

FURTHER EXPERIMENTS ON THE FIELD VOLE WITH TUBERCLE BACILLI

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THE susceptibility of the field vole to experimental infection with bovine, human and avian bacilli respectively was the subject of a previous paper (Griffith, 1939).

Bovine bacilli proved to be the most virulent for the vole, and all the strains, whether injected parenterally or introduced by feeding, gave rise to generalized progressive tuberculosis which was characterized by caseation of the lesions, especially the glandular, and great multiplication of the bacilli.

Eugonic human bacilli multiplied in the tissues of the vole and in some instances might have been a contributory cause of death but did not, except locally and occasionally elsewhere, provoke macroscopic tuberculous lesions.

Avian bacilli acted in much the same way as human bacilli, having little tendency to produce macroscopic lesions; multiplication of bacilli was, however, less on the whole than with human bacilli.

One dysgonic human strain was tested and produced in a vole slightly more widespread disease than eugonic human strains, but nothing comparable with that found in voles injected with bovine bacilli. Wells (1938) also showed that bovine bacilli, when injected intraperitoneally in doses of 0.001 mg. of culture, were much more virulent for the vole than human bacilli. These results by different observers suggested that the vole might be used in place of the rabbit to differentiate standard bovine from standard human strains.

Before final conclusions could be drawn regarding the value of the field vole in type determination additional experiments were essential, not only with standard bovine and human strains but also, and more particularly, with strains which varied from either of these types either in cultural characters or in virulence or in both these respects.

Lack of voles prevented me then from continuing my experiments, but later about thirty voles became available from local sources. As my work on the subject of experimental tuberculosis in the vole has now come to an end, I am reporting on the results of experiments which I have been able to complete since 1939 with the help of Dr J. A. Young and my assistant, Mr W. Nicholson.

The voles were used to ascertain whether or not this species of animal could be substituted for the rabbit to differentiate between the bovine and human types of tubercle bacilli. Six groups of strains were tested: (1) three bovine strains, virulent for rabbits, (2) three human strains of slight virulence for rabbits, (3) four 'dysgonic human' strains, (4) ten attenuated bovine strains, (5) two anomalous strains, (6) seven Nigerian strains. The B.C.G. strain was also tested. Each vole received 1.0 mg. of culture subcutaneously. The results of the experiments are summarized.

(1) VIRULENT BOVINE STRAINS

Three strains from human sputum, two of which were fully virulent and one slightly reduced in virulence for the rabbit, were each tested on a vole. All three strains were highly virulent for the vole and gave rise to severe rapidly fatal general tuberculosis, the lesions, particularly the glandular and pulmonary, showing extensive caseation and extremely numerous tubercle bacilli.

Table 1. *Voies inoculated with bovine strains virulent for the rabbit*

No. of vole	Strain	Duration of life	Results
73	C.J.S. 998 (slightly attenuated)	D. 38 days	Body emaciated. Large caseous ulcerating mass locally involving gland. All glands large and caseous except mesenteric which were partly caseous. Spleen enlarged, contained caseous tubercles. Liver, ? a few microscopic foci. Lungs, more than half replaced by firm caseating masses. Kidneys, a few minute opaque cortical tubercles. <i>Micro.</i> : Lungs, t.b. + + + +; submaxillary gland, t.b. + + +; spleen, t.b. + +; liver, t.b. +.
102	Sputum culture	D. 38 days	Local lesion caseous and ulcerated, left inguinal gland incorporated; left iliac enlarged and opaque. Small tubercles in right inguinal and iliac glands. Condition of other glands obscured by decomposition. Lungs, moderate number of large caseous tubercles. Liver, numerous grey points. Spleen enlarged, no definite tubercles. <i>Micro.</i> : Very numerous t.b. in inguinal gland, liver, lung and spleen.
103	Sputum culture	D. 50 days	Local lesion and left inguinal, 1 x 1 cm., together formed caseous mass. Nearly all other glands caseous to some extent. Lungs, sparsely scattered caseating nodules up to the size of hempseeds. Kidneys, seven opaque tubercles. Liver and spleen, nothing definite. <i>Micro.</i> : T.b. numerous in the lesions.

(2) EUGONIC HUMAN STRAINS

Three eugonic human strains from human sputum were tested on four voles. One strain did not produce any disease in a vole after 110 days and cultures were negative. Another vole inoculated subsequently with this strain died prematurely in 17 days; tubercle bacilli were fairly numerous in the organs. Two strains caused slight disease in two voles, which died (but not from tuberculosis) in 49 and 171 days. The lymph glands, except those adjacent to the sites of inoculation, were normal in appearance and the lungs contained sparsely scattered tubercles. The local glands of one vole (98) showed

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dry caseation, the disease there being retrogressive, and tubercle bacilli were not numerous in the glands and organs.

Table 2. *Voles inoculated with human strains slightly virulent for the rabbit*

No. of vole	Strain	Duration of life	Results
67	C.S. 400	D. 110 days	No lesions. Cultures negative
71	C.S. 400	D. 17 days	Small local abscess. Adjacent inguinal glands enlarged, not opaque. Normal elsewhere. <i>Micro.</i> : Inguinal gland, t.b. +; spleen, sparse t.b.; liver, none. <i>Cultures</i> : Numerous colonies liver and spleen
98	C.S. 563	D. 171 days	Small caseous collection locally. Left inguinal gland about 4 mm. in length, partly watery cyst with dry caseous focus at one end. Left iliac slightly enlarged, very dry caseation almost throughout. Other glands normal. Lungs, left caudal lobe translucent grey patch on dorsum, 2.5-3 mm. showing a few minute opaque foci; elsewhere scattered tubercles, some grey, four with caseous centre (one had a transparent centre with a caseous ring around it). <i>Micro.</i> : Left inguinal and iliac glands and spleen, t.b. scanty; lungs, t.b. + +
99	Scot. 572	D. 49 days	Local lesion, 5 x 5 mm., caseous, not ulcerated. All glands normal except left inguinal gland which was slightly enlarged and had one small tubercle. Liver, one pinhead caseous tubercle. Lungs, pneumonic, sparsely scattered caseous foci. <i>Micro.</i> : Inguinal gland, t.b. + + +; liver, spleen and lung, no t.b. seen. <i>Cultures</i> : Lung, moderate number colonies, eugonic human

(3) DYSGONIC HUMAN STRAINS

Four strains of this type, all from human sputum, were tested each on one vole. One strain did not produce macroscopic lesions in 104 days, and tubercle bacilli were found microscopically only in the inguinal glands. The results with the remaining three strains were indistinguishable from those with eugonic human strains.

Table 3. *Voles inoculated with dysgonic human strains*

No. of vole	Sputum strain	Duration of life	Results
94	A. 403	D. 104 days	No sign of tuberculosis. <i>Micro.</i> : Inguinal glands, t.b. + +; liver, lung and spleen, no t.b.
101	A. 446	D. 90 days	Local caseous lesion, 1.5 cm. x less than 1.5 cm. Lungs, ? grey focus. Other organs and all glands normal to naked eye. <i>Micro.</i> : Inguinal gland, t.b. + + +; lung and submaxillary gland, t.b. + +; spleen, one t.b. seen. <i>Cultures</i> : Inguinal gland and lung, numerous colonies
93	C.S. 531	D. 112 days	Caseous ulcer, 5 mm. across. Left inguinal gland, size of split-pea, and right inguinal a little smaller, both caseous throughout. Lungs, three submiliary grey tubercles. Other glands and organs normal. <i>Micro.</i> : Inguinal gland, t.b. + + +; liver, no t.b. <i>Cultures</i> : Inguinal gland, numerous colonies; liver, scattered colonies
95	C.S. 504	D. 64 days	Caseous local lesion, 5 mm. across. No caseation of glands. Lungs, sparsely scattered opaque tubercles. Other organs normal. <i>Micro.</i> : Inguinal gland, t.b. +; liver, no t.b. <i>Cultures</i> : Inguinal gland, moderate number colonies; liver, negative

SUMMARY OF EXPERIMENTS WITH NORMAL STRAINS

Bovine strains are highly virulent for the vole and cause rapidly fatal general progressive tuberculosis, characterized by caseation of the lesions, particularly the glandular, and by great multiplication of the bacilli.

Human (eugonic and dysgonic) strains are much less virulent than bovine strains. The bacilli may multiply in the tissues of the vole and sometimes be a contributory cause of death, but they do not, except locally and occasionally elsewhere, provoke tuberculous tissue changes leading to the formation of visible lesions.

(4) ATTENUATED BOVINE STRAINS

Having shown that bovine strains which are highly virulent for the rabbit produce in the vole on subcutaneous inoculation a characteristic form of general progressive tuberculosis I proceeded to test on the vole ten bovine strains which had become reduced in virulence either through residence in human or animal tissues or/and during cultivation on artificial media. The cultures were mainly old laboratory strains which had been originally diagnosed as bovine (by their manner of growth on artificial media and pathogenicity

Table 4

Strain	Origin	Year	Original virulence	How long cultivated	Present virulence
Mr T. M. 724 (e)	Sputum	1936	Much attenuated	2 yr. 10 m. (4 m. in G.P.)	Unchanged
Mrs T. M. 683 (e)	Sputum	1934	Much attenuated	4 yr. (65 and 182 days in rabbits)	Unchanged
Equine VII	Equine tissues	—	Attenuated	60th generation (182 days in G.P.)	Chronic T. in G.P.
L. 210	Lupus	1914	Attenuated	24 yr.	Slight for rabbit 4635
L. 110 (E)	Lupus	1914	Standard	24 yr.	Moderate for rabbit 4634
L. 153	Lupus	1911	Attenuated	27 yr.	Not pathogenic for G.P.
L. 197	Lupus	1914	Standard	24 yr.	Moderate for rabbit 4687
L. 85	Lupus	1907	Attenuated	31 yr.	Not virulent for rabbit
L. 173	Lupus	1912	Attenuated	26 yr.	Not pathogenic for G.P.
17 B.V.	Bovine tissues	—	Standard	124th generation	Not pathogenic for G.P.

for rabbits and guinea-pigs) and maintained since then on plain egg. Table 4 gives the origin of the strains, their original and present virulence and the periods they had been in artificial cultivation. When tested on voles the strains varied widely in degree of attenuation, the most attenuated having lost entirely their pathogenicity for rabbit and guinea-pig. The object of the experiments was to determine whether or not bovine strains at whatever stage of attenuation would react in the vole differently from strains of human type.

Four of the strains produced general tuberculosis in the vole characterized by caseation of all or nearly all the lymphatic glands of the body, the voles dying (one was killed) in from 39 to 135 days. Another strain (L. 110 (E)) caused in vole 84, which was killed 71 days after inoculation, a varying amount of caseation

of most of the lymphatic glands and no macroscopic lesions in the organs. A further strain (L. 153) gave an intermediate result. The four remaining strains (L. 85, L. 173 and L. 197 and no. 17 B.V.) were only slightly virulent, giving rise to lesions which were confined to the seat of inoculation or to it and the adjacent glands. Of these four strains three (one virulent and two attenuated on isolation) were obtained from lupus and had since been a long time in cultivation and one was of bovine origin, fully virulent at first, which lost virulence entirely during cultivation on plain egg.

These experiments show that attenuated bovine strains which are able to produce progressive tuberculosis in rabbits or guinea-pigs cause caseation of the lymphatic glands in voles. On the other hand, bovine strains which have become so reduced in virulence as to be non-pathogenic or nearly so for the rabbit and guinea-pig exhibit limited pathogenicity for voles and cannot by this test be distinguished from strains of human type. The strains which were not virulent for the vole and other species of animals had been a long time in artificial cultivation—up to 31 years—and exhibited a higher degree of attenuation than has been observed in any bovine strain as a result of residence in human or animal tissues. The vole therefore does not differentiate between ordinary human strains and bovine strains which have become avirulent for the rabbit and guinea-pig through cultivation on artificial media. Of practical interest, however, is the question whether or not bovine strains which have become reduced in virulence through residence in human or animal tissues can be identified as belonging to the bovine type by means of the vole test.

Five bovine strains, attenuated on isolation, were pathogenic for the rabbit or the guinea-pig when retested on the vole and all reacted in this species like strains of the bovine type. Further experiments are, however, necessary with attenuated bovine strains obtained from lupus or equine tuberculosis before a final conclusion can be drawn on the value of the field vole in differentiating between naturally attenuated bovine strains and strains of human type.

Summary

The vole test was applied to ten strains of tubercle bacilli which soon after their isolation were classified as belonging to the bovine type and had since been kept in artificial cultivation for periods ranging from 3 to 31 years. Five of the strains reacted like strains of bovine type, producing general lymphatic gland caseation. One strain was slightly more pathogenic than human strains and the results of the remaining four could not be distinguished from those of strains of human type.

(5) B.C.G. STRAIN

The B.C.G. strain was also tested on a vole (no. 78), which died in 56 days. There was no disease. Cultures from spleen showed scattered colonies with opaque wrinkled centres and broad dull spreading margins, some hollow centered.

Table 5. *Voles inoculated with attenuated bovine strains*

No. of vole	Strain	Duration of life	Results
69	Mr T.	D. 39 days	Local ulcer covered with dry caseous scab. Left inguinal gland, 10 × 4 mm., caseous and softened throughout. Right inguinal, one caseous nearly throughout, other a caseous focus. Left iliac, 7 × 3 mm., partially caseous; right iliac, half that of left, showed network of caseation. Ilio-sacral, 2 mm., partial early caseation. Anterior mediastinal glands, speckled opaque foci. Other glands, minute caseous foci. Liver, scattered minute foci. Lungs, four or five glassy tubercles. Kidneys, one minute opaque focus. <i>Micro.</i> : Left iliac, t.b. + + +; submaxillary, t.b. + + +; spleen, liver and mesenteric glands, t.b. +. <i>Cultures</i> : Inguinal gland, numerous bovine colonies; liver, moderate number
72	Mrs T.	D. 54 days	Caseous scabby local lesion. Inguinal and iliac glands much enlarged and caseous throughout. All other lymph glands enlarged and caseous to some extent either wholly or partially. Spleen moderately enlarged, no foci. Lungs, one caseous tubercle (t.b. +) and a few glassy foci. <i>Culture</i> : Spleen and liver, moderately numerous 'bovine' colonies
86	Equine VII	D. 135 days	Locally, caseous mass, 5 mm. across. All glands caseous throughout except mesenteric which were partly caseous. Lungs, two greyish white tubercles. Spleen, two caseous tubercles. Kidneys, three tubercles. Liver normal
88	L. 210	D. 68 days	Local ulcer, 1 cm. in diameter, with fibrocaceous floor. Left inguinal and iliac glands extensively caseous. Right inguinal, small irregular caseous area. Left axillary moderately large, partly caseous. Right axillary, caseous focus. Anterior mediastinal small but caseous. Other glands, small caseous areas (t.b. + + +). Spleen, slightly enlarged, irregular pale grey areas in pulp (t.b. +). Lungs, four tubercles and a few microscopic foci
84	L. 110	K. 71 days	Small ulcer with granular tissue floor and near it three small subcutaneous abscesses. Left and right inguinal glands, 1.5 and 1 cm., caseous and softened. Left iliac enlarged and caseous almost throughout (t.b. + + + +). Right iliac, a caseous focus. Portal and renal glands slightly enlarged and caseous. Mesenteric glands, a few caseous foci (t.b. + + +). Spleen enlarged, no foci seen. Organs normal (t.b. +). <i>Cultures</i> : Moderate number colonies
89	L. 153	D. 178 days	Locally, minute ulcer and two spots of subcutaneous pus. Both inguinal glands slightly enlarged and caseous (t.b. + + + +). Iliac glands slightly enlarged, no caseation. Right anterior mediastinal, slightly enlarged and caseous. Spleen, two minute foci. Liver, moderate number grey and creamy (? one caseous patch), no t.b.
79	L. 153	D. 53 days	Local ulcer (2 mm.), caseous base. Left inguinal, much enlarged, no macroscopic caseation (t.b. + + +). Between lesion and gland dilated vessels and microscopic tubercles. Spleen enlarged, showed enlarged Malpighian bodies (t.b. sparse). Liver normal (t.b. sparse). Submaxillary glands normal (t.b. sparse). Lungs normal. <i>Cultures</i> : Spleen, numerous colonies. Liver, moderate number colonies
87	L. 197	D. 70 days	Local caseous mass 5 mm., in greatest diameter (t.b. + + +) with a few subcutaneous tubercles near. Left inguinal and left iliac, three or four caseous foci (t.b. + +). Left axillary, a caseous mass 3 mm. in diameter. No other gland affected. Spleen, not enlarged, indefinite foci (t.b. +). Other organs normal. <i>Cultures</i> : Liver, sparsely scattered colonies.

Table 5 (continued)

No. of vole	Strain	Duration of the	
83	L. 85	D. 263 days	Locally, a spot of pus. All glands normal. Liver, ? a few grey foci. No t.b. found in inguinal gland or in organs. <i>Cultures</i> : Inguinal gland, scattered colonies. Liver, no colonies
85	L. 173	D. 237 days	Locally, split-pea-sized abscess. Left inguinal gland, size of split-pea, purulent throughout (t.b. + + +). No disease elsewhere. <i>Cultures</i> : Left inguinal gland, numerous colonies. Liver, two colonies
82	No. 17 B.V.	D. 141 days	Locally, a small spot of pus (t.b. + + + +). Left inguinal gland enlarged. Other glands and organs normal. <i>Micro.</i> : Liver, no t.b. <i>Cultures</i> : Local lesion, moderate number colonies; liver, no growth

(6) TWO ANOMALOUS STRAINS

Two strains (M. 688 and M. 911) could not be classified as either bovine or human according to the usually accepted distinctions in cultural characters and virulence between these types. They were therefore submitted to the vole test.

Strain M. 688 was obtained from the cerebro-spinal fluid of a woman, aged 27-years, who died of tuberculous meningitis. The culture exhibited the cultural characters of tubercle bacilli of the bovine type and was highly virulent for the guinea-pig; but for the rabbit the culture was only slightly virulent and therefore resembled in pathogenic properties a strain of human type. The classification of this strain, which was first mentioned in 1934, was postponed, pending the results of further experiments. These showed that the strain was not 'dysgonic human' culturally or like ordinary 'attenuated bovine' in virulence for rabbits and guinea-pigs. A vole, however, inoculated with the culture died of general tuberculosis, all the lymphatic glands showing some degree of caseation.

Strain M. 911 was obtained from the lumbar spine of a boy, aged 10 years, and was atypical in cultural characters and also in virulence. In primary cultures on egg the colonies were dysgonic and resembled those of bovine tubercle bacilli, but in subculture on glycerinated potato the strain originally and after passage through the rabbit grew luxuriantly, like eugonic human bacilli. The virulence of the culture for the rabbit was irregular—for some rabbits nearly equal to that of bovine bacilli, for others not more virulent than a strain of human type—and was not increased by passage. There was therefore no evidence of the presence in the strain of virulent bovine bacilli.

A vole inoculated with the culture died in 108 days and beyond a small local lesion showed no obvious tuberculosis; the lungs, however, were congested and contained numerous tubercle bacilli.

The pathogenic effects of these two strains in voles were in sharp contrast. On the assumption that bovine bacilli only can cause in the vole general tuberculosis with caseation of the lymphatic glands the first, a meningitis strain, must be classified as belonging to the bovine type. The strain, however,

could not be distinguished from tubercle bacilli of the human type in virulence for the rabbit and the guinea-pig.

The second strain reacted in the vole like tubercle bacilli of the human type, though its virulence for some rabbits was high and approached that of tubercle bacilli of the bovine type.

The pathogenic effects of these two strains for the vole were the reverse of what might have been expected in this species from their virulence for the rabbit.

Table 6. *Voles inoculated with anomalous strains*

No. of vole	Strain	Duration of life	Results
68	M. 911	D. 108 days	Wheat grain type. Local collection of yellow pus, size of wheat grain. Inguinal glands normal in size, no caseation. Lungs, congested, posterior part of one caudal being haemorrhagic. <i>Micro.</i> : Local pus, t.b. + + + +; inguinal gland, t.b. + +; lungs, t.b. + + +.
55	M. 688	D. 82 days	Ulcerated lesion. Inguinal and iliac extensively caseous. Portal and submaxillary glands partly caseous. Other glands contained a caseous tubercle or two. Spleen enlarged, three or four caseous foci. Liver, a few minute opaque foci. Lungs patchily congested and hepatized. A caseous tubercle on mesentery and a caseous focus in wall of caecum. T.b. numerous in lesions

(5) NIGERIAN STRAINS

All the preceding experiments were made with strains obtained in this country. When voles became available the opportunity was taken of testing on this species seven of the strains which had been obtained by Dr J. A. Young from natives in Nigeria. These strains were dysgonic on all media, producing on egg in primary culture flat colonies and in subculture thin layers. On glycerin potato they formed very thin grey layers in which either no secondary colonies or only one or two appeared after prolonged incubation. These colonies were subcultivated on egg and transferred to potato on which they grew luxuriantly. In this particular they resembled the dysgonic human strains of this country, but they were more dysgonic.

Each strain was tested subcutaneously on a rabbit in a dose of 10.0 mg. (20.0 mg. in one instance). The rabbits were killed or they died in from 111 to 280 days and showed disease which varied widely in extent and distribution. In four of the rabbits the tuberculosis though generalized was slight and exhibited the same range of variation of pathogenic effects as eugonic human bacilli, except in rabbit 4679 which also had tuberculosis of the joints and eyes. In the remaining three rabbits the lungs were severely affected, but there were few if any lesions elsewhere and these were of the sort that may be produced by tubercle bacilli of the human type.

Severe tuberculosis of the lungs alone does not necessarily contraindicate infection with tubercle bacilli of the human type, which often cause slowly progressive lesions in the lungs of rabbits. If the rabbits are allowed to live for long periods (205, 211 and 280 days in these instances), the lungs may become practically replaced by tuberculous tissue and abscesses. Eugonic

bacilli of slight virulence have been recovered from lesions of similar duration and nature in rabbits inoculated with strains of eugonic human type.

All the strains were virulent for the guinea-pig.

For the vole the virulence of the strains varied widely in degree. Two produced severe generalized progressive disease with caseous changes and great abundance of tubercle bacilli in the lesions. The pathogenic effects of these strains were similar to those of virulent bovine strains. A further strain caused moderately severe generalized progressive tuberculosis, the right lung having become replaced by caseous substance. Two other strains gave rise to slight progressive generalized tuberculosis. The remaining two strains caused mainly local disease, but in these instances, as in the other voles with slight disease, the adjacent glands were caseous. Although the strains were identical in cultural characters and resembled tubercle bacilli of the human type in their range of pathogenic effects for the rabbit, they reacted irregularly on the vole. Some were practically as virulent as bovine strains; others had slight virulence, and in the periods of observation of 81 and 89 days caused mainly local disease, while the remainder reacted intermediately. In Table 8. the pathogenic effects of the seven strains for rabbit and guinea-pig are compared.

Further experiments with Nigerian strains on voles and other species of animals are urgently needed.

Table 7. *Dr J. A. Young's Nigerian strains*

Nq. of vole	Strain	Duration of life	Results
90	Y. 87	D. 83 days	Generalized tuberculosis, bone and muscular lesions: severe disease
91	Y. 94	D. 118 days	Generalized tuberculosis, one muscle lesion, lungs severely affected, other organs not; glands not so severely as above
92	Y. 97	D. 121 days	Ulcer. Inguinal glands caseous. Left prescapular gland, opaque spot. Submaxillary gland slightly enlarged and opaque. Other glands: Lungs, six creamy areas with grey margins up to 5 mm. <i>Cultures</i> : Liver and submaxillary gland, scattered colonies
96	Y. 89	D. 61 days	Ulcer, 5 mm. Inguinal glands, caseous. Portal glands, early caseation. Lungs, one creamy tubercle. Also one anterior mediastinal gland. <i>Cultures</i> : Liver, scattered colonies
97	Y. 98	D. 81 days	Ulcer. Inguinal glands caseous, also right iliac; left iliac, three tubercles. Lungs, one grey tubercle
105	Y. 99	D. 89 days	Caseous lesion. Left inguinal glands caseous. Anterior mediastinal gritty. Lungs, two small grey foci. <i>Cultures</i> : ?
104	Y. 90	D. 83 days	Ulcer. Inguinal, iliac and popliteal glands enlarged and caseous. Anterior mediastinal and mesenteric partly caseous. Two to six tubercles in most other glands. Lungs, right, caseous throughout; left, two small caseous areas. Spleen, four small tubercles. Kidneys, three tubercles. <i>Cultures</i> : ?

Table 8. *Virulence of Nigerian strains for rabbit and vole compared*

Strain	Voles	Rabbits
Y. 87	V. 90. Severe G.T.	R. 4620. D. 205 days. Lungs moderate, slight elsewhere
Y. 94	V. 91. Moderately severe G.T.	R. 4655. D., 211 days. Lungs filled chest two-thirds replaced by tuberculous tissue. Kidneys, four tubercles. Lachrymal gland, one tubercle

Table 8 (*continued*)

Strain	Voies	Rabbits
Y. 90	V. 104. Moderate G.T. (caseous pneumonia right lung)	R. 4612. K. 111 days. Slight G.T.
Y. 97	V. 92. Slight G.T. (a few glands and caseous areas in lungs)	R. 4656. K. 280 days. Lungs extensively tuberculous. Kidneys, three and five tubercles
Y. 89	V. 96. Slight G.T. (portal gland, early caseation, and one caseous tubercle in lung)	R. 4669. K. 178 days. Lungs, slight. Kidney, one focus
Y. 99	V. 105. Local T. and two tubercles in lungs	R. 4679. K. 111 days. Slight G.T. but also both eyes, lachrymal glands and femur epiphyses
Y. 98	V. 97. Local T. and one tubercle in lungs	R. 4670. K. 178 days. Local lesion. Lungs, slight

Y. 90 and Y. 99 were each inoculated into a rabbit (R. 4612 and 4613) in a dose of 0.01 mg. of culture. They died in 89 days of chronic moderate generalized tuberculosis, the lesions in the lungs resembling those set up by tubercle bacilli of human type.

CONCLUSIONS

1. Typical bovine strains cause progressive tuberculosis in voles, characterized by widespread lymphatic gland caseation and great multiplication of tubercle bacilli in the lesions.

2. Eugonic human strains are much less virulent than bovine strains for voles and do not cause caseation of the lymphatic glands except perhaps in the nearest.

3. Dysgonic human strains are indistinguishable from eugonic human strains by the effects they produce in the vole.

4. Attenuated bovine strains from lupus or equine lesions are identifiable with the bovine type by their reaction in the vole. Few experiments have, however, been done with this group of strains.

5. Of two equivocal strains one reacted in the vole like a bovine, the other like a human strain.

6. The Nigerian strains, though apparently uniform in cultural characteristics and falling within the range of tubercle bacilli of the human type in pathogenicity for the rabbit and the guinea-pig, differed widely in degree of virulence for the vole.

REFERENCES

- GRIFFITH, A. S. (1939). The relative susceptibility of the field-voles to the bovine, human and avian types of tubercle bacilli and to the vole strain of acid-fast bacillus (Wells, 1937). *J. Hyg., Camb.*, **39**, 244-59.
- WELLS, A. Q. (1938). The susceptibility of voles to human and bovine strains of tubercle bacilli. *Brit. J. Exp. Path.* **19**, 324-8.

(*MS. received for publication 23. VII. 41.—Ed.*)