpartum	—	8,000	"
Infant	8 days	Icterus, spleno- and hepatomegaly, hydrocephalus, microphtalmia, uveitis	8,000	Blood CSF
	2 mos.	Death	Not done	Brain

*By mouse inoculation

ing these women were begun by us in Paris some 15 years ago, and the over-all results of our research will be summarized here. In general, our data agree with the results of other investigators.[3, 6, 7]

This survey includes both women whose infection was acquired during pregnancy or at an unknown date and those having a high antibody titer due to infection acquired before pregnancy. A study of the offspring of the latter group was considered necessary, since the possibility of transmission from a chronically-infected mother has been suggested in a small number of scattered reports.

PROCEDURES AND METHODS

In the initial survey, sera obtained during pregnancy were stored frozen until tested with cord sera obtained at the time of delivery. Physical examinations of children were conducted when a high dye test (DT) titer (1:500) was present in the cord serum. These examinations were made at various times postnatally, the eldest child being 45 months of age. In this survey, the results of which will be shown separately, the mothers were not treated during pregnancy, nor were the children treated during the neonatal period.

In all the other studies, in order to observe seroconversions, pregnant women were screened, principally at the end of the second month; those who were seronegative were re-examined subsequently.

TABLE II. *TOXOPLASMA* SEROLOGICAL SCREENING SYSTEM AMONG PREGNANT WOMEN DURING SECOND MONTH OF PREGNANCY

Serological procedure		*Repeat serology*
*Dye test**	*IgM FAT*	
Negative	Negative	5th, 7th and 9th months†
Positive	Negative	None
Positive	Positive	2 to 3 weeks later‡

*Positive = $\geq$ 1:20
†To determine seroconversion
‡To determine rise in DT titer

In addition, we also attempted to select women whose infections had occurred earlier, shortly before pregnancy, or during the first weeks. For this purpose, limiting ourselves to an examination of patients with a high titer in the dye test proved to be insufficient. For example, an instance of severe congenital disease was observed (Table I) which was not anticipated because of a low maternal DT titer in the first trimester. This case might have been detected during pregnancy had the IgM fluorescent antibody test (FAT) been performed. This observation led to the adoption of the following system to screen pregnant women in whom there is a high risk of infection for the child (Table II).

At the time of the initial examination both the DT and the IgM FAT are performed. If both are positive, acute infection is suspected and a second serum is obtained two or three weeks later in order to determine whether the DT antibody titer has increased significantly. If only the DT is positive, no follow-up is considered necessary unless clinical evidence suggests acquired toxoplasmosis. If the DT is negative, it is repeated in the fifth, seventh, and ninth months to determine if seroconversion has occurred.

Women in whom an acquired infection was demonstrated were treated with Spiramycin, an antibiotic derived from *Streptomyces ambofacians*, which is therapeutically active in experimental *Toxoplasma* infections.[5]

Pyrimethamine-sulfadiazine treatment was not used in pregnant women for fear of hematological and teratogenic side effects. Spira-

TABLE III. CLINICAL TOXOPLASMOSIS AMONG 135 CHILDREN EXAMINED BECAUSE OF MATERNAL SEROCONVERSION OR HIGH INITIAL TITERS

*Maternal**			*Offspring*					
			Dye test					
			Negative		*Positive*		*Clinical toxoplasmosis†*	
Dye test	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
>1:500 in the first serum (2d month)	124	5.5	123	99	1	0.8	0	0
Significant rise or seroconversion	11	0.5	3	27	8	73	2	18
Totals	135	6	126	93	9	7	2‡	1.5

*2,238 pregnancies sampled
†Examined at various ages up to 3¾ years
‡Both with isolated chorioretinitis

mycin was prescribed in four divided oral daily doses of 2 to 3 gm. for six weeks. This schedule was repeated at two-week intervals until delivery.

Placentas obtained at delivery were digested with trypsin and inoculated into mice in order to isolate parasites. Children were examined clinically and DTs were performed on their sera. Most children were treated in the early neonatal period with Spiramycin when congenital toxoplasmosis was suspected, and with pyrimethamine and sulfadiazine when infection, even asymptomatic, was demonstrated.

RESULTS

Initial surveys (Table III). Only two of the 135 babies selected for follow-up among 2,238 deliveries, from their serological findings, had "clinical congenital toxoplasmosis." Both had only a retinal scar which was discovered at the initial examination of one child and later in the second.

Nine asymptomatic babies had positive dye tests when first examined between six and 45 months of age. One was from the group of mothers with high dye-test titers at the first examination. Eight (73%) were from 11 born to mothers who had had either seroconversions or significant rises in titer during pregnancy. These findings suggested

TABLE IV. PREVALENCES OF *TOXOPLASMA* DYE-TEST ANTIBODIES IN SEVERAL POPULATIONS OF PREGNANT WOMEN

Age group (years)	New York*		London†		Paris‡			
					French		Others§	
	No.	Positive (%)	No.	Positive (%)	No.	Positive (%)	No.	Positive (%)
15-19	552	16	1,579	15	93	80	23	56
20-24	1,127	27	990	27	390	81	72	53
25-29	1,309	33	442	33	351	86	100	78
30-34	689	40	133	34	201	95	57	77
≥35	371	50	25	36	171	96	41	80
Totals	4,048	32	3,169	22	1,206	87‖	293	70‖

*Kean, B. H.: Clinical toxoplasmosis—50 years. *Trans. Roy. Soc. Trop. Med. Hyg.* *66*:549-67, 1972.

†Ruoss, C. F. and Bourne, G. L.: Toxoplasmosis in pregnancy. *J. Obstet. Gynec. Brit. Comm.* *79*:1115-18, 1972.

‡Desmonts, G., Couvreur, J., and Ben Rachid, M. S.: Le toxoplasme, la mère et l'enfant. *Arch. Franc. Pédiat.* *22*:1183-1200, 1965.

§Spaniards, North African Moslems, and Portuguese.

‖84% over all (14,828 sampled).

that some children had had asymptomatic congenital infections (Table III).

Study population. In France the prevalence of *Toxoplasma* antibodies is very high. In Table IV results reported in 1965 from Paris are compared with those recently described by Kean[6] in New York and Ruoss[7] in London. Whereas 84% of pregnant women in Paris have antibodies, only 32% in New York and 22% in London give similar reactions.

In Paris the prevalence of *Toxoplasma* antibodies is greater in women of French origin than among immigrants. In the latter, antibody prevalence increased markedly with age; most acquisitions were observed among North African Moslems and Portuguese.

The observed incidence of seroconversion was approximately six per 100 per year. Since 16% of the total population had no antibodies, the incidence of acquired infections was nearly 10 per 1,000 per year.

Placentas. The results obtained from the inoculation of placentas will be discussed here (Table V). *Toxoplasma* was isolated from 27

TABLE V. ISOLATION OF *TOXOPLASMA* FROM PLACENTAS OF WOMEN WITH ELEVATED* *TOXOPLASMA* DYE-TEST TITERS

Maternal toxoplasmosis acquired	*Placentas*			
			Toxoplasma†	
	No.	*%*	*No.*	*%*
During pregnancy	97	48	25	26
Before pregnancy or unknown	105	52	2‡	2
Totals	202	100	27	13

*Dye-test titer $\geq$1:1,000 or $\geq$300 I.U./ml.
†Isolated in mice.
‡Mothers were first examined at sixth month of pregnancy.

(13%) of 202 placentas. When maternal infection was known to have been acquired during pregnancy (seroconversion, clinical data, or significant rise in titer), parasites were demonstrated in 26% of the specimens. Among women with infections acquired before pregnancy and in those whose date of infection was undetermined, only two were positive. Each of these mothers had had sublinical infection as evidenced by high, stable antibody titers. Since their initial sera were obtained at the end of the sixth month, their infections could have been acquired during the first four months of pregnancy. The IgM FAT performed in one of these two women was positive; this is strongly suggestive of recently acquired infection. There was not a single positive among the mothers known to have been infected prior to pregnancy. Thus, *Toxoplasma* was demonstrated only in placentas obtained from mothers with either definitely or possibly acquired infections during the pregnancy study.

There was a close correlation between *Toxoplasma*-positive placentas and congenital infections, since each of the related offspring had serological or parasitological evidence of toxoplasmosis. While fetal infection may not necessarily follow when the placenta contains demonstrable parasites,[8] no exceptions were observed in these patients. Conversely, only three congenital infections were noted among offspring with negative placentas. In one there was a technical problem in that much of the placental sediment was lost before inoculation. In the second, the child had a strongly positive DT, but was not bled until he was two years old. Thus, an acquired infection could not be

TABLE VI. TOXOPLASMIC LYMPHADENOPATHY IN SEVENTH MONTH OF PREGNANCY: CHILD UNINFECTED

Subject	*Stage or age*	*Clinical manifestations*	*Titers*		Toxoplasma *isolated**
			DT (I.U./ml.)	*IgM FAT (1:)*	
Mother	7 mos.	Lymphadenopathy	500	20	Lymph node positive
	8 mos.	Premature delivery	—	—	Placenta negative
Infant	4 days	None	300	0	Blood and CSF negative
	5 mos.	"	8	0	—
	10 mos.	"	<2	Not done	—

*By mouse inoculation

excluded. In the third case, parasitemia paradoxically was demonstrated in the newborn child while the inoculation of its placenta was negative. These experiences suggest that the inoculation of placental tissue into mice may be useful in the diagnosis of congenital toxoplasmosis.

Infection in the offspring. Only 11 abortions were noted among 378 pregnancies with either seroconversion or high dye-test titer. In six the abortion was induced because of fear of the fetal effects of congenital toxoplasmosis.

Since the initial samples used for serological surveys of *Toxoplasma* were the sera collected for routine syphilis serology at the end of the second month, opportunities to detect abortions caused by acute maternal toxoplasmosis were limited. Interestingly, only one spontaneous abortion occurred among the 14 cases of toxoplasmic lymphadenopathy diagnosed about the time of conception and still present during the first month of pregnancy. This suggests that acute toxoplasmosis may not be a frequent cause of such events.

At delivery, several different kinds of fetal result were observed. These variations will be described by examples from the present series.

In many cases *the fetus was not infected*, as is illustrated by the case in Table VI. Here, toxoplasmic lymphadenopathy developed during the seventh month of pregnancy and parasites were isolated from a lymph node. At delivery no organisms were recovered from the placenta and the normal infant had a negative dye test at 10 months of age.

TABLE VII. ASYMPTOMATIC MATERNAL TOXOPLASMOSIS DURING PREGNANCY: FATAL GENERALIZED CONGENITAL TOXOPLASMOSIS

Subject	*Stage or age*	*Clinical manifestations*	*Dye test titer (1:)*	Toxoplasma *isolated**
Mother	2 mos.	None	< 10	—
	6 mos.	"	4,000	—
	7 mos.	Premature delivery	Not done	Placenta positive
Infant	1 hr.	Hydrocephalus Ascites Death	"	Blood positive CSF positive Ascitic fluid positive

*By mouse inoculation

TABLE VIII. ASYMPTOMATIC MATERNAL TOXOPLASMOSIS DURING THE THIRD MONTH: SEVERE CONGENITAL TOXOPLASMOSIS

Subject	*Stage or age*	*Clinical manifestations*	*Titer*		Toxoplasma *isolated**
			DT (I.U./ml.)	*IgM FAT (1:)*	
Mother	2½ mos.	None	6	70	—
	4 mos.	"	1,000	250	—
	9 mos.	Delivery	800	150	Placenta positive
Infant	Birth	3,360 gm., APGAR 5	—	—	Cord blood positive
	5 days	Hydrocephalus Chorioretinitis CSF cells 70/ml. Protein 0.2%	600	20	Blood positive

*By mouse inoculation

In a few cases *severe congenital disease* was present in the newborn child. An example of this is summarized in a case (Table VII) in which seroconversion occurred between the second and sixth months of pregnancy. The baby had hydrocephalus and ascites and died within an hour after delivery. *Toxoplasma* was recovered from the placenta and, from the infant's blood, cerobrospinal fluid, and ascitic fluid.

Another mother (Table VIII) had a slightly positive dye test (1:20 or 6 I.U./ml.) when first bled at two and a half months of

TABLE IX. MATERNAL TOXOPLASMIC LYMPHADENOPATHY DURING THE EIGHTH MONTH OF PREGNANCY: ASYMPTOMATIC CONGENITAL TOXOPLASMOSIS

Subject	*Stage or age*	*Clinical manifestations*	*Titer*		Toxoplasma *isolated**
			DT (I.U./ml.)	*IgM FAT (1:)*	
Mother	7½ mos.	Lymphadenopathy	—	—	—
	8 mos.	"	300	> 20	—
	8½ mos.	"	800	Negative	—
	9 mos.	Delivery	—	—	Placenta positive
Infant	Birth	None	Cord 600	Negative	Cord blood positive
	1 day	"	— 600	"	Blood negative
	1 mo.	"	600	"	—
	4 mos.	"	400	"	—
	6 mos.	"	200	"	—
	8 mos.	"	800	"	—
	10 mos.	"	800	"	—
	13 mos.	"	600	"	—

*By mouse inoculation

pregnancy. The IgM FAT was positive at 1:70. Unfortunately, follow-up and treatment were delayed. The second sample obtained six weeks later showed a dye-test titer of 1,000 I.U./ml. At delivery the baby was in poor condition and had hydrocephalus and chorioretinitis. *Toxoplasma* was isolated from the placenta and cord blood. Relatively few cases of such severe disease in the newborn were seen during this study.

Subclinical infections were found in a number of apparently normal babies. An example of this is given in Table IX. Here the mother had toxoplasmic lymphadenopathy during the eighth month of pregnancy. Her IgM FAT was positive and turned negative two weeks later. The dye-test titer, meanwhile, increased from 300 to 800 I.U./ml. *Toxoplasma* was isolated from the placenta, the cord blood, and the baby's blood at 24 hours. The baby was treated. He was clinically normal and has remained so at 13 months, in the presence of a continuing, strongly positive dye test.

Another type of outcome, *delayed disease*, is illustrated by a case (Table X) in which toxoplasmic lymphadenopathy occurred during

TABLE X. LYMPHADENOPATHY DURING THE FOURTH MONTH OF PREGNANCY: DELAYED CONGENITAL TOXOPLASMOSIS

Subject	*Stage or age*	*Clinical manifestations*	*Titer*		Toxoplasma *isolated**
			DT (I.U./ml.)	*IgM FAT (1:)*	
Mother	3½ mos.	Lymphadenopathy	Not done	Not done	—
	4 mos.	"	700	"	—
	5 mos.	"	700	"	—
	8½ mos.	Delivery	300	"	Placenta positive
Infant	Birth	Normal	300	Neg. undil.	—
	1 mo.	"	160	"	—
	2 mos.	"	160	"	—
	3 mos.	"	80	"	—
	5 mos.	"	40	"	—
	7 mos.	Normal fundus	Not done	Not done	—
	10 mos.	—	40	Pos. undil.	—
	11 mos.	Chorioretinitis	120	"	—
	1 yr.	—	240	Negative	—
	1½ yr.	PSM retardation	600	"	—

*By mouse inoculation

TABLE XI. OUTCOME OF 180 PREGNANCIES WITH ACQUIRED MATERNAL TOXOPLASMOSIS

Category	*No.*	*%*
Clinically normal child		
Uninfected	110	61
Infected	46*	26
Subtotal	156	87
Congenital disease		
Mild	11†	6
Severe	7‡	4
Subtotal	18	10
Neonatal deaths	6§	3
Totals	180	100

*Seven not examined until 14 to 45 months postpartum

†Ten with isolated ocular lesions discovered during systematic fundus examinations; one had isolated intracranial calcifications

‡Five with involvement of eye and central nervous system present at birth; two with delayed disease

§Two with generalized toxoplasmosis; four fetuses lost to examination

TABLE XII. OUTCOME BY TRIMESTER OF 145 PREGNANCIES IN WHICH MATERNAL TOXOPLASMOSIS WAS ACQUIRED

Maternal acquisition			*Congenital toxoplasmosis*			
			*Present**		*Absent*	
Trimester	*No.*	*%*	*No.*	*%*	*No.*	*%*
1st	29	20	5	17	24	83
2d	79	54	20	25	59	75
3d	37	26	24	65	13	35
Totals	145	100	49	34	96	66

*Infected, regardless of disease

the fourth month of pregnancy. At delivery *Toxoplasma* was isolated from the placenta but the baby was normal. He remained so during the first few months of life except for vomiting sufficient to interfere with his treatment. The fundus was still normal during the seventh month. During the 10th month the dye-test titer increased and the IgM FAT, which previously had been negative, became slightly positive (undiluted serum). At 11 months chorioretinitis was noted. During the second year mental retardation was observed. Such delayed disease was infrequent in this study. In each case the child received incomplete postnatal treatment, leading to the conclusion that there might have been more disease had fewer infants been treated.

Congenital toxoplasmosis in relation to date of maternal infection. Among a total of 378 pregnancies with high dye-test titers in maternal sera at delivery, toxoplasmosis was not demonstrated in about 150 children whose mothers had become infected before pregnancy. The 180 cases in which toxoplasmosis was definitely or probably acquired during pregnancy are summarized in Table XI. Infections were not demonstrated in 61% of these children. Since infection was asymptomatic in 26%, a total of 87% either were normal or appeared normal. This includes all cases, whether treated or untreated during pregnancy.

The stage of pregnancy in which maternal infection was acquired may also be important in the determination of the child's fate. In the attempt to assess this effect, mothers were classified according to the trimester of pregnancy in which their infections apparently were

TABLE XIII. OUTCOME BY TRIMESTER OF 153 PREGNANCIES IN WHICH MATERNAL TOXOPLASMOSIS WAS ACQUIRED

Maternal acquisition			*Clinical disease in children*					
			Severe		*Mild*		*Absent**	
Trimester	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
1st	30	20	4†	14	1	3	25	83
2d	84	55	8‡	9	5	6	71	85
3d	39	25	0	0	2	5	37	95
Totals	153	100	12	8	8	5	133	87

*Contains uninfected and infected babies
†One neonatal death
‡Four neonatal deaths

acquired. This was possible in 145 pregnancies (Table XII). Infections were transmitted from mother to fetus in 17% of the cases in which maternal infections were acquired during the first trimester. (Actually, because of the serological survey system employed, the majority of first-trimester infections were acquired during the third month.) This proportion increased to 25% in the second trimester and to 65% during third trimester infections. Pregnancies which resulted in clinical disease are summarized in Table XIII. Eight further cases in which congenital toxoplasmosis was not proved are included in this table: three neonatal deaths, in which the fetus was not available for examination, are tabulated as severe disease, and five asymptomatic infants, in whom congenital and acquired infection could not be separated, are included as clinically normal. Most clinically diseased children were observed following first and second-trimester maternal infection. Late maternal infections usually yielded asymptomatic newborns: only 5% had a mild disease.

The effects of *maternal Spiramycin treatment* are tabulated in Tables XIV and XV. Only mothers treated for a minimum of three weeks were considered to have been treated. Categorization into treated and untreated groups was possible for all the 180 pregnancies in which toxoplasmosis was acquired. After excluding doubtful cases (fetus lost for examination or asymptomatic infants with possibly acquired infections), 169 remained for the estimation of the effects of maternal treatment on congenital infections. The difference is highly significant,

TABLE XIV. OUTCOME OF 169 PREGNANCIES IN WHICH MATERNAL TOXOPLASMOSIS WAS ACQUIRED ACCORDING TO SPIRAMYCIN TREATMENT

			Congenital toxoplasmosis			
	Pregnancies		*Present**		*Absent*	
Category	*No.*	*%*	*No.*	*%*	*No.*	*%*
Treated	96	57	22	23	74	77
Untreated	73	43	37	51	36	49
Totals	169	100	59	35	110	65

*Infected, regardless of disease

TABLE XV. OUTCOME OF 180 PREGNANCIES IN WHICH MATERNAL TOXOPLASMOSIS WAS ACQUIRED ACCORDING TO SPIRAMYCIN TREATMENT

			Clinical disease in children					
	Pregnancies		*Severe*		*Mild*		*Absent**	
Category	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
Treated	98	54	6	6	6	6	86	88
Untreated	82	46	7	9	5	6	70	85
Totals	180	100	13†	7	11	6	156	87

*Contains infected and noninfected babies
†Six neonatal deaths (1 treated and 5 untreated)

with 23% infected offspring in the treated group as opposed to 51% among the untreated (Table XIV).

The comparison is not as good when disease is considered (Table XV), since the total number of diseased babies is not significantly different in the two groups. Nevertheless, fewer severe congenital infections occurred in the treated group (one neonatal death) than among the untreated (five).

Spiramycin apparently does not cross the placental barrier freely, although it has been demonstrated in high concentration in this organ.[9] Thus, it seems unlikely that administration of Spiramycin to the mother would cure an already infected fetus. If this is true, the timing of treatment in relation to maternal acquisition would appear to be critical. This could explain why the number of infected off-

spring is much smaller in the treated group, while the proportion of clinical cases does not seem to have been affected.

The principal conclusions to be drawn from this study would seem to be that the diagnosis of acquired toxoplasmosis during pregnancy by no means indicates a hopeless prognosis for the child. Healthy, uninfected infants were born to approximately 50% of untreated mothers. The rate increased to 76% in mothers treated with Spiramycin during pregnancy. In addition, clinical disease occurred in only a small proportion of children infected *in utero*—only 11 to 13% of the offspring of 180 pregnancies.

Nevertheless, it should be emphasized that most infants were treated even though asymptomatic. This possibly reduced the number of overt cases. In this group, few delayed illnesses were observed, two severe and three mild. They occurred among children who for different reasons were either untreated or were treated inadequately.

REFERENCES

1. Desmonts, G., Couvreur, J., and Ben Rachid, M. S.: Le toxoplasme, la mère et l'enfant. *Arch. Franç. Pédiat. 22*:1183-1200, 1965.
2. Desmonts, G. and Couvreur, J.: Toxoplasmose congénitale. *21e Congrès des Pédiatres de Langue Française*. Paris, Expansion Scientifique Française, 1967, pp. 450-88.
3. *Colloque sur la Toxoplasmose de la femme enceinte et la prévention de la toxoplasmose congéntiale*. Lyon, Monographie du Lyon Médical, Specia ed., 1970.
4. Couvreur, J.: Prospective study of acquired toxoplasmosis in pregnant women with a special reference to the outcome of the foetus. In: *Toxoplasmosis,* Hentsch, D., editor. Bern, Huber, 1971, pp. 119-35.
5. Garin, J. P. and Eyles, D. E.: Le traitement de la toxoplasmose expérimentale de la souris par la spiramycine. *Presse Méd. 66*:957-58, 1958.
6. Kean, B. H.: Clinical toxoplasmosis—50 years. *Trans. Roy. Soc. Trop. Med. Hyg. 66*:549-67, 1972.
7. Ruoss, C. F. and Bourne, G. L.: Toxoplasmosis in pregnancy. *J. Obstet. Gynaec. Brit. Comm. 79*:1115-18, 1972.
8. Struck, E. and Janitschke, K.: Anzüchtungsversuche von Toxoplasma gondii aus Plazenten und Abortmaterial und serologische Prüfung der Frauen auf Toxoplasma-Antikörper. *Z. Geburtsh. Perinat. 176*:324-30, 1972.
9. Garin, J. P., Pellerat, J., and Maillard, M.: Bases théoriques de la prévention par le spiramycine de la toxoplasmose congénitale chez la femme enceinte. *Press Méd. 76*:2266, 1968.