

A COMPARISON OF THE RESPONSE OF YAWS AND SYPHILIS IN THE RABBIT TO THERAPY WITH MAPHARSEN AND NEOARSPHENAMINE

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It is the consensus of most investigators that clinical yaws is as difficult to cure as is syphilis (1), yet on the experimental side it appears that adequate therapeutic studies are wanting. Nichols (2) did make an interesting comparison of the two experimental diseases, though on the basis of more modern techniques his results must be considered to be inadequate since his only criteria of cure were the regression of lesions and the disappearance of positive serological reactions. Neither lymph node nor tissue transfers were made to determine sterilization, hence conclusive results were not obtained.

While a considerable amount of work (2-8) has been done on the comparative pathogenicity and immunology of yaws and syphilis in rabbits and in monkeys, there is a glaring paucity of information on the subject of therapy. It is, therefore, the object of this paper to fill in this gap, so far as present facilities permit. Information on this phase of the subject might possibly have some bearing on the academic question of identity of the two "diseases," providing the responses to therapy were significantly different.

The Nichols strain of *Treponema pallidum*, maintained in this laboratory since 1923, was used in these studies and the yaws strain was one generously supplied by Dr. Alan M. Chesney. The two diseases were maintained by testicular transfer in the same laboratory under as nearly similar conditions as possible. Rabbits with typical lesions were selected for the therapeutic studies and each animal was treated with a single intravenous injection of an arsenical drug. Seven days later the testicular lesion was removed, minced and extracted in 0.9 per cent sodium chloride solution. The extract so obtained was injected intratesticularly into two recipient rabbits which were then observed for from eight to twelve weeks for the appearance of lesions and positive blood Wassermann reactions. When the recipient animals failed to show lesions at the site of injection, or a positive blood Wassermann reaction, the original rabbit from which the transfer was made was considered cured. These criteria of cure were selected since it has been observed that the results of lymph node transfers, used so frequently in studies of rabbit syphilis, were irregular in rabbit yaws (4, 7, 9).

The results of mapharsen therapy in rabbit yaws and rabbit syphilis are given in table 1. It is evident that there is no significant difference in the

TABLE 1

Mapharsen therapy of rabbit yaws and rabbit syphilis using infectivity of testicular material as the criterion of cure*

DISEASE	DOSE OF MAPHARSEN† (MG. PER KG. OF BODY WEIGHT)	NUMBER OF RABBITS	NUMBER CURED	NUMBER NOT CURED
Yaws.....	2.0	5	1	4
Syphilis.....	2.0	4	2	2
Yaws.....	3.5	3	1	2
Syphilis.....	3.5	3	1	2
Yaws.....	5.0	3	3	0
Syphilis.....	5.0	3	2	1
Syphilis.....	7.0	2	2	0

* The testicle showing the largest lesion was selected for transfer which was made seven days after the administration of the drug.

† Single dose administered intravenously.

TABLE 2

Neosarsphenamine therapy of rabbit yaws and rabbit syphilis using infectivity of testicular material as the criterion of cure*

DISEASE	DOSE OF NEOARSPHENAMINE† (MG. PER KG. OF BODY WEIGHT)	NUMBER OF RABBITS	NUMBER CURED	NUMBER NOT CURED
Yaws.....	4	1	1	0
Yaws.....	7	4	3	1
Syphilis.....	7	3	1	2
Yaws.....	13	3	3	0
Syphilis.....	13	3	3	0
Yaws.....	20	3	3	0
Syphilis.....	20	3	3	0
Yaws.....	50	5	5	0
Syphilis.....	50	1	1	0
Yaws.....	100	1	1	0

* The testicle showing the largest lesion was selected for transfer which was made seven days after the administration of the drug.

† Single dose administered intravenously.

response of the two diseases to therapy with this arsenical, nor is there a significant difference in the response of the two diseases to therapy with neoarsphenamine, as indicated in table 2. The fact that the two experimental diseases are cured with about equal ease is in agreement with the clinical results of Pardo-Castello (1). The writers recognize that equal susceptibility to cure has no necessary bearing on the identity of the two diseases. Rabbits infected with *Trypanosoma equiperdum* are cured by certain arsenical drugs in about the same dosage as required for rabbits infected with *Treponema pallidum*, yet no one would conclude that the two diseases are identical. It may be noted that yaws and syphilis are cured with equal ease, yet they can usually be differentiated with readiness on the basis of physical signs, as claimed by Turner and Chesney (5).

The foregoing data, using testicular transfer as the criterion of cure, indicate that the therapeutic index of single doses of neoarsphenamine is superior to that of single doses of mapharsen in the treatment of rabbit yaws and rabbit syphilis. The rabbit tolerates 150 mgm. per kilogram of neoarsphenamine and mapharsen is tolerated at only 10 mgm. per kilogram, whereas the single minimal curative doses are 13 and 5, respectively.

These data should be read in the light of previously published evidence that multiple doses of mapharsen (10) are considerably more efficient than single doses whereas, according to Kolmer (11), neoarsphenamine is relatively less efficient. Consequently, the significance of this contribution resides in its bearing on relative curability of yaws and of syphilis and not on the determination of conditions for the development of maximal therapeutic efficiencies.

SUMMARY AND CONCLUSIONS

The comparative response of rabbit yaws and rabbit syphilis to therapy with single doses of mapharsen and neoarsphenamine has been determined, and from the data obtained it appears that there is no essential difference in the ease with which the two diseases may be cured.

REFERENCES

- (1) PARDO-CASTELLO: Arch. Derm. & Syph., **40**, 762, 1939.
- (2) NICHOLS: J. Exper. Med., **14**, 196, 1911.
- (3) NICHOLS: J. Exper. Med., **12**, 616, 1910.
- (4) TURNER: Am. J. Hyg., **25**, 477, 1937.
- (5) TURNER AND CHESNEY: Bull. Johns Hopkins Hosp., **54**, 174, 1934.
- (6) HASSELMANN: China Med. J., **45**, 1131, 1931.
- (7) PEARCE AND BROWN: J. Exper. Med., **41**, 673, 1925.
- (8) REASONER: Am. J. Trop. Med., **9**, 413, 1929.
- (9) CHESNEY: Personal communication.
- (10) TATUM AND COOPER: THIS JOURNAL, **50**, 198, 1934.
- (11) KOLMER: Principles and Practice of Chemotherapy with Special Reference to the Specific and General Treatment of Syphilis, W. B. Saunders Co., Phila., p. 346, 1926.