necessary to exhaust the "protein reserves" of their animals and reduce the rate of plasma protein fabrication significantly.

Since antibody formation appears to be influenced by dietary protein intake it seems likely in general that anything which interferes substantially with protein metabolism such as caloric inadequacy[8] for a sufficient length of time will also impair antibody formation.

One further point is apparent in the data of this experiment. The protein *content* of any body compartment is an insensitive indicator of the rate of turnover or fabrication of protein in the compartment. In Fig. 1 it can be seen that when the total circulating serum protein fell to about 50% of its initial value the rate of antibody production has fallen to 1% or less of its initial value. From previous experiments[12] we know that the circulating quantity of that portion of the globulin containing the antibody is reduced only to an equal or lesser extent than the total protein, *i.e.* 50% or less. Practically this means that the measurement of such quantities as serum protein concentration, total circulating serum protein or any one of its components may give little if any insight into the *rate* of production or turnover of the protein.

Summary. The present experiment investigated the rate of loss of the capacity to produce antibody in comparison with the rate of loss of protein from body compartments including carcass, liver and plasma. Young adult male albino rats were tested at intervals from 0 to 100 days after initiation of the low protein diet for agglutinin and hemolysin production. Blood volumes, hemoglobin, serum protein, liver and carcass protein were determined. It was found that all protein compartments and the rate of antibody production fell at approximately linear percentage rates per day, the antibody production falling much faster than the rest. Statistically significant depression of the antibody titers was not reached till the 30th day with hemolysins and the 17th day with the agglutinins.

[12] Benditt, E. P., unpublished observations.

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Chemotherapy of *Trichomonas foetus* Infections in Rabbits.*

BANNER BILL MORGAN, LOUISE LOMBARD, AND ALAN E. PIERCE.†

From the Department of Veterinary Science, University of Wisconsin, Madison, Wis.

No satisfactory therapeutic agent has been established for the successful treatment of bovine trichomoniasis. *In vivo* studies in laboratory animals of the trichomonacidal properties of various chemicals may offer useful information for future treatment trials in cattle. The purpose of this paper is to present the results of a study on the effect of 58 compounds on *Trichomonas foetus* in the vagina of rabbits. The majority of the compounds were selected from 350 chemicals previously tested *in vitro* by Morgan and Campbell.[1]

Witte[2] apparently was the first to successfully infect rabbits with *T. foetus* by vaginal

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† Wellcome Research Fellow of the Animal Health Trust (from the Ministry of Agriculture and Fisheries Laboratories, Weybridge, England).

[1] Morgan, B. B., and Campbell, H. M., *Am. J. Vet. Res.*, 1946, **7**, 45.

[2] Witte, J., *Arch. wiss. prakt. Tierheilk.*, 1933, **66**, 333.

inoculations. Trichomonads were recovered from the inoculated rabbits intermittently for 26 days. Nelson[3] was successful in infecting 2 rabbits intravaginally. According to Nelson[4] and Byrne and Nelson[5] 38 rabbits which were given intravaginal injections of *T. foetus*, 32 or 84% developed self-limiting infections with an average duration of 23 days. MacDonald *et al.*[6] inoculated 76 rabbits intravaginally with *T. foetus* with an incidence of 67%. Wittfogel,[7] Stableforth and Scorgie[8] and Trussell and McNutt[9] were unable to infect rabbits by the intravaginal inoculation of *T. foetus*.

Nelson[4] was the first to use the rabbit as a test animal for various therapeutic agents against *T. foetus*. Attempts to rid the organisms from the vagina of infected rabbits with 3 pentavalent and 1 trivalent arsenicals and sodium bismuthyl tartrate were unsuccessful.

Experimental procedure. Virgin female rabbits, of different breeds, obtained from various sources were used in the experiments. The animals were 6 to 8 months of age and weighed from 5 to 8 lb.

The bacteria-free strain of *T. foetus* used in this work was isolated by Morgan and Wisnicky.[10] Forty-eight to 96-hour-old cultures were used. The organisms were cultivated on a modification of Schneider's citrate: whole egg and defibrinated bovine blood slants overlaid with buffered saline citrate solution with 5% bovine serum. The number of trichomonads was determined by hemacytometer counts. A standard suspension of 3 million organisms per ml was used for inoculation purposes.

Rabbits were inoculated with 10 ml of a trichomonad suspension into the vagina by means of a sterile glass tube 7 inches long and ¼ inch in diameter. In the initial screening tests only 1 rabbit was used for each drug. A rubber adapter was attached to the free end of the glass tube and the trichomonads introduced by means of a glass syringe.

Microscopic identification of *T. foetus* was made from recently collected vaginal samples. A sterile wooden applicator stick with a cotton pledget attached was enclosed in a glass tube and inserted into the vagina. The glass tube was withdrawn, the swab rotated and a mucus sample obtained. Material adhering to the cotton was mixed with 0.7% saline; placed on a slide and examined.

Throughout the course of these studies the external genitalia of the rabbits were washed with a disinfectant prior to inoculation of infective material or collection of mucus samples. All rabbits were sampled prior to the experiments and the material plated on blood agar to determine the presence of bacteria. In a number of rabbits a gram negative rod was isolated in pure culture. Whether this bacterium was part of the normal flora of the vaginal tract of the rabbit could not be determined; however, its presence apparently had no effect on the course of the subsequent *T. foetus* infection.

Vaginal inoculation of *T. foetus* infected from 20 to 80% of the rabbits. The factors responsible for variation in susceptibility are not well understood. Microscopical examinations were made during the first 5 days following the infective inoculation and only those rabbits which showed a considerable number of organisms in the collected discharges were utilized in the experiments. Where the infection appeared to be mild during this time the rabbits were discarded. By making this selection the infection persisted in the 30 untreated controls for a minimum of 20 days.

Fifty-eight rabbits were treated with various compounds after showing an infection for 5 days. Three drugs which inhibited *T. foetus* were further tested utilizing 10 rabbits for each drug and 10 controls. Liquids and jellies were introduced in the vagina with a glass

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3 Nelson, P., *Arch. Path.*, 1937, **23**, 744.

4 Nelson, P., unpublished thesis, Library, University of Wis., 1938.

5 Byrne, H., and Nelson, P., *Arch. Path.*, 1939, **28**, 761.

6 MacDonald, E. M., *et al.*, *J. Immunol.*, 1948, **59**, 295.

7 Wittfogel, H., *Inaug. Diss. Hannover*, 1935, p. 68.

8 Stableforth, A., and Scorgie, N., *Vet. Rec.*, 1937, **49**, 253.

9 Trussell, R., and McNutt, S., *J. Infect. Dis.*, 1941, **49**, 453.

10 Morgan, B. B., and Wisnicky, W., *J. Am. Vet. Med. Assn.*, 1942, **100**, 471.

TABLE I.

Therapeutic Agents Used for Treatment of Vaginal Infections in Rabbits Induced by *Trichomonas foetus*.

1. Phemerol (*p-tert*-Octylphenoxyethy-oxyethyldi-methyl benzyl-ammonium-chloride) (Liquid) (.01%)
2. Sulfaguanidine (Powder)
3. Povage (Silver chloride-thiourea complex salt + 3-chloro-4-hydroxy diphenyl + osmo-kaolin (Powder)
4. Vioform (5-chloro-7-iodo-8-hydroxyquinoline) (Powder)
5. Sodium bicarbonate (Liquid) (5%)
6. Carbarsone (p-Carbaminophenyl arsonic acid) (Powder)
7. Negatan (Polymerized disulphonic-dioxydimethyl-diphenylmethane acids) (Suppository 10% negatol)
8. Tyrothricin (Water soluble jelly) (.01%)
9. Ceepryn vaginal powder borated (Cetylpyridinium chloride (.5%) + boric acid + kaolin + dextrose) (Powder)
10. Entozon granulate (2,3-Dimethoxy-6-nitro-9-(*y*-diethylamino-*B*-hydroxypropylamino) acridine dihydrochloride + 2-orthoxy-6,9-diamino-acidrine lactate + amyl saccharine + sodium biborate) (Liquid) (2%)
11. Iodine (Tincture) (Liquid) (0.5%)
12. Lugol's Solution (Iodine (5 gr.) + potassium iodide (10 gr.) + water (100 cc)) (Liquid)
13. Trypaflavine (2,8-Diamino-10-methylacridinium chloride) (Liquid) (1%)
14. Proflavine dihydrochloride (3,6-diaminoacridine dihydrochloride) (Liquid) (3%)
15. Meta Cine Douche Powder (Citric acid + papain + lactose + methyl-salicylate + eucalyptol + menthol + chlorthymol) (Liquid) (3%)
16. Silver picrate (1% dispersed in kaolin) (Powder)
17. Zonite (Sodium hypochlorite + sodium hydroxide + sodium chloride) (Liquid) (3%)
18. Merpectogel (Phenylmercuric nitrate (1:24,000) + pectin jelly) (Jelly)
19. Caprokol (Hexylresorcinol 1:1000 + alcohol + water soluble jelly) (Jelly)
20. Chinosol (8-Hydroxyquinoline sulfate) (Liquid) (5%)
21. Amertan (5% tannic acid + merthiolate) (Jelly)
22. Gentian violet jelly-merthiolate (Jelly)
23. Lactic acid (Liquid) (5%)
24. Acetic acid (Liquid) (5%)
25. Penicillin 10,000 units per cc (total 100,000 units) (Liquid)
26. Streptomycin (1000 units per cc) (total 10,000 units) (Liquid)
27. Mercuric chloride (Liquid) (.01%)
28. Metaphen (4-nitro-anhydro-hydroxy-mercury-orthocresol (Metaphen 1:2500)) (Liquid) (.5%)
29. Copper sulfate (Liquid) (10%)
30. Floraquin (5,7-diiodo-8-hydroxy-quinoline (Diodoquin) + boric acid + lactose + anhydrose dextrose) (Powder)
31. Lysol (Cresylic acid + neutral soap + glycerine) (Liquid) (0.25%)
32. Sodium perborate (Liquid) (5%)
33. Phenylmercuric acetate (Liquid) (.01%)
34. Chiniofon (7-iodo-8-hydroxyquinoline-5-sulfonic acid) (Powder)
35. Picric acid (Liquid) (1%)
36. Pine Oil Disinfectant (Liquid) (5%)
37. Potassium permanganate (Liquid) (1%)
38. Hydroxyquinoline benzoate (Liquid) (5%)
39. Sulfo-merthiolate (Sodium p-ethylmercuri-thiophenylsulfonate) (Powder)
40. Malachite Green (Liquid) (1%)
41. Actidione (Liquid) (1%)
42. Subtilin (Liquid) (5%)
43. Bovoflavin-salbe German proprietary compound (Ointment)
44. Propylene glycol dipropionate (Suspension in water) (20%)
45. Sodium 3-(gamma-hydroxymercuri-*B*-methoxypropyl-4-hydroxybenzoate) (Liquid) (1%)
46. Negatan No. 34 (Solution) meta-cresol sulfonic acid + formaldehyde (Liquid)
47. Sulfo-merthiolate (sodium p-ethylmercuri-thiophenylsulfonate, Lilly) 1:1000 (Jelly)
48. Gentian violet 1% with merthiolate (sodium ethylmercuri thiosalicylate, Lilly) 1:1000 (Jelly)
49. Quinacrine hydrochloride (Powder)
50. Pantaquine (6-Methoxy-8-(5-isopropyl-amino-pentylamino) quinoline phosphate (Liquid) (10%)
51. Sodium recinoleate (Liquid) (5%)
52. Potassium dithioformate (Liquid) (5%)
53. Sodium isopropylsulfonate (Liquid) (5%)
54. Sodium hydrogen sulfasalicylate (Liquid) (5%)
55. Sodium diethyldithiocarbamate (Liquid) (5%)
56. 2 methoxy 6-chloro-9 (2'-diethyl-amino-4'-butylamino) acridine 2 HCl (5%)
57. 2-methoxy 6 chloro-9 (*a*-di-*n*-propylamino) acridine 2 HCl (Liquid) (5%)
58. 7-chloro-4-bis (dimethylamino-2-propylamino) quinoline (Liquid) (1%)

syringe (10 ml per animal). Powders were insufflated into the vagina with a small insufflator at the rate of ½ g per rabbit. After treatment the rabbits were examined at various intervals for 3 to 5 weeks and sacrificed after 6 to 8 weeks. The evaluation was based on one application of a given drug.

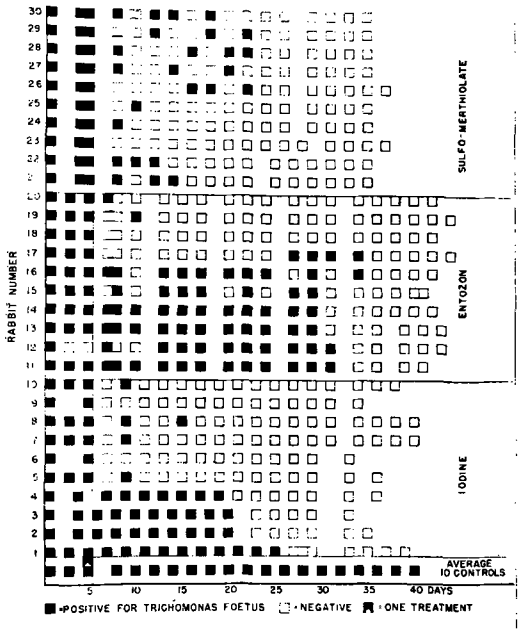

FIG. 1.
Results of *in vivo* tests with sulfo-merthiolate, entozon and iodine on *Trichomonas foetus;* 10 control rabbits.

Results. Table I indicates the 58 therapeutic agents used for treatment of the vaginal infections produced by *T. foetus;* of these compounds tested, only 3 appeared to reduce the duration of infection in the rabbits; entozon, iodine and sulfomerthiolate. Entozon, iodine and sulfo-merthiolate eliminated the infection, in 1, 4 and 5 days, respectively. The infection in all the other drugs tested persisted for at least 15 days following the treatment. None of the compounds tested at the dosage employed produced any symptoms of toxicity nor was there any apparent damage to the mucous membranes of the vagina on postmortem examination. The 3 drugs when used on 10 rabbits each appeared to shorten the duration of infection when compared with 10 untreated controls (Fig. 1). The results, however, are considered inconclusive.

Summary. A standardized, controlled *in vivo* technic utilizing female rabbits has been described for testing the trichomonacidal properties of various therapeutic compounds against *Trichomonas foetus.* A total of 58 compounds was tested by this method. Only 3 compounds: entozon, iodine and sulfomerthiolate appeared to reduce the duration of infection.

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Effect of Alpha Naphthylthiourea (ANTU) on Serum Cholesterol in Thyroidectomized Dogs.

WALTER FLEISCHMANN, JANE L. STUBBS, AND WILLIAM P. MCSHANE.
From the Physiology Section, Medical Division, Army Chemical Center, Maryland.

Chronic poisoning of dogs with alpha naphthylthiourea (ANTU) is accompanied by a marked increase of the cholesterol content of the plasma. After discontinuing administration of ANTU the plasma cholesterol diminishes rapidly.[1] ANTU like other thiourea derivatives depresses the function of the thyroid gland. This underfunction leads to compensatory enlargement of the gland. Richter[2] who introduced ANTU as a rodenticide described hyperplasia of the thyroid in rats poisoned with the drug. The antithyroid effect of the drug has also been demonstrated by cytological studies of the thyroid of rats

[1] Chanutin, A., Gjessing, E. C., and Ludewig, S., PROC. SOC. EXP. BIOL. AND MED., 1947, **64**, 174.

[2] Richter, C. P., *J. Am. Med. Assn.,* 1945, **129**, 927.