SMALLPOX AS A CAUSE OF FALSE POSITIVE REACTIONS TO THE KAHN TEST*

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During the last decade considerable interest has been shown in the occurrence of biologic false positive (B.F.P.) reactions to the standard tests for syphilis, and a vast literature on the subject has grown up. Moore and Mohr (1952a,b) first classified B.F.P. reactions into two categories:

(a) *Acute*.—Occurring during or shortly after a wide variety of non-syphilitic infections, and returning to negative in less than 6 months.

(b) *Chronic*.—Persistently positive for months or years.

Formidable lists of infections which may precede acute B.F.P. reactions are given in modern textbooks of venereology and in the many articles dealing with the subject. While it is widely reported that "viral infections" and vaccination against smallpox are potent causes of acute B.F.P. reactions (Stokes, Beerman, and Ingraham, 1954; Willcox, 1950; Moore and Mohr, 1952a,b; Stokes and James, 1949), smallpox itself is rarely mentioned (Mackey, 1956).

Present Investigation

During the early months of 1956, a severe epidemic of smallpox occurred in Ibadan, and over 1,000 cases were admitted to the Isolation Hospital. Since it had been stated that smallpox might be a cause of B.F.P. reaction we decided to investigate the incidence of positive Kahn tests among patients convalescent from smallpox. We restricted our investigation to adult males, since we had already observed a base-line of 8.5 per cent. Kahn positive tests among 2,257 adult male prospective blood donors in Ibadan in 1956.

Materials and Method of Kahn Test

Materials.—Standard Kahn Antigen was obtained monthly from the Venereal Diseases Reference Laboratory, London Hospital, London, and flown

out to Nigeria in sealed bottles. This was stored in a dark cupboard in an air-conditioned room kept at 75°F. The saline used was 0.9 per cent. "Analar" sodium chloride made up in glass-distilled water.

Method.—The standard three-tube test was employed, with the modification that all reagents were heated to 37°C. before mixing, and the tubes placed in a 37°C. water bath for 15 minutes after shaking.

Specimens of blood for Kahn testing were taken from patients on the day of discharge from the Isolation Hospital—estimated as the 14th to 28th day of the disease. Where a patient was for some reason retained in the Isolation Hospital for a longer period, a specimen was collected on the estimated 28th day. Patients' accounts as to the duration of their disease were often vague, and sometimes deliberately misleading, so that duration of disease had to be estimated clinically on admission. This time for the taking of the specimens was chosen because in acute infections there is an incubation period of about 2 weeks for the development of the B.F.P. reaction (Kahn, 1954).

Results

Of 108 adult male smallpox convalescents so tested, 34 (31.5 per cent.) were found to have positive Kahn tests. This compares with 8.5 per cent. positive reactions among adult male blood donors, and the difference is statistically significant ($P = 0.01$).

Cases were classified as "mild", "moderate", or "severe" according to the severity of the smallpox. The positive results in each group are given below:

Smallpox	No. of Cases	Positive	
		No.	Per cent.
Mild	25	6	25
Moderate	48	15	32
Severe	35	13	37

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While the figures show an increasing incidence of positivity with increasing severity of the smallpox, the numbers are too small to be statistically significant.

Follow-Up

The follow-up was complicated by the fact that a proportion of the smallpox patients had received penicillin, or other antibiotics of known anti-treponemal potency, to combat secondary infection during the course of the disease. We felt that, where such drugs had been given, a reversal from sero-positive to sero-negative could hardly be ascribed to the natural reversal of an acute B.F.P. reaction. Such patients were therefore excluded from the follow-up.

Of the 34 patients who had a positive Kahn test during their convalescence from smallpox, 14 had received "anti-treponemal" antibiotics. Of the remaining twenty, eleven were subsequently traced. Dealing as we were with patients whose addresses were sketchy in the extreme, our surprise was, not that so few could be found, but that so many were traced. Of the eleven traced, four had reverted to negative at the end of 3 months, and seven were still positive. After 6 to 7 months the remaining seven also gave a negative Kahn test.

Discussion

We are conscious that this study is incomplete in many respects. Ideally we should have demonstrated in each patient that the Kahn test was negative at the onset of smallpox, but this was impracticable for two reasons:

- (1) Many of the patients were so covered with smallpox lesions on admission that it would have been extremely difficult to perform venepuncture without the needle passing through a pock, a procedure which we would hesitate to perform for what, from the patient's point of view, was an investigation of only academic interest.
- (2) It is the local practice to hide patients with smallpox, or else drive them out into the bush. Thus, despite the vigilance of the Medical Officer of Health and his staff, many of the patients admitted to the Isolation Hospital were not in the first day or two of the disease.

Similarly, in the absence of facilities for performing the *Treponema pallidum* immobilization test or one of the other "specific tests", as opposed to the

"relatively non-specific" Kahn test, we cannot be sure that the positive results found among our convalescent smallpox patients were in fact B.F.P. reactions. Stokes and James (1949) state:

"There is reason to suspect that a sero-negative status in a syphilitic person may be converted into a sero-positive state by some of the agencies that can produce a B.F.P. state".

Ibadan is in an endemic yaws area, and we cannot be certain that some of our patients were not old yaws cases, in whom either the onset of smallpox was sufficient to cause a temporary return to sero-positivity, or the natural or post-therapeutic advent of sero-negativity coincided with the 7 months' period that followed the smallpox. The 100 per cent. attainment of sero-negativity within 7 months, among the patients followed-up, and their universal denial of a history of yaws, makes such a hypothesis unlikely, but it is still not impossible.

Despite these limitations, we feel justified in considering that the results of our investigation are suggestive that smallpox is a potent cause of acute B.F.P. reactions to standard tests for syphilis.

Summary

Kahn tests performed on 108 adult male smallpox patients in the immediate convalescent period showed a statistically significant increase in the percentage giving positive results, as compared with adult male blood donors from the same area. Of the patients giving positive results who could be followed up, all had reverted to negative in 6 to 7 months.

These results are considered suggestive that smallpox is a potent cause of acute biologic false positive reactions.

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