INVESTIGATIONS ON THE LEUCOCYTIC BLOOD PICTURE DETERMINED BY THE ARNETH-SCHILLING METHOD IN APPROXIMATELY 100 PATIENTS WITH BONE OR JOINT DISEASES CHIEFLY OF TUBERCULOUS NATURE

BY

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With the improved methods of examination of recent years, early diagnosis has undoubtedly become easier and more certain than in the past, but if we examine the records of a coast hospital we soon find that most patients have had quite a long history of illness before the underlying disease has been brought under treatment.

Even with the use of von Pirquet's reaction, or possibly other tuberculin tests, radiography, blood sedimentation rate, and careful case recording, it is often the case that a considerable period of time elapses before a diagnosis of surgical tuberculosis is certain.

Are there any other available methods which may be employed in order to reach a definite diagnosis more rapidly? This was a question with which I was faced during my work at Stavern Coast Hospital. In the larger text books no other methods were mentioned, but as I had learned the Arneth-Schilling method of blood counting during work in other institutions, and had seen the value of the method in other diseases I considered the possibility of obtaining some help from this method.

In the edition of Schilling's book I had, there was no account of the use of the method in bone or joint tuberculosis but it was described as valuable in investigating the influence of pulmonary tuberculosis upon the blood picture. During the

year of my appointment at Stavern the blood pictures of quite 110 patients were examined and where pathological shifts could be demonstrated I carried out serial examinations—up to 7 in some patients.

After I had carried out these investigations I received information that some German workers had published preliminary accounts of similar investigations (Zeitschrift für orthopädische Chirurgie, 1930, p. 229 and Deutsche Zeitschrift für Chirurgie 220—297 Hauer & Nitsche, Berlin, and Stein, Wien).

These observers claim that there is reason to believe that such investigations may be of considerable value. In particular, the German workers had large series of examinations, 14 on average, extending over considerable periods—up to two or three years. It was not possible for me to obtain such series as all the counts had to be carried out in my spare time, and as my appointment at the coast hospital was of necessity limited in duration I had considered my material rather too small for publication. However, as the results are in agreement with those in Hauer and Nitsche's provisional publication I have thought fit to give an account of my investigations.

The patients considered most suitable for investigation were in various stages of tuberculosis and were without demonstrable secondary infection or focal sepsis. Out of consideration to Bjørn-Hansen and Gording's work on the leucocytic blood picture in joint disease resulting from focal sepsis I made a series of similar investigations on the Pirquet-negative patients under our care for joint disease. These patient's blood pictures are collected into a special table or are specified in the diagnostic groups.

The technique employed was the usual one, described by Bjørn-Hansen and others. When possible a blood sedimentation-rate determination was made either on the same day or as soon as possible after the blood films.

As appears from the tables the material consisted of the following:—

Group I: Spinal Caries and Sacro Iliac Tuberculosis: 27 males, 13 females = 40

Group II:	Tuberculous Coxitis::	13	males,	7	females	= 20
Group III:	Tuberculous Coxitis & some focal sepsis:	9	„	11	„	= 20
Group IV:	Bone Tuberculosis of various localisations, also Arthritis Deformans, Chronic Osteomyelitis etc.:	15	„	8	„	= 23

A few patients of less interest have not been included in these groups.

A total of 228 blood counts were carried out on these patients during 1930—31; in the case of patients in the quiescent recovery stage where the blood picture showed but slight deviation from the normal, only single examinations were made. Patients with progressive disease or with complications were examined repeatedly—up to 7 times. During the same period 282 blood sedimentation-rate determinations were carried out, i.e. this was done rather more frequently.

Radiograms were taken as a rule every three months or, in the case of new patients with uncertain diagnosis on admission, every month. If there was any suspicion of complications radiograms were taken more frequently.

The classification I have adopted is due to the fact that I wished to group together the cases with disease in any given organ-system, in order to determine, if possible, the effect of the special systems upon the blood picture. As this point was not discussed in any of the literature I could find in the Coast Hospital's excellent special library, I had thought it possible that, particularly in children with spinal caries, one might find more pronounced deviations than a true inflammatory process would cause. At that time little information was available as to the blood picture in children, but since Hauer & Nitsche, from numerous investigations, have been able to construct reliable curves the position is otherwise. In normal children it was found that the relative proportions should be set at 50—60 % for the lymphocytes, while the leucocytes vary; it was specially emphasised that rod-nucleus types were rarely above 2.5—5 %.

It was found, however, that the leucocytic blood picture in surgical tuberculosis is on the whole similar to that in pulmonary tuberculosis but the changes appear more slowly as, indeed, is usually the case with the clinical course of the disease.

In order more fully to analyse the leucocytic blood picture in surgical tuberculosis we may employ the same classification as is used for pulmonary tuberculosis viz: "Haematogenous spread", "Exsudative Phase" and "Productive Phase".

Frequently we find no changes in the blood picture *before the exsudative phase,* when the segmented neutrophile cells increase and (juvenile) there is a relatively greater increase of the rod-nucleus and younger types, with decrease of lymphocytes and monocytes and eventual disappearance of eosinophile and basophile cells.

Clinically and radiologically this corresponds to rarefaction, obscured outlines, structural degeneration; further, abscess formation, sequestration and sinus formation; while the productive phase, with organisation, sclerosis and calcification, is accompanied by a blood picture showing reappearance and steady increase of basophile and eosinophile cells, decrease and then disappearance of the young types and rod nuclei, decrease of neutrophiles and increase of lymphocytes and monocytes.

In many patients the blood sedimentation rate (S.R.) follows the clinical course of the disease, but we know from many observations that this test is occasionally unreliable, especially in the early stages of tuberculosis. *Sophie Tillisch* has demonstrated this fact in this country. The same is the case in focal sepsis (*Bjørn-Hansen*). The above mentioned German observers claim that the blood picture shows definite changes in 30 % more cases than does the S. R. With their large figures they are perhaps justified in this conclusion. My own investigations also show that the blood picture is superior to the S. R. in a number of cases, in particular a considerable number of cases of spinal caries. This was not only found in patients whose general condition was good but also in previously ambulant, recently admitted patients in comparatively poor condition.

In my opinion the *leucocytic* blood picture is of greatest importance *in early cases of surgical tuberculosis, before there are visible clinical or radiological changes,* and in which the S. R. shows no abnormality, but in which the need for immobilisation is so great.

Patient No. 22, Arne P., born 1906. Diagnosis: spinal caries —In patient at Coast Hospital first 30.7.30 to 28.12.30, readmitted 1.5.31. Pirquet +, Wassermann reaction ÷.

History:

As a child he had a playmate with tuberculosis of a foot. Previous illness: Pertussis, Measles, Cervical Adenitis (1930). (Gram negative bacilli found, also leucocytes). In 1929, after a sprain, his left ankle became swollen and painful; it improved upon rest but became worse on movement. *X-ray,* May 1930. Rarefaction of ankle joint. Admitted to "C-H" for this affection. During the examination the patient stated that since June he had complained of weakness in his back; he had occasionally carried a heavy trunk. He had gained 15 kg. in weight in 2 months during treatment with rest before admission. Tuberculosis of medial malleolus was found, with an abscess. Incised and scraped 4.8.30. (T.B. + in tissue). The spine was X-rayed, the only suspicious feature being some bulging of the psoas shadow on one side. S.R.: (30.7) 7 mm, (2.9) 12 mm (13.10) 6 mm, (5.12) 9 mm (1 hour).

The wound over the tibia healed by first intention and the patient was allowed up early. Occasional pain in the back but the mobility of the trunk was normal and a further series of X-rays showed nothing but the bulging psoas shadow seen on admission. As the patient wished to continue his studies as a dentist abroad he was allowed to take his discharge on 28.12.30, with considerable misgiving, however, and was warned to return immediately if any new symptoms appeared. The patient's leucocyte picture on two occasions was as follows:

	Baso	Eosino.	Transition	Juvenile Young nuclei.	Rod nuclei.	Segm.	Lymph.	Mono.
14.10.30:	¼%	3%	0%	½%	0.75%	55%	35%	45%
24.10.30:	0%	3%	0%	4%	8 %	40%	25%	20%

S.R. during the corresponding period: *7 mm, 12 mm, 6 mm, 9 mm.* That is: a well marked shift to the left and absence of basophile cells with increase of monocytes. More than 200 cells were counted.

During his journey abroad he developed high fever with increasing pain in the back and was admitted to a university clinic. The suspicious psoas region was discovered there and an attempt was made at aspiration under anaesthesia. This was successful and opaque medium was injected to ascertain the origin of the abscess. The aspiration cannula was allowed to remain in position for drainage and a fistula resulted. After a time the patient was allowed to return to Stavern and on 1.5.31 we found that the abscess originated in the first lumbar vertebra. This vertebra showed rarefaction and loss of structure but the outline was good and there was no collapse.

The blood picture now showed:

	Baso.	Eosin.	Trans.	Juvenile Young.	Rod.	Segm.	Lym ph.	Mono.
4.5.31	¼%	¾%	0%	3%	11.5%	37.5%	36.5%	10.5%
11.6.31	1%	2%	0%	1%	15%	45.5%	20.5%	15%

S.R.: 7.5.31: *31 mm.* 9.7.31: *35 mm.*

The patient's general condition was very good throughout this period.

This patient's blood picture shows that the changes which were definite on 24.10.30 increased somewhat when the caries arrived at the stage of sinus formation. There were: decrease of eosinophiles, relatively greater increase of rod nuclei than segmented forms, and increase of lymphocytes at the expense of the monocytes. After 14 days insolation (28.5—11.6) the eosinophiles

and basophiles increased but there was otherwise little change. S.R. showed no significant change in the autumn of 1930 but after appearance of the sinus it was considerably increased.

There were several patients who had similar changes in the blood picture—more pronounced that those of the S.R. viz. Nos. 8, 9, 17, 23, 25, 26, 29, 32, 33, 37.

Patient No. 37 had a quiescent tubercular knee and was ready for discharge but as she complained of "rheumatism" in her back I took a blood film and found the following picture:—

	B.	E.	T.	(J) Y	R.	S.	L.	M.
6.12.30	1%	4%	1%	4%	5%	29.5%	26%	28.5%

The patient's S.R. had given the following figures:
24.6.30: *17 mm.* 22.8.30: *12 mm.* 2.9.30: *16 mm.* 31.1.31: *10 mm.* 1.5.31: *9 mm.*

On more careful scrutiny of her X-ray film from 3.9.30 changes were seen in L II. A plaster bed was applied and the pains rapidly subsided.

Blood picture on 2.5.31:

B.	E.	T.	(J) Y.	R.	S.	L.	M.
1%	1%	½%	0%	1%	47%	40%	9.5%

Blood picture on 2.5.31:—

B.	E.	T.	(J) Y.	R.	S.	L.	M.
1%	1%	½%	0%	1%	47%	40%	9.5%

Another patient, also with a quiescent tubercular knee was found on 20.9.30 to be suffering in addition from spinal caries S.R. had been as follows:
26.6.30: *5 mm*, 5.11.30: *5 mm*, 23.1.31: *8 mm*, 24.4.31: *7 mm* (?)
Blood picture:

	B.	E.	T.	(J) Y.	R.	S.	L.	M.
15.1.31:	½%	3%	0%	1.5%	6%	51%	25%	13%
1.5.31:	½%	2.5%	0%	1%	5%	50%	28%	13%
13.6.31:	0%	1.5%	½%	½%	4%	55%	26%	12.5%

i.e. more pronounced changes than corresponding S.R.

We observed in some patients how an intercurrent acute appendicitis influences the blood picture, this was particularly evident in patient No. 26, with spinal caries.

On 24.4.31 the blood picture showed the following inactive phase:—

B.	E.	T.	(J) Y	R.	S.	L.	M.
1.5%	2%	0%	0%	6%	64%	19%	7.5%

On 26.4.31 the patient developed abdominal pain and vomiting. Pulse rate 80, tongue moist, pain and rigidity at Mc Burney's point.

Blood Picture:

B.	E.	T.	(J) Y.	R.	S.	L.	M.
0%	0%	0%	2%	23%	66.5%	24.5%	4%

Appendicectomy was performed the same day; the appendix being much swollen, with gangrenous mucosa. Blood Picture 4.5.31:—

B.	E.	T.	(J) Y.	R.	S.	L.	M.
0.5%	5.5%	1%	1%	7%	53.5%	22.5	9%

Corresponding deviations were found in patient No. 39, with spinal caries.

In tuberculous hip disease and knee disease similar blood pictures were found and the deviations could be even greater than in the cases of spinal disease. This was especially evident in hip disease with abscess. In patient No. 9, with hip disease, the details were as follows:—

After an injury to the hip in the winter 1930 the patient began to limp in March of the same year. He was treated with plaster and extension from 24.5.30 and was admitted on 28.10.30 to "C-H" where he was treated by extension with aspiration of the abscess. Blood picture:—

	B.	E.	T.	(J) Y.	R.	S.	L.	M.
10.11.30:	½%	1.5%	0%	1.5%	1.5%	59%	28%	8%
8. 1.31:	0%	3%	0%	7.5%	20%	45%	15.5%	9%

S.R. was influenced to a lesser degree i.e. there was less fluctuation in this:—

S.R.: 23.1.31: *75 mm,* 13.4.31: *60 mm,* 6.7.31: *67 mm.*

In patients with tuberculosis of foot, elbow and other bones we found similar blood pictures to those in spinal caries, hip and knee disease.

Not many patients with other conditions were examined but among those grouped as "various" there were some cases of arthritis deformans, osteomyelitis, polyglandular dysfunction and chronic osteomyelitis.

In patients with chronic arthritis and focal sepsis we found the condition described by Bjørn-Hansen and others, namely frequent left shift with little or no effect upon the S.R. I may also mention that in these patients eosinophilia might be found with accompanying left shift while patients with tuberculous disease who had a blood picture showing left shift seldom had increase of eosinophiles. (In a number of children with spinal caries eosinophilia was found but I believe that this was due to the fact that they had just previously been vaccinated against whooping-cough.)

SUMMARY.

(1) By investigation of the leucocytic blood picture in fully 100 patients with surgical tuberculosis it was found that the blood picture on the whole is parallel to the development of the disease in the same way as in pulmonary tuberculosis, but that the changes appear more slowly.

(2) The leucocytic picture shows its changes earlier than the blood sedimentation rate, and fluctuations in the blood picture proceed more rapidly. These investigations confirm the German observer Stein's finding that the method is superior to the S.R. in 20—30 % of cases.

(3) In some cases of surgical tuberculosis the leucocytic picture may show definite changes before the disease can be diagnosed by any other method.

(4) The changes in the blood picture in tuberculous joint disease are to some extent different from those in non tuberculous conditions (Focal Sepsis, Arthritis Deformans, Osteitis Fibrosa).

RÉSUMÉ.

1°) Dans des recherches sur la formule leucocytaire du sang chez une centaine de malades atteints de tuberculose chirurgicale, on trouva que, d'une manière générale, le tableau sanguin suivait l'évolution de la maladie, de même que dans la tuberculose pulmonaire, mais que les modifications se manifestaient plus lentement.

2°) La formule leucocytaire montre des modifications à un moment plus récent que la sédimentation globulaire et les fluctuations du tableau sanguin sont plus rapides. Ces recherches ont confirmé les trouvailles de l'investigateur allemand Stein qui estime que cette méthode est supérieure à celle de la S.R. dans 20 à 30 % des cas.

3°) Dans certains cas de tuberculose chirurgicale, la formule leucocytaire peut présenter des modifications sensibles, avant qu'il soit possible de diagnostiquer la maladie par n'importe quelle autre méthode.

4°) Les modifications du tableau sanguin se manifestant dans les maladies tuberculeuses articulaires different, dans une certaine mesure, de celles qui apparaissent dans les états non tuberculeux, (sepsis focale, arthrite déformante, ostéite fibreuse).

ZUSAMMENFASSUNG.

1) Bei einer Untersuchung des leukozytären Blutbildes bei genau 100 Patienten mit chirurgischer Tuberculose wurde gefunden, dass das Blutbild im ganzen der Entwicklung des Leidens in derselben Weise folgt wie bei der Lungentuberkulose, nur dass die Veränderungen langsamer auftreten.

2) Die Leukozytenformel zeigt ihre Veränderungen früher als die Blutsenkungsgeschwindigkeit, und Schwankungen im Blutbild gehen schneller vor sich. Diese Untersuchungen bestätigen die Ansicht des deutschen Beobachters Stein, dass die Methode in 20—30 % der Fälle der S.R. überlegen ist.

3) In einigen Fällen von chirurgischer Tuberculose kann die Leukozytenformel bestimmte Veränderungen bereits nachwei-

sen, bevor das Leiden durch irgend eine andere Methode diagnostiziert werden kann.

4) Die Veränderungen im Blutbild bei tuberkulösen Gelenkleiden sind bis zu einem gewissen Grade verschieden von denen bei nicht tuberkulösen Zuständen (fokale Sepsis, Arthritis deformans, Osteitis fibrosa).

LITERATUR

Gording & *Björn-Hansen* (Oslo): Nord. med. tidsskr. 1931 Bd. 3. Nr. 22. p. 337: Fokalinfeksiöse sympt. av tons. og dental opr. Undersökelser av det leucocytaere blodbillede.

Hauer (Berlin) & *Nitsche* (Berlin-Dahlem): Zeitschr. für Orth. Chir. 1930 Bd. III, p. 229: Weisses Blutbild und Senkungsreaktion bei Knochen-Gelenktuberkulose.

Schilling, Viktor: Praktische Blutlehre 1931.

Stein, Georg: Zentralbl. für Chir. 1930, Nr. 19. — Deutsch. Z. f. Chir. 219, 297. Ueber das Blutbild bei chirurg. Erkrankungen.

Tillish, Sophie: Tuberkulosemötet i Oslo 1927.