

Treponemal IgG and IgM response in experimentally infected chimpanzees

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In recent years our studies of experimental syphilis have centred in the use of the chimpanzee as an animal model for the disease. Chimpanzees have been infected with *Treponema pallidum*, *T. carateum*, and *T. cuniculi*. The characteristics of these infections have been described in part or in whole elsewhere (Brown, Kuhn, Tolliver, and Norins, 1970; Chandler, Kaufmann, and Kuhn, 1972; Kuhn 1970, 1971, 1973; Kuhn, Medina, Cohen, and Vegas, 1970; Kuhn, Varela, Chandler, and Osuna, 1968; Kuhn, Brown, and Falcone, 1968). This paper presents changes observed in serum and cerebrospinal fluid (CSF) obtained sequentially from chimpanzees with and without experimentally induced treponematoses.

Material and methods

(1) *Animal infections*

The study included 24 adolescent or adult chimpanzees of either sex. Ten chimpanzees were inoculated only with *T. pallidum*, two with *T. cuniculi*, and nine with *T. carateum*, and three were not experimentally infected but had serological evidence of a previous treponemal infection. 3 years after the *T. carateum* (pinta) infection, four animals were challenged with 1×10^6 motile *T. pallidum* and four with 2.5×10^6 motile *T. pallidum*. One animal previously infected with *T. cuniculi* (cunicalosis) for 1 year was included with each of the last two groups. None of the infected animals received anti-treponemal treatment during the study.

(2) *Serum and cerebrospinal fluid*

A total of 409 sera and 349 CSF specimens were collected and tested. The distribution of the specimens by infection group is presented in Table I.

(3) *Serological tests*

The fluorescent treponemal antibody-absorption (FTA-ABS) test was performed according to the standard technique (USPHS, Manual of Tests for Syphilis, 1969), except that a 'broad spectrum' (not H-chain specific) fluorescein labelled anti-human IgG conjugate and a monospecific anti-human IgM conjugate were used, and test results were reported only as reactive and non-

TABLE I *Number of serum and CSF specimens collected from each infection group*

<i>Infection group</i>	<i>No. of animals</i>	<i>Sera</i>	<i>CSFs</i>
<i>T. pallidum</i> only	10	171	176
<i>T. carateum</i> before challenge	9	93	73
<i>T. carateum</i> after challenge	8	76	57
<i>T. cuniculi</i> before challenge	2	23	12
<i>T. cuniculi</i> after challenge	2	19	12
<i>Not infected</i>	3	27	19

reactive (Duncan and Kuhn, 1973). The tests are designated FTA-ABS-IgG and FTA-ABS-IgM.

For CSF testing both conjugates listed above were used in the provisional technique for the performance of the fluorescent treponemal antibody-cerebrospinal fluid (FTA-CSF) test, and the tests are designated FTA-CSF-IgG and FTA-CSF-IgM (Duncan, Jenkins, and Parham, 1972).

The venereal disease research laboratory (VDRL) slide tests for serum and for CSF, qualitative and quantitative, were performed according to the latest methods (USPHS Manual Tests for Syphilis, 1969) by personnel of the Venereal Disease Serology Unit, Center for Disease Control (CDC), Atlanta, Ga.

(4) *Total protein determination*

The trichloroacetic acid method was followed, except that the CSF was diluted 1 : 5 (USPHS, Manual of Tests for Syphilis, 1969).

Results

Serum and CSF were collected from the chimpanzees upon their arrival at the CDC facility, and at that time eight animals had some serological reactivity as shown in Table II (overleaf). CSF specimens and sera from the remaining sixteen animals were nonreactive.

Five animals with reactive sera (Nos 2, 5, 7, 11, and 22) and five with nonreactive sera (Nos 1, 6, 8, 16, and 20) were inoculated with *T. pallidum* only. The selection of the seroreactive animals and the limitations of the results were presented by Brown and others (1970). However, additional serological

TABLE II *Initial test reactivity of serum or CSF from eight chimpanzees on their arrival at the CDC facility*

Animal no.	Tests				VDRL	
	FTA-ABS IgG	FTA-CSF IgG	FTA-ABS IgM	FTA-CSF IgM	Serum	CSF
2	R	R	NR	NR	NR	NR
5	R	NR	NR	NR	NR	NR
7	R	R	R	NR	NR	NR
11	R	R	R	NR	NR	NR
12	R	R	NR	NR	R	NR
13	R	R	NR	NR	NR	NR
22	R	R	R	NR	R	NR
23	R	R	R	R	WR	NR

R = Reactive NR = Nonreactive WR = Weakly reactive

reactivity was detected by one or more of the tests after inoculation (Table III).

Eleven animals with nonreactive sera were selected for *T. carateum* or *T. cuniculi* inoculation. The interval in months between inoculation and the detection of serological reactivity is shown in Table IV.

Table V shows the change in test reactivity in the animals originally infected with pinta and cuniculosis and then challenged with *T. pallidum*.

The change in test results from reactive to non-reactive in specimens from twelve animals which had not received any treatment is shown in Table VI. Three animals, seroreactive on arrival at the CDC,

TABLE III *Interval in days between inoculation of chimpanzees with Treponema pallidum and detection of test reactivity*

Animal no.	Tests				VDRL	
	FTA-ABS IgG	FTA-CSF IgG	FTA-ABS IgM	FTA-CSF IgM	Serum	CSF
1	34	34	34	NR	34	60
2	R	R	22	NR	22	47
5	R	62	62	NR	14	37
6	27	27	27	NR	27	56
7	R	R	R	NR	33	63
8	22	34	14	NR	49	104
11	R	R	R	819	62	62
16	21	42	42	NR	103	103
20	48	61	20	NR	48	75
22	R	R	R	NR	R	105

NR = Nonreactive throughout study R = Reactive before inoculation

TABLE IV *Interval in months between inoculation of chimpanzees with T. carateum or T. cuniculi and detection of test reactivity*

Inoculum	Animal no.	Tests				VDRL	
		FTA-ABS IgG	FTA-CSF IgG	FTA-ABS IgM	FTA-CSF IgM	Serum	CSF
<i>Treponema carateum</i>	3	12	31	NR ^a	NR	15	NR
	9	17	NR	NR	NR	NR	NR
	10	2	27	NR	NR	15	NR
	14	28	28	NR	NR	28	NR
	15	8	12	NR	NR	8	NR
	17	28	28	NR	NR	28	NR
	19	8	13	15	NR	12	NR
	21	8	8	NR	NR	NR	NR
	24	8	8	8	NR	12	NR
	<i>Treponema cuniculi</i>	4	0.5	8.5	NR	NR	2
18		3	NR	NR	NR	NR	NR

^aNR = Nonreactive throughout study.

TABLE V Interval in days between *Treponema pallidum* challenge and reactive test results

Infection	T. pallidum challenge	Animal no.	Tests				VDRL	
			FTA-ABS IgG	FTA-CSF IgG	FTA-ABS IgM	FTA-CSF IgM	Serum	CSF
<i>T. carateum</i>	1×10^6	3	R	R	104	NR	33	62
		10	R	R	64	NR	R	33
		15	R	R	34	NR	R	67
		17	R	R	21	NR	R	33
<i>T. carateum</i>	2.5×10^3	14	R	R	62	NR	R	62
		19	R	68	R	NR	R	NR
		21	R	R	NR	NR	R	108
		24	R	R	R	NR	R	108
<i>T. cuniculi</i>	1×10^6	4	R	R	26	NR	R	63
	2.5×10^3	18	R	66	NR	NR	17	NR

R = Reactive before challenge NR = Nonreactive throughout study

TABLE VI Interval (months) required for test results to revert from reactive to nonreactive in untreated chimpanzees

Animal no.	Infection	Tests				VDRL	
		FTA-ABS IgG	FTA-CSF IgG	FTA-ABS IgM	FTA-CSF IgM	Serum	CSF
12	Not infected	R	28*	NR	NR	26	NR
13		R	7	NR	NR	NR	NR
23		R	R	13	13	20	3
1	<i>T. pallidum</i>	R	R	9	NR	R	R
6		R	R	2	NR	R	6
16		R	R	5	NR	R	10
3	<i>T. carateum</i> and <i>pallidum</i>	R	R	7	NR	R	R
14		R	R	2	NR	R	1
15		R	R	2	NR	R	R
17		R	R	7	NR	R	2
24	R	R	2	NR	R	R	
4	<i>T. cuniculi</i> and <i>pallidum</i>	R	R	2	NR	R	R

R = Reactive throughout study NR = Nonreactive throughout study * = Months required for serological reversal from reactive to nonreactive

were not experimentally infected and nine were experimentally infected with one or more strains of *Treponema*.

Table VII shows the time interval in weeks between *T. pallidum* inoculation and the detection of re-

activity by the VDRL CSF test along with the corresponding VDRL serum titres. As Table VII shows, the CSF of two animals did not become reactive in the VDRL test during a 15-week observation period; one of the animals had been

TABLE VII Interval (weeks) between *T. pallidum* inoculation of chimpanzees and detection of reactivity in the VDRL CSF test with the corresponding VDRL serum titre

Animal no.	No. of wks	VDRL serum titre (dilution)	Animal no.	No. of wks.	VDRL serum titre (dilution)
1	9	32	14	9	128
2	7	64	15	10	256
3	9	128	16	15	128
4	9	4	17	5	32
5	5	64	18	NR	0
6	8	64	19	NR	8
7	9	16	20	11	256
8	15	64	21	15	32
10	5	16	22	15	32
11	9	128	24	15	64

NR = Nonreactive 15 wks after inoculation with 2.5×10^3 *T. pallidum*

previously inoculated with *T. carateum* and the other with *T. cuniculi*, and both had been challenged with 2.5×10^3 motile *T. pallidum* organisms.

A total of 264 determinations of CSF total protein concentration was made (Table VIII).

Discussion

The literature on serological reactivity in pinta infection is relatively scarce. Pardo-Costello and Ferrer (1942) reported on work done with the older nonspecific lipoidal tests. In the initial stages no serological reactivity was detected, in the intermediate stage 60 per cent. of sera were reactive, and in the late stages 100 per cent. were reactive. In our studies, in which the modern cardiolipin-lecithin-cholesterol antigens and the more sensitive fluorescent treponemal antibody test were used, reactivity was detected in the serum and CSF of chimpanzees infected with pinta and cuniculosis. The interval between inoculation and the occurrence of serological reactivity in these animals was much longer than for the animals infected with syphilis. Excluding the FTA-CSF-IgM test, the interval between *T. pallidum* inoculation and detection of reactivity was 21 to 62 days for the FTA tests, 14 to 103 days for the VDRL serum test, and 37 to 105 days for the VDRL CSF test. In man, serological reactivity generally appears from 4 to 6 weeks after *T. pallidum* infection (USPHS, Syphilis, a Synopsis, 1968). FTA IgG reactivity was detected in the sera of the five nonreactive chimpanzees between 21 and 48 days after inoculation; CSF antibody reactivity occurred on the same date as serum reactivity in two animals and from 12 to 21 days after serum reactivity in the other three animals. Except for animal No. 22, serum from each

animal inoculated only with *T. pallidum* changed from nonreactive to reactive by one or more tests, and the VDRL titres increased to between 1 : 64 and 1 : 1024 after inoculation. Animal No. 22 had a titre of 1 : 1 at the time of inoculation, and this increased to 1 : 32 after inoculation.

For the animals infected with *T. carateum* or *T. cuniculi*, the interval between inoculation and serum reactivity in the FTA-ABS-IgG test ranged from 2 weeks to 28 months as compared with the maximum of 48 days for the animals infected with *T. pallidum*. CSF reactivity was detected on the same date as serum reactivity with specimens from four animals, and 4 to 25 months after serum reactivity in four animals. Sera from eight of the eleven animals became reactive in the VDRL test, with titres varying from 1 : 1 to 1 : 32. One animal infected with pinta died from an intercurrent infection 27 months after inoculation.

The intervals between inoculation and reactivity in serum for the two animals infected with cuniculosis were 2 weeks and 3 months for the FTA-ABS-IgG test. The CSF of one became reactive in the FTA-CSF-IgG test 8 months after the serum, and that of the other has remained nonreactive.

Reactivity developed later in the animals with pinta and cuniculosis infections than in those with syphilis, and the resulting titres were lower. However, the *T. carateum* and *T. cuniculi* inocula were considerably smaller in number than the *T. pallidum* inocula (Kuhn and others, 1968; Kuhn and others, 1970). Unlike those of the syphilitic animals, CSF specimens from the animals infected with pinta were nonreactive in the VDRL CSF test 3 years after infection, and those from the animals inoculated with *T. cuniculi* were nonreactive 1 year later. In the case of

TABLE VIII *Total protein concentration of CSF from 24 chimpanzees before and after inoculation*

Animal no.	No. of collections ^a	Protein concentration (mg./100 ml.)		Animal no.	No. of collections	Protein concentration (mg./100 ml.)	
		Range	Average			Range	Average
1	15	145-245	195	13	6	72-140	106
2	16	62-150	106	14	17	57-118	87
3	16	96-167	132	15	9	57-130	94
4	13	57-145	101	16	8	75-145	110
5	10	32-80	56	17	18	40-195 ^b	117
6	8	80-150	115	18	5	80-117	99
7	13	80-190	135	19	9	55-110 ^b	82
8	13	55-95	75	20	13	55-160	107
9	4	2.5-90	46	21	9	97-208	153
10	21	95-221 ^b	158	22	10	17-130	74
11	12	75-190 ^b	132	23	6	110-172	141
12	2	25-80	52	24	11	105-177 ^b	141

^a = Three tubes of CSF were taken at each collection

^b = Variability of protein content was detected in the three tubes from these animals on six occasions. The range and average are biased on the high side for animals 10 and 17 because of the following results:

Animal 10: Tube 1 = 221 mg./100 ml., Tube 2 = 167.5 mg./100 ml., Tube 3 = 135 mg./100 ml.

Animal 17: Tube 1 = 195 mg./100 ml., Tube 2 = 155 mg./100 ml., Tube 3 = 145 mg./100 ml.

one of the animals infected with cuniculosis FTA-CSF-IgG reactivity occurred 8 months after FTA-ABS-IgG reactivity. CSF from one animal infected with pinta was nonreactive throughout the study. Reactivity was detected by the FTA-ABS-IgM test in only two animals infected with pinta. Sera from two animals infected with pinta and one infected with cuniculosis were still nonreactive in the VDRL test after infection.

Of the three animals not experimentally infected, serological reversal to nonreactivity occurred in seven instances, although the animals had not received treponemal agents. At the end of the observation period, all specimens tested for IgM antibody were nonreactive, as were those tested with the VDRL tests. Only those tested for IgG antibody remained reactive at the end of the observation period.

Julian, Logan, and Norins (1969) reported that treponemal IgM antibody was detected earlier than treponemal IgG antibody. In the present study, three syphilitic animals reacted first by the FTA-ABS-IgG test, five were reactive by both the FTA-ABS-IgG and FTA-ABS-IgM tests on the same testing date, and two were reactive first by the FTA-ABS-IgM procedure. With one exception, all animals infected with pinta or cuniculosis became reactive first by the FTA-ABS-IgG test. Although all inoculated animals became reactive by the FTA-ABS-IgG test, three remained nonreactive by the VDRL serum test. The serological reactivity with pinta and cuniculosis infections seems to be biased towards tests detecting IgG antibody. With syphilis, all animals developed reactivity by the FTA-ABS-IgM test within a 2-month period after inoculation. Except for two animals infected with pinta, IgM reactivity was not detected in these infected animals until after they were challenged with *T. pallidum*. This restricted IgM antibody activity might indicate differences in the antigenic structure of the organisms or could possibly be attributed to the lesser antigenic mass employed.

O'Neill and Nicol (1972) reported that 127 of 128 human cases of untreated syphilis demonstrated both IgG and IgM serum antibody. However, for their 267 treated cases, a correlation between treatment and the disappearance of the IgM serum antibody was claimed. In our study it appears that the production of IgM antibody ceased spontaneously in ten of the animals because the test results changed from reactive to nonreactive, although they had not received anti-treponemal treatment. The FTA-ABS-IgM test on serum reverted ten times and the FTA-CSF-IgM test once. The VDRL test on serum reverted twice and on CSF five times.

Domonkos (1971) has stated that in patients with

pinta the CSF is generally normal. Saenz, Triana, and Armenteros (1940) reported that 10 per cent. of pinta patients showed CSF changes, namely increased globulin, syphilitic colloidal gold curves, and positive Meinicke reactions. Pardo-Costello and Ferrer (1942) reported that, when the spinal fluid of 23 patients with pinta was examined, twelve (52 per cent.) showed pathological changes similar to those encountered in cerebrospinal syphilis although there were no clinical manifestations. However, only seven of their patients had reactive CSF serological tests, and of these, six had increased protein and four had cell counts exceeding 5 per cu. mm.

In our study, two animals, one with pinta and one with cuniculosis, did not demonstrate CSF reactivity. The other nine animals demonstrated CSF reactivity within 8 to 31 months after inoculation, but the reactivity was confined to the FTA-CSF-IgG test. In the syphilitic animals, CSF reactivity was detected by the FTA-CSF-IgG tests within 62 days of inoculation. Only after challenge with *T. pallidum* did the CSF from the animals originally infected with pinta or cuniculosis develop reactivity in the VDRL CSF test, and this occurred in eight of the ten animals. The CSF of one cuniculosis-infected animal challenged with 2.5×10^3 *T. pallidum* organisms did not become reactive, whereas that of the other cuniculosis-infected animal, which was challenged with 1×10^6 organisms, did so. Of the seven VDRL CSF reactive pinta-infected animals, four had been challenged with 1×10^6 organisms and three with 2.5×10^3 organisms.

The question whether the IgG antibody passes the blood-brain barrier, damaged or intact, or is produced locally is still not resolved. However, from this study, there is evidence to suggest that there is passive transfer of the IgG antibody. Of the twenty animals inoculated with *T. pallidum*, all had reactivity in the CSF within 10 weeks of inoculation, whether they had had a previous treponemal infection or not. It appears from the results that there is a correlation between the VDRL serum titre and the appearance of reactivity in the VDRL CSF test. For eighteen of the twenty animals, the interval between *T. pallidum* inoculation and the detection of VDRL CSF test reactivity ranged from 5 to 15 weeks, with the corresponding serum titres ranging from 1:4 to 1:256 (Table VII). In no instance was there VDRL CSF test reactivity without a corresponding VDRL serum test reactivity after inoculation. However, we have previously shown that VDRL CSF reactivity with nonreactivity of the VDRL serum test can occur in chimpanzees after the syphilis has progressed over a number of years (Duncan and Kuhn, 1972). *T. carateum* has not, to our knowledge, been reported

in the CSF of humans infected with pinta, but *T. pallidum* has been detected in both humans and chimpanzees (Stokes, Beerman, and Ingraham, 1944; Duncan and Kuhn, 1973). The presence of *T. pallidum* in the CSF could be responsible for local antibody production, but it is difficult to explain the presence of IgG antibody in the animals infected with pinta and cuniculosis, except by passive transfer.

The possibility that IgM antibody is produced in the spinal column also seems very remote. It appears that IgM antibody does not cross the blood-brain barrier, damaged or otherwise. Eighteen of the 21 experimentally infected animals had IgM antibody detected in their sera, but they lacked IgM activity in the CSF. This lack of activity in all these infected chimpanzees is similar to the absence of reactivity in the CSF of man infected with *T. pallidum* (Duncan and Kuhn, 1973). Mattern, Sandor, and Pillot (1965) tested 35 CSF specimens for treponemal IgM antibody from patients with active neurosyphilis and all were nonreactive. Wilkinson (1973) found IgM treponemal antibody in only two out of nineteen CSF specimens from patients with neurosyphilis and stated that it was rare to find treponemal IgM antibody in the CSF in neurosyphilis. Results of these three studies suggest the FTA-CSF-IgM test is not a practical means of detecting treponemal IgM antibody of the central nervous system.

The VDRL CSF reactivity with specimens from the syphilitic chimpanzees and not with those infected with pinta or cuniculosis points to a number of possibilities:

- (1) It may be evidence that there are two types of IgG antibody, one reactive in the VDRL procedure and one detected by the broad-spectrum anti-IgG conjugate used in the FTA-CSF-IgG test;
- (2) It may be evidence of differences of the antigenic components of these treponemes;
- (3) The mass of *T. carateum* or *T. cuniculi* inoculum may not have been antigenically sufficient;
- (4) It may point to a greater damaging of the blood-brain barrier by *T. pallidum* than by *T. carateum* or *T. cuniculi*.

Derwelis, Butler, and Fineg (1970) reported on the total protein concentration obtained on CSF from twenty chimpanzees by the 10 per cent trichloroacetic acid method. They found the concentration to vary between 58 and 280 mg./100 ml. (average 131.5). In this study, 264 CSF specimens were subjected to the 10 per cent. trichloroacetic acid method, and the range was found to be between 2.5 and 245 mg./100 ml. The CSF was collected in three tubes, each containing approximately 2.0 ml. The protein determinations were usually performed on

pooled fluid from all three tubes or a fluid from only one of the three tubes collected. The protein content was found to be higher in most animals than in man, and the concentration varied from one testing date to another. The specimens were obtained before and after infection, and a consistent pattern was not obtained after inoculation. In all instances, only clear cerebrospinal fluids that were free of blood or coagulum were used. In a number of instances, when the tubes were examined macroscopically, it was noted that the first tube would have a large coagulum or be completely jelled, the second would have only a small coagulum floating in the fluid, and the third would be completely liquid. In these cases the third tube was used for the determination. Variation in concentration among tubes was not considered until by chance all three tubes of a collection were examined. In a number of instances the protein content varied from one tube to the next (Table VIII). Since satisfactory controls were used when the determinations were made, it seems apparent that for accurate sampling all three tubes should if possible be pooled before determining the protein content. Unfortunately, because of temporal and physical limitations at the chimpanzee facility, adequate cell counts on the CSF specimens could not be obtained.

One other interesting observation was made during this study. A baby male was born to animal No. 4. This animal had been inoculated with *T. cuniculi* and 1 year later challenged with *T. pallidum*. The baby was born 25 months after the challenge. Serum from the baby was reactive by the FTA-ABS-IgG test but nonreactive by the FTA-ABS-IgM test. Therefore, serologically, the baby did not have a congenital infection, since it had only maternal treponemal IgG antibodies.

Summary

Samples of serum and cerebrospinal fluid from 24 chimpanzees with and without treponemal infections were sequentially collected and tested. The animals were infected with *Treponema pallidum*, *Treponema carateum*, and *Treponema cuniculi*. Sera were examined by the VDRL slide test, the FTA-ABS-IgG, and FTA-ABS-IgM tests. Cerebrospinal fluids were examined by the VDRL slide test and the provisional FTA-CSF-IgG and FTA-CSF-IgM tests. Sera from the animals infected with syphilis became reactive in all procedures within 103 days of infection, and the CSF reactivity was limited to the VDRL and FTA-CSF-IgG tests. Sera from animals infected with pinta and cuniculosis were predominantly reactive in the tests detecting IgG antibody, and CSF

reactivity was limited to the FTA-CSF-IgG test. After challenge with *Treponema pallidum*, the serological reactivity of the animals previously infected with pinta and cuniculosis became similar to the pattern shown for the animals infected with syphilis. The protein content of CSF is generally higher for chimpanzees than for man: it varied from testing date to testing date, and did not follow a definite pattern after experimental infection. Serological tests indicated that a baby chimpanzee born 25 months after its mother was infected with *Treponema pallidum* was not congenitally infected.

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Résultats de la recherche des IgG et des IgM tréponémiques chez les chimpanzés infectés expérimentalement

SOMMAIRE

Des échantillons de sérums et de liquides céphalo-rachidiens obtenus chez 24 chimpanzés, avec ou sans infections tréponémiques, furent recueillis consécutivement et examinés. Les animaux avaient été infectés par *Treponema pallidum*, *Treponema carateum* et *Treponema cuniculi*. Les sérums furent examinés par le test du VDRL sur lame et ceux de l'FTA-ABS-IgG et de l'FTA-ABS-IgM. Les liquides céphalo-rachidiens furent examinés par le test du VDRL sur lame et les épreuves "provisoires" FTA-CSF-IgG et FTA-CSF-IgM. Les sérums provenant d'animaux inoculés de syphilis devinrent positifs à tous les examens dans les 103 jours et la positivité du LCR se limita aux épreuves du VDRL et du FTA-CSF-IgG. Les sérums des animaux inoculés de pinta ou de cuniculose furent positifs principalement vis-à-vis des épreuves détectant l'anticorps IgG et la positivité du LCR se limita au test FTA-CSF-IgG. Après inoculation de *Treponema pallidum*, la réactivité sérique des animaux antérieurement infectés de pinta ou de cuniculose présenta le même tableau que chez les animaux infectés de syphilis. La teneur en protéines du LCR est généralement plus élevée chez les chimpanzés que chez l'homme: elle varie selon la date de l'examen et n' a pas d'allure particulière après l'infection expérimentale. Les épreuves sérologiques montrèrent qu'un jeune chimpanzé, né 25 mois après que sa mère eut été infectée par *Treponema pallidum*, n'avait pas lui-même été atteint d'une infection congénitale.