tuberculosis in this species, and also in the bank vole *Clethrionomys glareolus*, the wood mouse *Apodemus sylvaticus*, and the shrew *Sorex araneus*. The disease, which was widely spread in Britain, caused a chronic inflammation, particularly in the subcutaneous tissues and the lymphatic system; but it proved not to be the cause of the fluctuations in vole population that had been the original object of the study.

Clinical interest now centred upon the possible use of the vole bacillus for protecting man against tuberculosis, for it appeared that the vole bacillus was not pathogenic for man, though it caused the Mantoux reaction to become positive. This organism was thought to be a form of *Mycobacterium tuberculosis*, though there were certain differences—for example, its growth was inhibited in culture media containing glycerin, and it presented curved or hooked forms, especially when seen in the tissues. The war interrupted the development of this idea, but by 1946 Wells[5] felt in a position to say that he thought the vole bacillus was incapable of producing other than localized disease, and that a large scale trial comparing it with B.C.G. was justifiable. The trial[2] was mounted in 1949 by the Medical Research Council, B.C.G. and vole bacillus vaccines being compared. Wells inoculated the patients at the two hospitals in question[1] in May 1950. The vaccine was administered by a multiple puncture technique in order to avoid the troublesome ulcers[5] that usually followed subcutaneous injection.

Wells died in 1956, and it seems that interest in the vole bacillus died with him. His last recorded opinion of the vaccine[6] recognized that lupus occurred rather more frequently after it than it did after B.C.G. and that local lymphadenopathy was somewhat more troublesome. But he seems to have considered that the vole bacillus was at least as good a prophylactic against tuberculosis as B.C.G., and that it had the theoretical advantage of being an organism that existed in its natural state of virulence and was not, like B.C.G., artificially attenuated, with the consequent twin dangers of eventually losing useful antigenic properties or of reverting to a more virulent phase. (It is not suggested that this latter eventuality is more than a theoretical possibility, the major disaster at Lübeck in 1935 having been attributed to contamination of the vaccine.[7]) Incidentally, Wells was critical of the Czechoslovakian work with the vole bacillus, in which an organism was used that had been attenuated by prolonged culture on artificial media, whereas he had been careful to maintain the virulence of his own vaccine by repeated passage back into voles.

Maguire's discovery raises two points upon which it is interesting to speculate. Firstly, an incidence of 17 cases of lupus murinus among 110 patients vaccinated is much higher than the 3% reported[2] in the M.R.C. trial, and it suggests that it would be well worth while to review as many of the subjects of the original trial as possible. L. J. Witts,[4] in his obituary on Wells, mentions that extensive trials of the vole bacillus vaccine were also being made in Rhodesia, and further information might be forthcoming from this quarter. Secondly, there is no evidence to suggest that the vole bacillus has caused anything more than local disease, whereas B.C.G. may very rarely cause generalized, even fatal, tuberculosis.[8] If the vole bacillus is really incapable of causing generalized disease might it not be worth while to reconsider its use as a prophylactic, particularly as lupus murinus is treatable? It might be possible to modify the lupus-producing proclivities of the vaccine, either by controlling the dose, by analogy with the observations of O. Horwitz and J. Meyer[8] in B.C.G. lupus, or by modifying the technique of vaccination, as suggested by P. D'Arcy Hart and his colleagues.[2] In fact this outbreak of lupus murinus, far from constituting an absolute contraindication to the use of the vole bacillus, as might seem to be the first obvious conclusion, might really be seen as an opportunity for reconsidering the value of the vole bacillus as a prophylactic agent that produces a purely local infection. There is no doubt, however, that Wells considered a living vaccine, however good it might be, as second best should a killed vaccine ever become a practical possibility.

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Jakob–Creutzfeldt Syndrome: an Infective Disease?

Increasing interest in the so-called "slow virus" diseases of the nervous system has raised the possibility that certain obscure and as yet unexplained diseases of the brain and spinal cord may be of similar aetiology. Kuru, a progressive disorder characterized by increasing cerebellar ataxia and dementia, which occurs in the Fore tribe in New Guinea, can be transmitted to chimpanzees when material from affected human brains is inoculated[1] into them. Work is now in progress to find out whether there is any possibility that commoner human diseases such as multiple sclerosis and motor neurone disease could also prove to be due to transmissible agents.

The term "Jakob–Creutzfeldt disease" has been widely and erroneously used by neurologists and physicians in Britain for many years to identify a syndrome, often familial, in which features of Parkinsonism are accompanied by progressive dementia, signs of corticospinal tract degeneration, and sometimes peripheral amyotrophy due to anterior horn cell disease. Such a clinical picture, evolving over a period of some years, is not uncommon, and resembles the so-called Parkinsonism-dementia complex which has been found to occur frequently in the Mariana Islands in the Pacific. Such cases occurring sporadically or in more than one member of a family in western Europe and in the United States are probably better described as examples of corticostriatonigral degeneration.

The condition which A. Jakob and H. G. Creutzfeldt originally described is a disorder characterized by dementia of comparatively rapid progression accompanied by frequent myoclonic jerking and other less constant findings, often

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[2] Brownell, B., and Oppenheimer, D. R., *J. Neurol. Neurosurg. Psychiat.*, 1965, **28**, 350.
[3] Nevin, S., McMenemey, W. H., Behrman, S., and Jones, D. P., *Brain*, 1960, **83**, 519.
[4] Gibbs, C. J., *et al.*, *Science*, 1968, **161**, 388.

including ataxia and sometimes evidence of pyramidal tract disease. Few patients suffering from this progressive disorder survive for more than six to nine months after the onset. In most cases the electroencephalogram shows striking abnormalities characterized by diffuse and irregular mixed spike and delta wave activity. B. Brownell and D. R. Oppenheimer[2] have confirmed that the most striking pathological changes in these cases are, firstly, spongiform changes in the cerebral cortex, and, secondly, degeneration of cerebellar granular cells. The condition seems to be similar to, if not identical with, the so-called subacute spongiform encephalopathy first described by S. Nevin and his colleagues.[3]

In a typical case of spongiform encephalopathy of the Jakob–Creutzfeldt type C. J. Gibbs and his colleagues[4] found that a biopsy of the brain showed a typical status spongiosus of the cortical grey matter. Inoculation of some of this material into a chimpanzee was followed after 13 months by the appearance of a subacute, progressive, non-inflammatory, and degenerative brain disease. The clinical course of the illness in the chimpanzee was similar to that observed in the human patient, and the neuropathological findings were also similar. The authors could find no evidence that the disease was of spontaneous origin or that it was transmitted by contagion from chimpanzees with kuru. They conclude that the condition is almost certainly caused by a transmissible agent, which has yet to be identified.

Anorexia Nervosa

J. F. Seidensticker and M. Tzagournis[1] recently suggested that anorexia nervosa is a symptom complex rather than a disease entity. This is in line with the view expressed by E. L. Bliss and C. H. H. Branch[2] that the condition is best regarded as a state of nervous malnutrition found in patients with a variety of psychiatric syndromes who have also lost a considerable amount of weight. Other investigators[3–6] have applied stricter criteria and have divided the syndrome into primary and secondary forms. Neither includes malnutrition due to physical disease or natural famine, but the secondary form covers the states that can occur in severely ill psychiatric patients—such as severely depressed or schizophrenic patients who refuse to eat because they believe that their food is poisoned.

The term primary anorexia nervosa is reserved for those patients, predominantly female, who usually become ill in adolescence, avoid eating food, and are characterized as a group by their athleticism, higher than average intelligence, and high social class origins. More specifically H. Bruch[7] has drawn attention to their "pursuit of thinness," while A. H. Crisp[8] has recently claimed that primary anorexia nervosa can be distinguished psychopathologically from feeding disorders of childhood and adult life on the basis of its being primarily a disorder related to the weight changes of puberty, the patient having a phobia of normal adolescent weight. This phobia, sometimes denied by the patient but usually revealed in treatment aimed at restoring the full weight, has its basis in the psychological implications of normal post-pubertal weight for the patient. By avoiding such weight she avoids adolescent experience and whatever distress has been associated with this. The phobia also usually ensures that the metabolic effects of the disorder are coloured by predominant carbohydrate starvation, which comes from the patient's conviction that starchy foods are the ones to be particularly avoided. Eventually the condition can become complicated by bouts of overeating with or without vomiting, which, if persistent, can lead to severe disorders of electrolyte and fluid balance.[9 10] Epilepsy, which occurs in about 10% of patients, appears mainly to have its basis in such severe metabolic abnormalities.[11 12]

It has also been claimed that patients with anorexia nervosa overlap clinically, individually, and within the family with some sections of the obese population. Childhood feeding problems, initial overweight, high growth rate, and adolescent dieting behaviour, as well as emotional difficulties in the adolescent patient and her family, have been proposed as some of the multiple factors leading to the development of this particular disorder at a time of crisis. Such factors probably also influence its sex distribution.[8] Occasionally the illness appears to have developed later in life. In such instances the patient may be denying earlier disability, but a later onset can genuinely occur and is then often preceded by a phase of definite obesity.

The disorder probably occurs fairly frequently, mild cases recovering spontaneously and never reaching the doctor. Parents are sometimes less aware of such mild degrees of the disorder in their children than are headmistresses and others less personally involved. The individual with anorexia nervosa is a reluctant patient, usually needing to stay as she is. She is usually brought protestingly along by her mother. Most clinicians believe it is important to restore weight to normal levels as a first measure, and this often requires intensive inpatient medical and nursing care and supervision.[4 5 8] Patients will often successfully resist this, unless they believe that they can also be helped with the psychological problems they are being asked to face through gaining a full amount of weight. They will otherwise usually resist gain in weight above about 100 lb. (45 kg.) and will continue to avoid carbohydrate in their diet—or will be secretly planning to do so as soon as they leave hospital. Psychotherapy is often time-consuming with such patients, and demands considerable skill, often needing to be directed at the family as a whole.

These patients are manipulative and extremely fearful, and not all can be helped by such intensive treatment. Indeed, some patients, especially those chronically ill, relapse into a more severe state than before if they are pressed to gain too

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