colonic diverticula in the experimental situation. Wierda² found diverticula of the colon of three rats fed on a high fat diet for from 90 to 111 weeks. Each rat had a diverticulum of the colon within 2 cm. of the caecum, and one had a second diverticulum along the length of the large bowel. No colonic diverticula were found in rats on the same diet sacrificed when 25 to 50 weeks old. Carlson and Hoelzel³ reported the development of diverticula—usually one, or occasionally two or three, in number—within 1 cm. of the caecum in about 20% of a group of 252 rats in life span studies on various diets. Rats on bulky diets showed the least evidence of diverticulosis, but diverticula developed in those rats kept on a low residue diet and, more particularly, in those who were first fed a bulky diet and who were later switched to a low residue diet.

We have recently had the opportunity of studying the intestines of 38 black and white Lister rats fed on a low roughage diet for between 52 and 70 weeks. The diet comprised 60% sucrose, 20% casilan, 15% arachis oil, and 5% mineral salts and vitamins. Weight at death varied from 350 to 450 g. In one rat a rather sacular caecum was found, but histological examination revealed no evidence of diverticula. The colon in all the other animals was free from diverticula but was invariably very contracted and contained little food residue.

Diverticular disease of the colon is becoming an increasingly important problem in current clinical practice, and yet its aetiology remains essentially unknown. The production of colonic diverticula in the experimental animal would obviously be of considerable value in the investigation of this condition. Our own negative findings in this small series should not discourage others from investigating the association between diet and colonic diverticula both in different strains of rats and in other experimental animals.

A longer period of study than ours is obviously necessary.

We wish to thank Professor John Yudkin for access to the experimental material.

—We are, etc.,

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Of Voles and Men

SIR,—A leading article on vole bacillus vaccination (1 March, p. 527) was based upon a recent study by Dr. Anne Maguire. Unfortunately her report¹ contained a number of factual misstatements about the Medical Research Council's trial of this vaccine. These have been given quite undue publicity by your leading article, and we therefore wish to correct them.

All the subjects in the Medical Research Council's trial of B.C.G. and vole bacillus vaccines in the prevention of tuberculosis were children in their penultimate term at school, and aged about 14½ years on entry to the study. No institutional patients were included. The trial started in September 1950 in the London area, and vole bacillus vaccine was not used until the trial was

extended to the Birmingham and Manchester areas in January 1951. The trial was undertaken by the Medical Research Council's Tuberculosis Research Unit, under the general direction of their Tuberculosis Vaccines Clinical Trials Committee. Full progress reports on this trial appeared in 1956,² 1959,³ and 1963.⁴

Dr. Maguire's report¹ concerns a group of about 180 mongol and other mentally defective patients given vole bacillus vaccine at Calderstones and Brockhall Hospitals in May 1950, when they were over 15 years of age. They thus comprise a completely separate group of subjects given a different batch or batches of vole bacillus vaccine at an earlier date than the participants in the M.R.C. trial. Dr. Maguire's group was included in a series of studies of vole bacillus vaccine, mainly in similar subjects, which was started by the late Dr. A. Q. Wells and his colleagues in 1944, with a grant from, but otherwise independently of, the Medical Research Council. Most of Wells's studies were made in mentally defective subjects living in institutions because they were known to be a group which was particularly susceptible to tuberculosis and therefore in particular need of the protection which vaccination was believed (and later found) to confer; when his studies started there was no effective tuberculosis chemotherapy, and, of course, no chemoprophylaxis. Two reports on this series of studies appeared in 1954,^{6,7} and provide the first accounts of lupoid reactions at the site of vole bacillus vaccination.

Dr. Maguire's confusion of these two quite separate investigations has clearly led to the blatant inaccuracies in the second and third sentences of your leading article. But this does not excuse your failure to put her findings in their proper perspective by an adequate review of the literature on this topic. In particular, you make no mention of the important report by Wylie, Bennett, and Swithinbank⁸ on the lesions found in Dr. Wells's studies. Nor apparently did you consult any of the main reports on the M.R.C. trial²⁻⁴ (all of which appeared in your columns), only a commentary⁵ upon the first of these reports. Moreover, you have misquoted this commentary; the incidence of lupus which required treatment, at the vaccination site, was about three per thousand subjects given vole bacillus vaccine in the M.R.C. trial, not 3%.

Wylie and others⁸ found a much higher incidence of lupoid reactions among mongols than among other mental defectives, and stated that they had not seen any such reactions among mentally normal subjects. They attributed this predisposition to lupoid formation in mongols to the peculiar texture and histology of the skin, rather than to an increased susceptibility to tubercle bacilli. They suggested that "the most important single factor in the development of a lupoid reaction seems to be secondary infection" at the vaccination site, that opportunities for secondary infection in mental deficiency institutions were high, and that scratching of the papules at the eruptive stage might also predispose to their subsequent infection.

The first report on the M.R.C. trial² stated that 22 cases of lupoid lesions requiring treatment (increased to 23 in the second report³) had been discovered by examination of the vaccination sites in the vole bacillus vaccinated participants. All had been referred for treatment before July 1955—that is, all had developed within four and a half years of entry to the trial. No further cases were discovered, despite continued examination of the vaccination sites, up

to January 1959³—that is, during the next three and a half years. The third report⁴ contains no further reference to this topic because there was nothing further to report, and no further lesions of this type have come to notice, although the M.R.C. Tuberculosis and Chest Diseases Research Unit maintained personal and postal contact with participants until September 1960, and postal contact until December 1967. Thus a continuous review of the M.R.C. trial subjects has been made. No further review, as suggested in your leading article, appears to be called for, especially as Maguire reports that the lesions began to appear, in her patients also, between two and three years after vaccination.¹ Moreover, all the 23 cases in the M.R.C. trial occurred among the 3,778 participants given the "standard" batches of vaccine (substrains 2 to 4) and none among the 2,039 given the "sub-standard" batches (substrain 1).^{3,9} (This last substrain, incidentally, showed a protective efficacy against tuberculosis of 74% during a 10-year period, which is of the same high order as the other substrains of vole bacillus vaccine, and as the B.C.G. vaccine.) Wylie and others⁸ had also found an association between the development of lupoid lesions and the strength of the vaccine. Moreover, in 1959 Wells and Wylie¹⁰ described a method of preparation of vole bacillus vaccine which appeared to avoid the risk of development of lupoid lesions; 385 of their subjects had been given vaccine prepared in this way more than four years previously, and none had developed a lupoid lesion.

The explanation of the very different findings in the subjects now examined by Maguire,¹ compared with those in the M.R.C. trial, may thus be attributed both to differences in the populations studied and to technical shortcomings in the earliest batches of vole bacillus vaccine prepared by Wells.

If you had taken these reports into consideration in your leading article, we believe that this would have strengthened the case, which you advanced in your final paragraph, for a reconsideration of vole bacillus vaccination. Mitchell¹¹ reviewed the evidence in the light of his own observations, and put forward the same case, in 1962. His conclusion then was that "the development of lupus at the vaccination site may now be considered to be of historical interest only and is no longer a contraindication to the use of vole bacillus vaccine as a vaccinating agent in the future." There is nothing in Dr. Maguire's report¹ which need modify this conclusion.—We are, etc.,

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