

ANTHRAX

**William Smith Greenfield, M.D., F.R.C.P.,
Professor Superintendent, The Brown Animal Sanatory
Institution (1878–81)**

**Concerning the priority due to him for the production of the first
vaccine against anthrax**

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SUMMARY

The purpose of this paper is to draw attention to the fact that W. S. Greenfield, working at the Brown Animal Sanatory Institution in London, prepared an effective vaccine against anthrax and described his results some months before the experiment of Pasteur at Pouilly-le-fort. Partly through lack of financial support and partly due to opposition by the antivivisectionists, Greenfield was forced to confine his experiments to a small number of animals, but his results were nevertheless conclusive. He showed that by continuous subculture in a fluid medium that the anthrax bacillus progressively lost its virulence, until it was harmless even to the most susceptible animal, the mouse. The injection of suitably attenuated organisms into cattle rendered them immune to the subsequent injection of virulent anthrax bacilli. Greenfield's work has been overlooked or neglected, and he has never received the credit due him. It is only fitting that his work should be acknowledged in the centenary of the year in which it was described. The following account is composed primarily of quotations from his published papers. For additional information on Greenfield, reference may be made to the series of papers by Wilson (1979*a, b*). It may be pointed out that the method of attenuating the virulence of bacilli recorded by Pasteur in relation to the bacillus of fowl cholera was, like that of anthrax vaccine, anticipated by Greenfield.

A hundred years ago an editorialist announced the 'appointment of Dr Greenfield as Superintendent of the Brown Institute for Animals, in lieu of Professor Burdon-Sanderson. . . The Brown Institute was the one place which the Government had been able to look to for really original research in great questions of pathological research and comparative hygiene. . . It is hardly safe to continue to indulge in that hope. . . with a hospital physician in search of patients and practice installed at the head of the institution, *more Britannico*, it will be little short of a miracle if it does not sink into relative insignificance. And this is no ill compliment to

Dr Greenfield, who cannot be expected, whatever be his acquirements or energy – and he is distinguished for both – to fulfil the quite incompatible functions of a practising physician, a hospital physician, a lecturer, and the director of the chief British laboratory of research in comparative pathology’ (7 December 1878).

The essayist was in error, and it is the purpose of this centenary paper to note Greenfield’s accomplishments, in his own words to the extent possible. The Professor Superintendent of the Brown was required to give annual lectures, and it is to these that one turns to begin to appreciate the insight Greenfield brought to his position.

‘At the present time it seems to me that the relationship of lower organisms, especially of bacteria, to contagion is a topic of especial interest’ (17 January: 1880*a*).

‘...if we once admit that each distinct contagious disease is dependent on a lowly organism, we are led almost irresistibly to conclude that each of these organisms or contagia is a separate species...if this view be correct, or even approximately so, we may be able not only to isolate the organism upon which each disease depends, but we may be able to cultivate it under suitable conditions; we may draw its form, measure its size and that of each of its constituents; we may ascertain under what conditions it will grow and develop, and what is perhaps of the highest importance, how its growth may be checked by such means as will not be deleterious to the animal body, and thus lay the foundations of a true preventive medicine’ (24 April: 1880*b*).

‘It is now generally regarded...that the contagium of anthrax resides in the organism discovered by Delafond...and called...by Cohn *Bacillus anthracis*’ (5 June, 1880*c*).

‘...I have, with the sanction of the Committee [of the Brown Institution], been much engaged in an inquiry on behalf of the Royal Agricultural Society, into the nature, causes, and prevention of anthrax and anthracoid diseases. This inquiry is in continuation of those which were so happily initiated by Dr Burdon-Sanderson in 1876...which appeared to show, first, that when anthrax is communicated by inoculation to bovine animals through rodents, the animals so infected, although exhibiting severe symptoms, recover; and, secondly, that such animals are less liable than others to infection by the same process’ (10 April: 1880*d*).

‘...I think it must be allowed that they [*Bacillus anthracis*] are more irritant in their action, and cause death more rapidly when directly inoculated in the fluid from an animal just dead of the disease, than when cultivated, at least such is the conclusion from my own observations. (Footnote: Further experiments, completed since the delivery of this lecture have led me to the conclusion that the poison becomes progressively less virulent in successive generations of artificial cultivation. I have thus been able to obtain a modified virus, which when inoculated produces much less severe symptoms, and appears to be partially protective against future more severe attacks.)’ (5 June: 1880*c*.)

‘Since the delivery of this lecture these experiments have been continued, and some of them have been detailed in the *Journal of the Royal Agricultural Society* (Part I, 1880). These, together with still further experiments not yet published,

show that protection is conferred, which is great in degree and lasts a considerable time; and that this is true whether the poison is directly drawn from the guinea-pig or is cultivated, provided only that symptoms are produced by the first inoculation' (10 July: 1880*d*).

Mr Joseph Lister, F.R.S.: 'And I have great pleasure in being able to inform the Section, by Dr Greenfield's permission, that the question has been answered in the affirmative; and that one bovine animal, inoculated seven months ago with virus from a rodent, has proved itself, on repeated inoculations, entirely incapable of contracting splenic fever, . . .' (Delivered 12 August 1880, published 4 September 1880.)

The *Lancet* Paris correspondent wrote: 'The chief event last week was M. Pasteur's long-promised communication to the Academy of Medicine, on the attenuation of the virus of fowl's cholera. . .' (6 November 1880). In Annotations in the following week: 'We have drawn attention to the chief features of Mr Pasteur's communication. . . to point out that its most important fact has been already anticipated by one of our own investigators in the same field. The fact is that successive cultivations may attenuate a virus, which, thus weakened, still confers protection against the inoculation of the virus in the most virulent form. The anticipation to which we refer is by Dr Greenfield (*Lancet*, 5 June 1880, p. 866). . .' (13 November: 1880).

'The results in bovine animals. . . are strictly analogous with those obtained with rodents, allowing for the greater power of resistance of bovine animals to the virus. . . . If an animal dies of anthrax of modified form and slow course, and another be inoculated from it, the latter usually dies more rapidly, and the next in succession still more rapidly, so that by cultivation in the animal body the maximum potency of the virus may be speedily recovered' (1 January: 1881*a*).

' . . . there is some evidence that there exist forms of blood-poisoning in connection with certain trades in this country which are really derived from anthrax, such as probably the "wool-sorters' disease" of which Dr Bell of Bradford has just reported a case in which he found anthrax bacilli in the blood¹⁵ (*Lancet*, 27 December 1879, p. 579). (Footnote 15 read: I may mention that I have been able to prove the identity of this disease with the splenic fever of cattle by recent experiments.)' (10 July: 1880*e*.)

René Valléry-Radot (1902): 'On that Monday, 28 February [1881] Pasteur made his celebrated communication on the vaccine of splenic fever and the whole graduated scale of virulence.'

Greenfield noted: 'Since the publication of my first experiments the subject has been attracting much attention in France and quite recently a number of experiments have been published which afford striking confirmation of my own results' (1881*b*).

In *Lancet* Annotations: 'The appointment. . . of Dr Wm. Smith Greenfield to the Chair of Pathology of the University of Edinburgh is a most creditable and auspicious event' (23 April: 1881).

'Gentlemen, coming before you to-day for the first time as the formal occupant of the Chair of Pathology in this University, it is fitting that I should address to

you some statement of the past history of the chair, and of the present relations of my subject to the study of medicine. . . I have no idea of giving you now any description. . . of the past and present state of what has recently been called "bacterial pathology" . . . but I may venture a few words to indicate its importance to you as a subject of study, and to point out its bearing on the pathology of the future. . . . The admirable scientific and practical experiments which Lister worked out when a professor in this university. . . have established with certainty the fact that these blood-poisonings are effected through the agency of bacteria. Might it not be then that splenic fever was merely one of these common blood-poisonings. . . ? . . . about three years ago. . . it was discovered by Dr Sanderson and Mr Duguid that a cow might be inoculated with splenic fever from a guinea-pig, and, though suffering severely, not die of the disease. In continuing these experiments, I found that a cow once so inoculated resisted the results of further inoculation to a very remarkable degree. . . I found that if one cultivated the bacillus under particular conditions it gradually lost its activity, and at last became practically inert. It at once occurred to me that, by making use of this fact, I might obtain a virus so far modified as to be sufficient when inoculated to ensure protection, and yet not to endanger the life or safety of the animal inoculated. And this I found could be done with success?" (1881c). (*Journal of the Royal Agricultural Society*, vol. xvi, part i, April 1880, and vol. xvii, part i; *Proceedings of the Royal Society*, 17 June 1880; *Lancet*, 18 December 1880, and 1 January 1881; *British Medical Journal*, December and January 1880-1.)

'M. Pasteur has recently published the results of a very large series of experiments made by a precisely similar method, and with results fully confirming those which I published more than a year ago. And although I venture to claim for England whatever merit may be due to priority for the discovery, I none the less rejoice that the facts should have been so fully established in France. My experiments were made with a small and inadequate sum of money furnished by the generosity of a private society, and in the face of all the difficulties interposed by law. . . .' (29 October and 5 November: 1881c).

John Simon, F.R.S., on the Cruelty to Animals Act: 'A second name which I have mentioned is that of Professor Greenfield, who has so highly distinguished himself in developing, by means of experiments, the preventive medicine of splenic fever. Dr Greenfield, in order to perform his inoculation experiments, had, of course, to become a license-holder under the Act; and his experience of the hindrances which attach to that position is expressed to me in the following terms: "It is my deliberate conviction, as a result of my experience, that these hindrances and obstacles are so numerous and so great, as to constitute a most serious bar to the investigation of disease, and even of such remedial measures as would by common consent be for the direct benefit of the animals experimented upon. When to this is added all the annoyance and opprobrium which are the lot of the investigators, it is to be wondered that anyone would submit to being licensed"' (1881).

Greenfield was a multi-faceted physician. As a clinician he wrote about wool-sorters' disease: ' . . . death appears often to be due to compression of the lungs by

pleural effusion, evacuation of the fluid should be tried'. He then turns to preventive actions. 'Stringent regulations with regard to the destruction of the carcasses and hides of affected animals would do more to stamp out the disease than any other measure. But as the disease is often imported from distant countries, by means of wool, hair, or hides, which retain the contagion for long periods of time, it is only by the thorough systematic disinfection of these and the destruction of all the material which is known to be infected, that the disease can be thoroughly prevented. Up to the present time [1881] there is no enactment in England, even in respect of animals known to have died of the disease, which enables anyone to interfere with such disposal of the carcase or the offal as the owner sees fit' (1883).

Professor A. M. Drennan (1958) to Professor F. G. Young: 'I must apologize for my long delay in replying to your letter . . . about the late Professor Greenfield – who was my first Chief of Pathology and whom later I succeeded . . . Your diagnosis is, I think, correct about a "prophet losing honour in his own country" for a number of things which he described, and sometimes recorded, were afterwards re-discovered and published by others whose names are now attached to them! . . . In his lectures Greenfield gave the results of many of his original observations with supporting evidence, but he was strangely reluctant to publish latterly . . . The result is that much valuable information never got further than the verbal stage. But those of us who were privileged to work with him gained that information and also many stimulating suggestions for further work . . . Greenfield was a man who just was not appreciated and was not concerned about advertizing himself. Personally I admired him and learned much from him and I am delighted to think that at last his worth and priority may be brought to notice.'

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