Bacillæmia in Leprosy

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1. Its value in diagnosis. Certain investigators, Sarjito and Sitanala in Batavia¹ and Campos in Brazil,² claim to have found the Mycobacterium leprae in the blood both of nodular and maculo-anæsthetic cases of leprosy. The investigators in Batavia moreover state that of 129 apparently healthy "contacts" examined bacilli were found in six of these cases. The "thick film" method was employed and blood obtained by puncturing an apparently healthy finger. What then is the diagnostic value of blood examination in our South African cases?

Technique:

- 1. A thick film is prepared as for malaria. It is important though that the film be not too thick.
- 2. Allow it to dry and then fix it gently over a flame.
- 3. Dehæmoglobinise with tap water immediately after fixing.
- 4. Set film aside to dry and stain by the Ziehl-Neelsen method. (We have found that the best results are obtained by staining with warm carbol-fuchsin for 1-2 minutes, washing well with water, decolourising in one per cent. H_2SO_4 for 15-20 seconds, again washing well with water and counterstaining with methylene blue for 15 seconds. The bacilli in the blood do not appear to be very acid-fast hence the weak acid, and as bacilli are often very scanty the leucocytes should be stained a pale blue so that the organisms in them can be easily seen.)

The method of withdrawing blood is important. Taking blood from an apparently healthy area is not devoid of error, for bacilli are frequently found in areas of skin showing neither infiltration nor erythema on superficial examination. This is often the case with the finger and the writer has frequently been struck by the number of extracellular bacilli in a blood picture taken from an apparently healthy finger as compared with the scarcity of such bacilli in blood taken from a vein in the same case. Care should, however, be exercised in withdrawing blood from the vein not to drain bacilli from the skin, for in 14 cases of nodular leprosy blood taken from a selected vein was bacteriologically positive in 12 cases, a skin scraping from the neighbourhood of the vein positive in 13 cases, and in one case both the skin and blood were negative. Therefore to reduce the possibility of error to a minimum 0.5 c.c. of normal saline was injected into an apparently healthy vein through a fine needle so as to wash out any bacilli that might have got into the needle

during its passage through the tissues of the skin. 0.5 c.c. of blood was then taken, the needle withdrawn from the syringe and a thick film prepared from a drop of blood taken from the contents of the barrel.

Result (N.B.—Cases of nodular leprosy were taken at random in the compounds, some early, some advanced):

No. of Cases Examined No. Bacteriolog. Positive 15 15 (100%)

Bacillaemia is therefore the rule in nodular leprosy and not only the case during acute exacerbations of the disease.

*Differential Count (cells with Bacilli):

Large mononuclears		80%
Small mononuclears	•••	3%
Polymorphs	•••	17%

—In one instance a giant cell with pale eccentric kidney shaped nucleus was found packed with bacilli.

In the blood taken from the finger a large mononuclear with pale oval nucleus is frequently seen, often with heavy infection, but these cells are probably always from the skin (connective tissue derivatives).

The baccilli vary greatly in morphology. A number are straight well-stained rods, but fragile and beaded bacilli, diptheroid rods and spore-like forms also occur. In the plasma they may be seen singly or in bundles.

An interesting phenomenon observed in one case was the clumping together of 6 leucocytes, 5 with bacilli, to form what appeared to be a small embolus.

In a series of 200 cases in which the Thick Blood Film was prepared either from a healthy looking finger or vein the results tabulated below were obtained :—

Nodul	lars B1.+	Wass+V	Vass <u>+</u> V	Vass—B	1. <u>+</u> Wass	s+Wass-	-B1	-Wass+W	/a ss —
79	62 (78 [.] 5°/。)	30 (48°/ _°)	7	25 1((12)) 5 7°/ _°)	5	7 (8 [.] 8°/ _°)	2	5
Mucul	o-Anæst	91 hetics	$2^{\circ}/_{\circ}$ B1+E	31—Was	s+Wass	+Wass-	-Wass	not täken	
121	(incl. 6 co	ontacts)	0 1 (10	21 37 0°/ _°)	2	76	6	contacts	

^{*} In skin scrapings the bacilli are chiefly extracellular, a few being intracellular in the tissue cells. For practical purposes therefore a blood was accepted as *positive* only when bacilli were found in the essential leucocytes, the large and small mononuclears and polymorphs; cases with bacilli in the plasma only being regarded as doubtful.

† The old classification of maculo-anaesthetic and nodular leprosy is used for the sake of convenience, for in cases with active cutaneous macules (now classified with nodular cases as "cutaneous" leprosy) the blood picture was consistently negative. It will therefore be seen-

(a) Bacillaemia is the rule only in the nodular type of leprosy. The few exceptions were cases in comparatively good health but the possibility of errors of technique should also be considered. It appears that a leprotic bacillaemia is an indication of lowered resistance. In maculo-anaesthetic cases we presume that the blood has a degree of immunity and the bacilli therefore locate themselves either in the nerves or skin (macules), whereas in nodular leprosy, because of markedly impaired resistance, the disease becomes more generalised and bacilli are found in the blood stream as well (cf. Mitsuda's skin reaction and Bargehr's specific skin reactions.³).

(b) Examination of the blood is of no practical value in diagnosis. Bacilli are often found only after prolonged search and are far more readily demonstrated in these (nodular) cases by skin scrapings or nasal smears. All cases in which M. leprae were found in the blood had positive noses.

(c) A positive Wassermann frequently accompanies nodular leprosy with bacillaemia (48% of above mentioned cases). At present there is still much confusion as to the true value of the Wassermann reaction in leprosy. Rhee⁴ and others mention the close relationship between the quantity of lipoid and the frequency of a positive Wassermann in leprous serum. One might remark though that 27 out of the 30 Wassermann positive cases referred to above were strongly positive. If syphilis can be accepted as the underlying cause it might play an important part in predisposing to the infectious nodular type of the disease. (Naturally there are other factors to be considered also: climatic, dietetic and racial. Cochrane⁵ speaks of the South African community as not being highly "leprolised." Also other concurrent diseases may predispose to this type of leprosy.)

2. The Blood during an Acute Exacerbation. In view of Professor de Langen's⁶ interesting

infection, using an emulsion of a leproma prepared from a nodular case during an acute exacerbation of the disease, thick blood films were made from several cases during such reactions.

Result :---

Cases Examined 5

Blood Positive 5

Blood Picture

a. Extracellular in plasma

Several globi, also fairly numerous bacilli singly and in clumps—well stained "vegetative" rods, beaded bacilli, coccibacilli and spore-like forms.

b. Intracellular

Numerous intracellular bacilli chiefly in the large mononuclears (large monos. 79%, polys. 21%). A few cells with single bacilli but the majority of the cells with heavy infection. Again a polymorphic variety as in the plasma but noteworthy were the number of long and short fragile delicately stained bacilli.

The feature in all was the abundance of bacilli both in the leucocytes and in the plasma. Are these bacilli as virulent as those obtained from the lepromas? The frequency of metastatic lesions would tend to suggest this possibility. Further proof is however necessary. The blood of these acute cases may be of importance in the spread of the disease by insect vectors, e.g. by mechanical transmission, —a point perhaps of public health interest.

3. The value of Much's modification of Gram's method in bacillaemia. Because the bacilli in the blood do not appear to be very acid-fast and there is a strong possibility that many are decolorised by the acid when the ordinary Ziehl-Neelsen stain is employed, Much's method of staining was adopted in 3 cases

stain the bacilli take on varying tints of violet according to their degree of acid-fastness. The blood films were prepared as before and neutral red was used as the counterstain. Results were most encouraging the violet bacilli standing out clearly against the pale red background, and there is no doubt that far more bacilli were seen in the films stained by this method than in corresponding films stained by the Ziehl-Neelsen method. The beaded nature of many bacilli, the frequency of heavy mononuclear infection and the number of bacilli free in the plasma were clearly demonstrated.

4. Bacillaemia and Prognosis. As M. leprae occurs as a constant feature only in the blood of nodular lepers a bacillaemia is a very unfavourable indication. In four cases, up till recently classified as maculo-anaesthetic and apparently "quiescent," bacilli were found in the blood. On further examination all four were now found to be early diffuse nodulars, retrogressing rapidly with skin scrapings from face positive. They were all young girls who had reached the age of puberty and this would account for the

unfavourable change in their conditions. Whether a bacillaemia precedes signs of nodular infiltration cannot be said at present. Certainly in the cases mentioned infiltrated areas teeming with bacilli were easily found after our suspicions had been aroused by blood examination.

Kren⁷ mentions that a certain parallelism exists between the presence of the tubercle bacillus and the clinical symptoms : " So long as tubercle bacilli circulate in the blood we cannot speak of cure." - The same remark can be aptly applied to leprosy with bacillaemia.

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