REFRESHER COURSE FOR GENERAL PRACTITIONERS

THE DIAGNOSIS OF SMALLPOX.—I

BY

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It is not too wide of the mark to suggest that a large part of the difficulty in the correct diagnosis of smallpox is created by the facility with which the disease can be portrayed in a written description. These canonical descriptions of the "typical" case of smallpox and the "typical" case of chicken-pox, which are enshrined in every textbook, encourage the belief that such clear-cut issues are usually encountered. The plain fact is that, in its typical form, the diagnosis of smallpox presents little difficulty; when the disease occurs in a person who has been vaccinated some time previously, however, almost every rule can be broken, so that a correct clinical diagnosis may be extremely difficult.

The roots of clinical experience of any disease require constant nourishment from a day-to-day acquaintance with it; the relative freedom of Great Britain from smallpox in recent years makes such conditions impossible. It is fortunate, therefore, that the virologist has now achieved both precision and rapidity in his examination of suspected material. While it will be obvious that the clinician should exercise reasonable discretion in the demands he makes upon the already overburdened resources of the virus laboratory, it is essential to make the important point that there is now no room for the confident assertion of a dogmatic clinical opinion in doubtful cases; the final answer must rest with the laboratory.

Pathogenesis of Smallpox

An understanding of the behaviour or natural course of an infectious disease is an essential prelude to its management. In smallpox such understanding must depend very largely on an analogy with another infection. The studies of Fenner on the pathogenesis of ectromelia, an infectious disease of mice, have supplied a useful working hypothesis which may be applied to smallpox. Such work as has been done on the disease itself tends to confirm the accuracy of the analogy. It would seem likely that reception of the virus is followed by a transient viraemia (Fig. 1). This

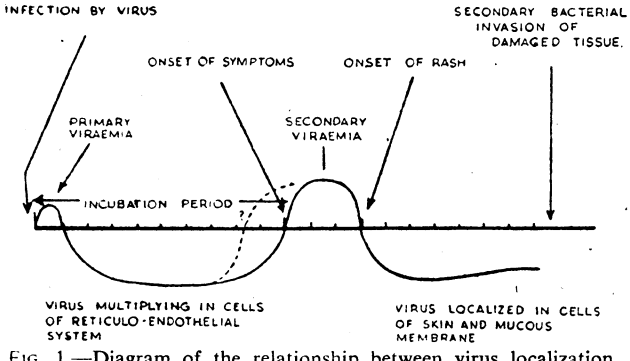

FIG. 1.—Diagram of the relationship between virus localization and clinical symptoms in smallpox.

primary viraemia inaugurates the incubation period during which time the virus is presumed to multiply in the reticulo-endothelial tissues. At the end of the incubation period the virus bursts into the blood stream (*secondary viraemia*), to be disseminated through it to all tissues of the body. Parasitizing of cells and multiplication of the virus now takes place—most obviously in the skin and mucous membranes, but probably also in many other tissues. The period of secondary viraemia is probably of short duration; further multiplication of virus occurs locally in and around the infected cells.

Although such an account may tend to oversimplify the matter, it forms a useful picture of the pattern of the disease and helps us to understand certain points which require emphasis:

(1) Vaccination after exposure may fail to prevent the disease. Once the primary viraemia has occurred prevention of the disease will depend upon a race between the multiplication of virus within the reticulo-endothelial system and the elaboration of virus-neutralizing antibodies as a result of the stimulus of vaccination. Early vaccination may, but will not always, prevent the disease: late vaccination, as Ricketts has said, "will merely add to the patient's troubles."

(2) The occurrence of the secondary viraemia in a susceptible individual sets in motion a sequence of events which it seems impossible at present to modify—namely, the localization and multiplication of virus in tissue cells. This will produce the typical skin lesions, and when these are numerous, as in the unvaccinated, a profound toxaemia due to a combination of local virus proliferation and tissue destruction will be a natural sequel. When the rash is profuse, too, the interference with normal skin function may well play a decisive part in enhancing the already grave intoxication.

(3) This local tissue destruction will permit the entry of a new phase into the disease—namely, secondary bacterial contamination. Added to the load which the patient already bears, this may well prove the final insult. Although, in theory, it is now possible to deal with this aspect of infection, it will be obvious that the contribution of chemotherapy is limited. For, in the severe unmodified attack the effects produced by virus proliferation, tissue destruction, and interference with skin function will be the main deciding factors—effects which will be uninfluenced by antibiotics. Chemotherapy is more likely to be successful in limiting the worst features of the modified disease and in mitigating the disfiguration which, even in such cases, can result from unrestrained sepsis.

Prodromal Illness

The onset of smallpox is usually fairly abrupt. The temperature rises sharply—102 to 105° F. (38.9 to 40.6° C.)—and there are all the signs and symptoms of a generalized toxaemia, of which severe frontal headache, backache, nausea, and vomiting are the most constant features. Slight shivering or even rigors are common, particularly in adults, and the clinical picture is very suggestive of severe influenza. Conjunctival injection, suffused facies, dry coated tongue, marked prostration, and even violent delirium may all be noted in the most severe cases and heighten the resemblance to influenza possibly with lung involvement. This initial toxaemia, which usually lasts two to three days, is almost invariable in smallpox. Although its duration bears little relation to the subsequent illness or to the previous vaccinal state, the severity of the symptoms is usually related to the subsequent severity of the disease. By contrast, such a form of onset is unusual in chicken-pox, in which the first manifestation of the disease is often the appearance of the eruption. Although there are, of course, exceptions (and, particularly in adults, it should be remembered that chicken-pox can be a severe disease), it may be taken as a useful general rule to regard with great suspicion any case of apparent chicken-pox in which the rash has been preceded by a period of toxaemia.

During this prodromal period rashes, sometimes of fleeting duration, may be observed. The worst omen attaches to the purpuric form in which haemorrhage occurs into skin and mucous membranes and from mouth, bowel, or vagina. This, purpura variolosa, is usually seen in unvaccinated persons and is invariably fatal. Erythematous, macular, or pleomorphic rashes are occasionally seen. As a general rule the significance of these rashes is not so serious, although a vivid, intense, almost 'erysipelatous erythema is sometimes seen accompanying the purpuric form.

The Rash

The smallpox eruption, then, makes its appearance some 48 to 60 hours after the onset of a prodromal toxic illness. As a rule, coincident with its appearance the temperature drops sometimes to normal and the patient feels temporarily relieved of some of his toxic symptoms. The first lesions are usually observed on the forehead or the wrists, but, dependent upon the degree of modification, further lesions rapidly appear during the following 24 to 36 hours. It will be most convenient to trace the development of the rash through its sequence of changes. The description of the rash can be considered under three headings: first, the individual element; secondly, the distribution of the rash; and, thirdly, the variations that may be encountered.

The Individual Element

Macule to Papule.—Although the initial spots are macular and not raised above the normal skin, they rapidly become papular. The papules are usually rather small, of a dusky red colour, rounded, hard, and well defined. To the finger they feel in or almost under the skin and "shotty." The base of the papule is soon surrounded by a ring of erythema. The papules continue to increase in numbers, sometimes for as long as 48 hours; by this time some of the earlier lesions may begin to show vesication at the summit.

Vesiculation.—Although the change from papule to vesicle occurs more or less synchronously, in the more profuse rashes, as has already been indicated, the early papules have often begun to vesicate before the papular rash is complete, so that there may be as much as 24 hours between vesiculation in the upper and lower extremities. The vesicle is regular in shape with a rounded base, rather larger than the papule—about ¼ in. (0.6 cm.) in diameter—but, like it, giving the sense of lying deeply in the skin. Rather flat-topped to begin with, as the vesicle matures a central umbilication will often be observed, while later still the lesion may be dome-shaped. As development of the most profuse rashes takes place, neighbouring lesions tend to coalesce, particularly on the face, the forearms, and the back of the trunk. The skin feels hot, and in the most severe cases is very tender to the touch. Oedema is often a noteworthy feature, particularly obvious in the face.

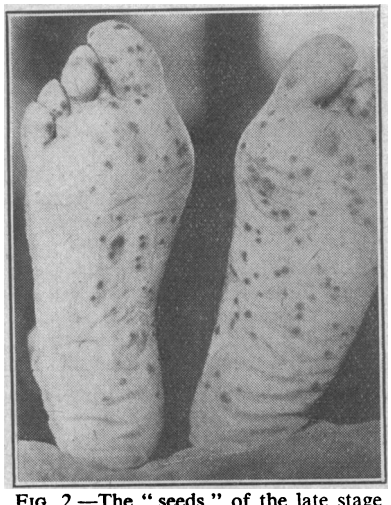

FIG. 2.—The "seeds" of the late stage of smallpox.

Pustulation.—The contents of the vesicle are at first fairly clear, but over a period of two to three days a gradual milkiness appears which eventually merges into the yellow or purulent lesion. The size of the lesion has again increased slightly, but, except where confluence has altered the shape, the individual lesion preserves its circular base and rather full dome-shaped top. The red or pink areola so well marked during the earlier stage now gradually disappears. The change from vesicle to fully matured pustule may take from three to four days.

Desiccation.—In the most severe cases large areas of epidermis overlying the vesicles—more commonly on the back—almost slough off, as in an exfoliative dermatitis, leaving an exposed red raw surface. Such cases will often fail to reach a stage of desiccation. More favourably the pustules either rupture—when the skin is normally soft—or, particularly in the palms or soles, dry up without bursting. The exuded pus forms a hard brownish crust or scab which in confluent cases completely involves the face in a thick mask. Under the tougher skin of the hands or feet shrivelled brownish "seeds" are formed (Fig. 2) which can only be cleared by the slow process of opening up each lesion with a sharp needle or tenotomy knife.

Thus, in summary, the classical smallpox lesion may be described as uniform in size, regular in shape, and deep-set in the skin; progressing from stage to stage in a leisurely but inexorable fashion. In contrast, the lesion of chickenpox shows much variation in size and shape, lies very superficially on top of the skin, progresses rapidly in 24 to 48 hours from papule to scab, and appears in a series of crops.

The Distribution

As has already been described, the earliest elements of the eruption appear on the forehead, face, and wrists. Thus at the outset the character of the distribution is announced by its predilection for the peripheral areas of the body (see Fig. 3). This is a diagnostic point of great importance and contrasts with chicken-pox, in which the lesions increase in number as the centre of the body is approached. But, although this general distribution will usually supply a valuable pointer to the diagnosis, just as much importance must be attached to the focal distribution: to the sites on which the rash is most concentrated as well as the areas which are avoided. Although the reason remains obscure, the smallpox virus shows a preference for skin cells overlying areas which are subject to trauma and minor irritation. The protection afforded by the clothing probably explains the

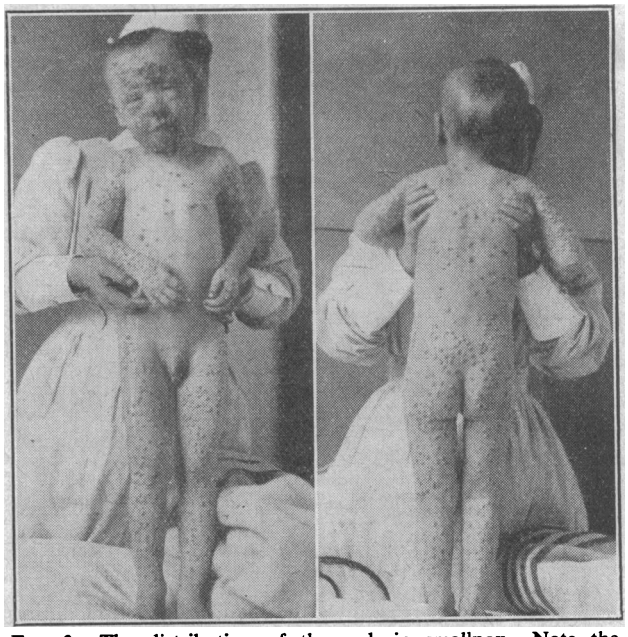

FIG. 3.—The distribution of the rash in smallpox. Note the heavy involvement of the face, the sparing of the abdomen, and the comparative freedom of the popliteal fossa compared with the front of the knee.

gross distribution. In examining the patient, especially when the rash is sparse, particular attention must be given to such sites as the malleoli, the mastoid process, the elbows, the line of well-marked tendons, and parts of the body abraded by tight- or ill-fitting clothing. Although the bony prominence itself is not infrequently devoid of rash, there is a tendency for the lesions to group themselves in profusion around it or to run alongside the line of trauma (see Fig. 4). In contrast, there may be a complete absence

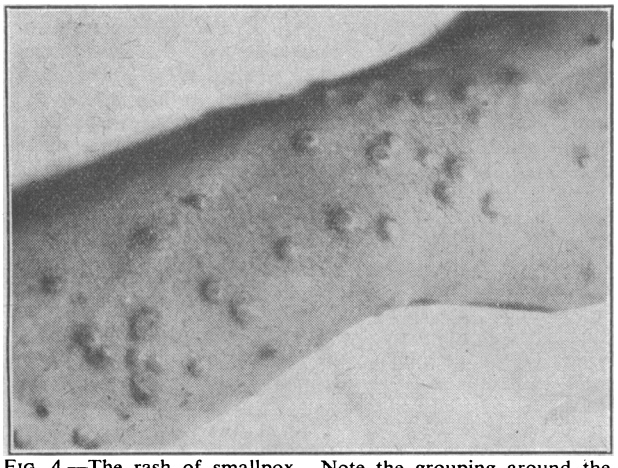

FIG. 4.—The rash of smallpox. Note the grouping around the wrist and the lesions running along the line of a prominent vein.

of lesions from sheltered areas such as the flexures. The axilla, says Ricketts, is a mine of information. Whereas in smallpox it often entirely escapes, it is almost always affected in chicken-pox. In the latter infection the focal distribution is much more irregular and little preference is evident between the sheltered and the exposed areas.

It may be stated as a general rule that, on the body as a whole, the rash of smallpox prefers the upper to the lower—the forehead more than the face, the head more than the trunk, the arms more than the legs (Fig. 3). On the arms and legs the rash is more profuse on the extensor surfaces and on the lower parts—the hands and wrist more than the arm, the foot and ankle more than the leg. Sheltered areas tend to be spared. In chicken-pox many of these points are reversed, so that the arms and legs are spared rather than the trunk, flexor surfaces are involved as much as extensor, and hollows such as the axilla show no immunity. The whole picture is more erratic and variable.

[*Part II will appear in our next issue.*]

John Newport Langley, the centenary of whose birth falls on November 10, was a pupil of Michael Foster at Cambridge, and in 1903 succeeded him as professor of physiology there. His most important work was on the autonomic nervous system. He mapped out the sympathetic pathways to various organs and fixed the position of the relay cells upon their course. He also investigated the mechanism through which the nervous impulse starts the contraction of muscle fibre. With Gaskell he built up much of our knowledge of the sympathetic system. In 1878 Foster had founded the *Journal of Physiology*, but by 1894 it had become embarrassed by debt. Langley paid off the debt and became both owner and editor. This was an important event in British physiology, for Langley not only insisted that every paper published should be a contribution to knowledge, but he also set the high standard of form and style which has ever since been associated with that journal. He died on November 5, 1925.

DICKENS'S DOCTORS

A surprising number of doctors appear in the pages of Dickens, many of them anonymous, and a delightful dissertation on them was given by Mr. Bernard Darwin in the form of the David Lloyd Roberts memorial lecture to a distinguished audience at the Royal Society of Medicine on October 29. Dickens, he said, probably knew more about medicine than the ordinary layman of his time, and he evidently liked doctors. He had a great feeling for suffering, and in *Our Mutual Friend* gave a charming and not over-sentimentalized account of the Children's Hospital in Great Ormond Street. Later he gave a public reading of the *Christmas Carol* for that institution, and charmed about £3,000 out of the pockets of his audience. It was true that he laughed at doctors, but that was his way—perhaps his only way—of making his point. There were some ramshackle doctors among the doctors he depicted, but no sinister figures such as appeared among his lawyers, like Dodson and Fogg. Moreover, there were no murderers among his doctors, although at about the time he was writing *Little Dorrit* the exploits of Palmer of Rugeley were making an enormous impression on the public mind, including the mind of Dickens himself.

Bob Sawyer

In Mr. Darwin's opinion, far and away the most attractive of Dickens's medical creations was Bob Sawyer. There were two great moments in *Pickwick*, one in chapter 20 when the elder Weller made his first appearance, making Sam shrink into a little Cockney by comparison, and the other in chapter 30 at Manor Farm when Sam tells his master of the arrival of a couple of "Sawbones," one of whom was the redoubtable Bob. There were people who did not like Bob Sawyer, regarding him as a noisy and vulgar young man. But, after all, of what was he accused? Of smoking in the street, a practice which everybody followed to-day, and of calling waiters by their Christian names, a habit now not unknown in the highest circles. Too exacting a standard of manners was apt to be demanded. On the other hand, there were phases of his practice which might have been considered as "infamous in a professional respect." He sent his boy round leaving wrong bottles of medicine at houses in order to get himself known, and the same useful boy would call him out of church in the middle of the service on the presumption that a patient had been taken suddenly ill, making people exclaim what a practice this young man Sawyer (late Nockemorff) must have. But Bob Sawyer was a zealous doctor. When the Eatanswill editors had a fight, or when Mr. Winkle fell on the ice, Mr. Sawyer hovered round with his lancet, ready to bleed if necessary, and everyone would recall his wisdom when Mr. Pickwick fell into the pond and was taken home and put to bed and given unlimited quantities of hot punch. Bob Sawyer declared that there was nothing like hot punch in such cases, and that if hot punch did ever fail to act as a preventive it was because the patient had fallen into the vulgar error of not taking enough of it. In the end Bob Sawyer, with his inferior companion, Benjamin Allen, got surgical appointments with the East India Company, and, having each had yellow fever 14 times, resolved to try a little abstinence, after which they did well. Frankly, Mr. Darwin found it difficult to accept this termination, which was out of character. Dickens could not bear the unhappy ending. His characters must be cushioned and pensioned off. It was not altogether Dickens's fault. He did try in one of his books—*Great Expectations*—to have a different ending, but his publishers told him the public would not stand for it, and, of course, the customer was always right.

A Mort of Doctors

Dickens might have thought he had been rather hard on the medical profession in creating Bob Sawyer, and tried