Local Treatment

Finally, the specific local treatment must be directed: (1) to free the tissues from the scar-like natural barriers to the irritating metabolites; and (2) to improve the circulation and eliminative functions, especially that of the skin, to remove these metabolites. For this purpose many recommend short-wave diathermy, and so far as I have had experience of it it would seem to be a satisfactory and successful method of treatment; but naturally my own experience lies in hydrotherapeutic measures, and I have found possibilities of successful treatment in these which have not tempted me to use any others.

I believe in a combination of massage and deep baths with an undercurrent douche. An hour's massage is given on alternate days three times weekly, and the baths on intervening days. In my experience this is quite sufficiently strenuous treatment for most people, and that to try to concentrate it further is likely to do more harm than good. As a rule the first week's treatment tends to stir up the pains; a fortnight's treatment is therefore the least time that should be expended, and for most cases three to four weeks is advisable.

The massage given must not be just any massage. This is not realized by many masseurs and masseuses, and doctors are often disappointed in the results of the treatment ordered simply because the right treatment is not given. The masseuse must first educate her fingers so that she can easily locate the thickened nodules, bands, and plaques in the fibrous tissue of the body. She must at her first contact with the patient explore his body so as to discover the exact position and relations of the thickenings, especially those that are tender and apparently responsible for the particular pain and tenderness complained of by the patient. She must then so arrange the position of the patient that the muscles are sufficiently relaxed to enable her to press the nodules against subjacent bone. She must remember that her object is not to increase the tone of muscle fibre, and that therefore all hacking and slapping, often too much beloved by the masseuse as a spectacular demonstration of her manipulative skill, are harmful and to be eschewed at all costs. Her sole object is painstakingly to discover the nodule and rub it away against the subjacent bone. She must at the time realize that such a process may be intensely painful, at all events for the first two or three treatments, though the tenderness often suddenly diminishes after that. She must not, therefore, dwell too long on any one spot, but move from one area to another as her intuition informs her will allow her patient to derive the maximum benefit from her treatment, without being discouraged by being made to suffer too much pain. Without this intuition the masseuse is not likely to be very successful. Above all, she must keep her patient warm, for both types are abnormally sensitive to cold; she must therefore practise making her manipulations under the bed-clothes, and must work by touch rather than by sight.

The baths I favour are deep immersion baths, which should be given quite hot at a temperature of 102 to 103° F. Fibrositic patients as a rule stand heat well, and there is little risk of heat exhaustion, as is the case with rheumatoid patients. In this bath should be an undercurrent douche given at a temperature of 107° F. and applied at pressure to the areas of pain and stiffness, since the heat and percussion effect of the douche are admirable stimulants to the local circulation.

Given the correctness of the premise that fibrositis is in many, if not most, cases metabolic in origin, this line of treatment would seem to be logical, and in my experience has proved itself valuable in relieving the patient of his symptoms for a period which may in favourable cases extend to many years.

Conclusions

1. The metabolic factor in the genesis of rheumatic diseases has been too much neglected ever since the essentially metabolic disease, gout, was rigidly, perhaps too rigidly, excluded from the group.

2. This especially applies to fibrositis, which in the majority of cases is metabolic in origin.

3. Infective foci, if they exist, may be the direct cause of fibrositis, but may act by upsetting the metabolic balance and thus cause its onset.

4. Fibrositis may occur in those suffering from sub-thyroidism or autonomic imbalance.

5. The characteristic thickenings of fibrositis are due to a fibrous barrier of resistance laid down round irritative metabolites.

6. These thickenings may exist before clinical manifestations show themselves. The latter occur when a threshold of irritation is passed.

7. Treatment consisting in removal of septic foci and administration of vaccines is, as a rule, disappointing.

8. The dietary, endocrine, and autonomic balance must be readjusted, and the thickenings removed by short-wave diathermy or massage and hot baths.

BLOOD EXAMINATIONS IN THE PROGNOSIS AND TREATMENT OF PULMONARY TUBERCULOSIS

BY

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I propose to confine my remarks almost entirely to that branch of laboratory work on which I feel that I am best qualified to speak, namely, certain methods used in the assessment of blood changes in pulmonary tuberculosis and their clinical interpretation.

The criteria commonly relied upon in the investigation of blood changes in pulmonary tuberculosis are the total and differential leucocyte reaction, the Arneth count or one of its modifications, and the sedimentation rate of erythrocytes. I propose first to outline the variations in these reactions which may be expected in health and disease, in order to facilitate subsequent discussion of the clinical significance of those changes which are found in cases of phthisis.

Total and Differential Leucocyte Reaction

Recently the importance in pulmonary tuberculosis of the "three key cells," the neutrophil, the lymphocyte, and the monocyte, has been brought into prominence, and much has been done to elucidate the leucocyte response in different phases of the disease. Sabin¹ and her co-workers in America^{2,3} believe that the monocyte, or its derivative the epithelioid cell, in which living bacilli appear to thrive, is a "liability rather than an asset to the body." The function of the lymphocytes, on the other hand, is almost certainly that of surrounding the tubercle, cutting it off from the healthy tissue, and perhaps eventually destroying it, or at least facilitating its conversion into fibrous tissue. The differential leucocyte count is therefore regarded as a method of evaluation of the tissue damage which has resulted from infection. In brief, "the monocyte represents tubercle formation, the neutrophil represents tubercle

* Read in opening a discussion in the Section of Tuberculosis at the Annual Meeting of the British Medical Association, Oxford, 1936.

undergoing abscess formation, and the lymphocyte represents the healing phase of the tuberculous lesion" (Medlar and Pesquera³).

There are, of course, no fixed normal figures for the total or differential leucocyte counts, owing to the wide variations which may be found in different healthy individuals. Shaw¹⁶ has shown that during a twenty-four-hour day the total leucocytes per c.mm. of man exhibit two tides, each occupying approximately twelve hours with a variation of 2,000 or more per c.mm. The neutrophils are the cells most affected, and the tides occur regardless of food and exercise.

The Nuclear Count

Since Arneth first classified the neutrophile polymorphs into five groups according to the number of lobes to the nuclei, and later added complicated subgroups, the tendency among other workers has been to attempt to simplify the count. The Schilling modification is well known, and Bonsdorff has reduced the Arneth count to even simpler proportions. This method has been quite extensively used in this country, particularly by Lyle Cummins⁵, who found it, together with the differential leucocyte count and the sedimentation rate, of value in the assessment of cases of phthisis.

The *Bonsdorff Count*⁴ consists in the enumeration of the number of nuclei in 100 polymorph neutrophils. Although this number is subject to slight physiological variations it should, according to Cook and Ponder, be approximately 274, for these workers state that in health the number of cells in each class is fairly constant: *Class I* (undivided nucleus), 12; *Class II*, 25; *Class III*, 44; *Class IV*, 15; and *Class V*, 4. Some observers, however, state that the normal Bonsdorff count should be rather lower than this.

The Sedimentation Rate

The significance of the rapidity with which blood resolved itself into its different constituents appears to have been first appreciated by Hippocrates⁷. In 1918 the ancient Greek notion was demonstrated by Fahraeus⁸ and Katz⁹ to be intimately associated with health and disease, and in 1921 Westergren¹⁰ pointed out the relation between sedimentation rate and activity of tuberculous processes. Since that date the method has been in almost universal use. In this country Lyle Cummins⁵, Trail¹¹, Heaf¹² and many others have applied it in the management of cases of phthisis, and the test is now regarded as a valuable indication of activity or arrest of pulmonary disease, and by some as a significant prognostic agent. It is agreed that serial tests are of infinitely greater value than isolated readings.

The usefulness of the test in following up cases from one institution to another has been diminished by the tendency for different workers to use different techniques. The original Westergren method appears to be still most universally used, but a very large number of modifications have been introduced, and it is unfortunately not an easy matter to express one method in terms of another. It is beyond the scope of this paper to discuss the merits and demerits of the different methods, but there does not seem to be any adequate reason for departing from Westergren's original method in cases where it is possible to obtain blood from a vein. The use of a 200-mm. tube (Westergren) is, I think, to be preferred to the 100-mm. tube, in that "packing" of the cells at the bottom of the tube occurs earlier in the shorter tube, and consequently in rapidly sedimenting bloods the higher readings tend to be inaccurate. The sedimentation curve flattens too soon with the shorter tube.

The mechanism giving rise to changes in the leucocyte reaction and the sedimentation rate in pulmonary tuber-

culosis is at present imperfectly understood, and the significance of these changes can thus only be appreciated by repeated comparisons between clinical condition and blood picture. As the result of the analysis of nearly 2,000 cases of pulmonary tuberculosis from this point of view I am venturing to express my opinion as to the value of these methods in prognosis and treatment. I have used the following procedure.

Technique

Tests are made as near midday as possible. Blood is taken from a vein in the antecubital fossa with a 2 c.cm. Record syringe and an ordinary serum needle. A few drops are expelled on to a clean slide for making smears and (if necessary) a total count. The syringe is then held vertically, and the excess of blood is expelled into a piece of cotton-wool held round the needle; 1.6 c.cm. of blood is transferred to a small test tube containing 0.4 c.cm. of 3.8 per cent. citrate solution, and well mixed. Smears are next made from the uncitrated blood previously mentioned on clean slides, using a narrower slide or a standard slide with the corners chipped off as a "spreader." It is essential that smears should be of the correct thickness, particularly for the Bonsdorff count; it is better to make them too thin than too thick. The sedimentation tube (Westergren) is then filled to the 0 mark, and placed in a specially made stand with a cork at the bottom and a spring clip at the top. It is essential that the diameter of the tube should not be less than 2 mm., that it should be clean and dry, and that it should be quite vertical in the stand. Normal variations in room temperature do not produce a significant change in the sedimentation rate.

The length of the column of clear fluid is read at the end of one hour. (The normal figure is stated to be 3 or under for males, and 7 or under for females.) The whole of this procedure only occupies two or three minutes. The sedimentation reaction tube should be put up as soon as possible after the blood has been drawn. Blood smears are subsequently stained with the Leishman stain, and examined under the 1/12 objective. The Bonsdorff and the differential counts are carried out at the same time; for the latter at least 200 cells should be counted. There is normally little or no difficulty in differentiating lymphocytes from monocytes. Monocytes appear as large cells, with a round or horseshoe shaped nucleus, showing finely drawn basi-chromatin and a faintly granular cytoplasm.

I emphasize the following points in the technique. It is very desirable, I think, that the blood specimens should be taken from a vein wherever possible. The finger-prick method seems to be unduly subject to error owing to the difficulty in avoiding pressure in the attempt to obtain a sufficient quantity of blood. It would appear that there may be other sources of error in this technique, for Simpson¹⁷ in describing a series of experiments in which blood smears were taken at brief intervals from the same individual recorded a capricious irregularity in the counts, comparable to the density of smoke rising from a fire!

In a similar experiment in which I took six blood smears from an individual at 10-minute intervals, using the stab method and the vein puncture method alternately, I found marked variations in the leucocyte picture by the former method, but constant results by the latter. At the same hour the following day the counts by vein puncture remained unchanged, but there was again a certain variation using the stab method. The sedimentation rates were constant for both methods throughout.

The percentage of cells is apt to vary very considerably in different parts of the slide, and it is of course essential that the whole length and breadth should be covered during the count. The Bonsdorff count requires practice. If the smear is thick an accurate count is impossible; if it is too thin searching for cells becomes tedious. The nuclei should not be joined by more than a fine chromatin filament if they are to be regarded as separate. For those who have not been accustomed to doing these counts it is perhaps as well

to begin on normal individuals who should have approximately 274 nuclei in 100 polymorphs. The personal factor should not, I think, introduce an error of more than ten in a complete count. I no longer use the total leucocyte count, since it does not greatly increase the information to be derived from the differential count, but it does add to the time and labour involved.

Comparison of These Methods

I give some examples of the type of blood pictures which result from the use of these methods in the difference phases of pulmonary tuberculosis.

Case 1.—Quiescent Case	Case 2.—Active Disease	Case 3.—Terminal Condition
Neutrophils ... 55 %	Neutrophils ... 63 %	Neutrophils ... 68 %
Class I ... 13	Class I ... 25 %	Class I ... 50
Class II ... 36	Class II ... 36	Class II ... 34
Class III ... 38	Class III ... 35	Class III ... 13
Class IV ... 13	Class IV ... 4	Class IV ... 3
Class V ... 0	Class V ... 0	Class V ... 0
Bonsdorff count 251	Bonsdorff count 218	Bonsdorff count 169
Lymphocytes ... 36 %	Lymphocytes ... 25 %	Lymphocytes ... 19 %
Eosinophils ... 4 %	Eosinophils ... 1 %	Eosinophils ... 0 %
Monocytes ... 5 %	Monocytes ... 11 %	Monocytes ... 13 %
Sed. rate ... 7	Sed. rate ... 35	Sed. rate ... 71
Index ... 264	Index ... 161	Index ... 55

The first is a picture from a quiescent case, showing a blood which approximates to the normal, although a certain degree of "shift to the left" is still apparent from the Bonsdorff count. The second is from a case in which there is activity, but a fair measure of resistance. The third is from a case of extensive active disease in which the resistance has quite given way and toxæmia is profound.

In these cases it will be seen that the various factors which make up the haemogram are in agreement. Thus in Cases 2 and 3 a rapid sedimentation rate is accompanied by a low Bonsdorff count, a low lymphocyte percentage, and a high monocyte percentage. Similarly in the first case, all the elements approximate to the normal. It might be supposed that in every case of active phthisis there would be the same correlation between the different criteria employed, each of which is regarded as an index of activity of tuberculous processes. This unison is by no means the rule however. It is common in pulmonary tuberculosis to find a normal sedimentation reaction associated with a comparatively low Bonsdorff figure; or a low lymphocyte-monocyte ratio occurring with a high Bonsdorff count. This may be particularly observed in serial counts on the same patient; improvement may occur in one of the criteria and not in the others. The question arises as to which of the criteria employed gives the most reliable indication of the patient's progress and pathological condition. I submit the opinion which I have formed of the relative value and significance of the three methods under discussion, based upon the association of the blood findings with the clinical condition and progress of a large number of cases of pulmonary tuberculosis.

THE SEDIMENTATION RATE

This is the easiest test to perform, the least liable to technical error, and in consequence the test most universally used. The interpretation which can be placed upon it, however, calls for considerable modification in different types of case. I have found that, taken by itself, it has very little prognostic value in pulmonary tuberculosis. Many active cases are admitted to hospital with a poor sedimentation rate, but this often improves rapidly under routine treatment, when other factors in the blood picture are far more difficult to influence, and often regardless of focal activity. Moreover, instances are common in which the sedimentation rate remains within normal limits, although it is apparent from clinical and x-ray evidence that an active lesion is present. On the other hand, in a

certain type of case a rapid sedimentation rate is compatible with a very chronic lesion associated with little or no toxæmia. It has in fact been notable in my own series of cases that many of the higher readings for the sedimentation rate have occurred in this type of case.

Fluctuations in the sedimentation rate seem almost comparable with variations in the patient's weight—most patients gaining weight when under treatment often regardless of underlying pathological processes. In fact I would suggest that one important factor in the production of a rapid sedimentation rate is disturbed metabolism. A rapid rate is frequently found in association with dyspnoea and with cases in which bronchitis is a prominent feature. Chronic bronchitis uncomplicated by tuberculosis does not usually occasion an acceleration of the rate¹³.

Toxæmia no doubt plays a direct as well as an indirect part in accelerating the rate, but it is notable that acute infiltrative toxic types of case frequently give lower readings than the more chronic forms. Prolonged rest in bed, except in the most advanced cases of phthisis, will often bring the sedimentation rate to within normal limits. The other factors in the blood picture may not however be correspondingly improved.

I have concluded, therefore, that the sedimentation rate, taken by itself, is not a reliable indication of a patient's state of resistance to his disease or of the state of activity of his lesion; nor can it be used alone, for the comparison of the condition of one patient with another. I believe, however, from clinical observation that it is a valuable indication of disturbed metabolism and the constitutional disturbance resulting from the disease, and as such it has a definite place in the blood picture. I do not believe, however, that minor fluctuations in the rate are of sufficient significance to justify the extreme precautions against inaccuracy which are sometimes advocated.

THE DIFFERENTIAL COUNT

When one considers that in any case of pulmonary tuberculosis there must be many separate lesions in different phases of development and healing it is not surprising that inconsistencies in the differential count are met with, and that such counts are often difficult to interpret. In counts repeated daily for two or three weeks, however, I have found that the percentages of cells remain fairly constant in the absence of clinical change in the patient. Repeated differential cell counts at longer intervals during treatment do, in a large number of patients, show quite definite changes. In a patient who has improved, the percentage of lymphocytes may be doubled at the expense of the neutrophils, the monocytes percentage may be decreased, and eosinophils previously absent may reappear. On the other hand the reverse process will be observed where uncontrolled activity of disease has supervened. I think it is unwise to attempt too close an interpretation of minor fluctuations in the cell percentages, if only for the reason that there is liable to be a small error in performing the count, unless four or five hundred cells are counted. However, in my experience an adult patient with 35 to 40 per cent. of lymphocytes at the commencement of his treatment has a better prospect in his fight against his disease than one with only 20 per cent. A relative lymphocytosis appears to indicate a good potential resistance to the disease. There are many exceptions, however, to such a generalization, and I believe that to rely solely on this aspect of the blood picture for definite information would often be misleading.

THE BONSDORFF COUNT

This is invariably deflected from the normal when there is any auto-inoculation from a tuberculous focus. In some

2,000 cases of phthisis I have found very few which did not show a certain degree of shift to the left, or lowering of the Bonsdorff count, and most of the exceptions have been in quiescent cases. The Bonsdorff count cannot be correlated purely with the extent of disease, and activity may apparently depress the count to a far greater extent in one case than in another. As a general statement one can say, I think, that the Bonsdorff tends to be lower in acute forms of the disease than in the more chronic type. I have concluded that this count is a reliable indication of toxæmia in pulmonary tuberculosis.

Clinical Deductions

It would appear therefore that in pulmonary tuberculosis the sedimentation rate, the differential leucocyte count, and the Bonsdorff count each represent a different aspect of the patient's reaction to his infection. I would suggest that increase in the sedimentation rate represents constitutional disturbance, decrease in the Bonsdorff figure represents toxæmia, while it has been shown by many workers that the differential leucocyte count reflects the changes which are occurring in the diseased areas in the lungs.

Lyle Cummins, using the blood picture as one factor in the assessment of cases of phthisis, proposed a system whereby marks were allotted in respect of the different criteria, in order to reduce a complicated series of figures to a simpler and more easily comparable form. It is certainly necessary, in view of the fluctuations which occur in the component figures of serial haemograms, to have a method of summarizing the information derived from each source. In my own work I have adopted the principle of balancing those factors in the haemogram which can be described as "assets" to the patient against those which are "liabilities." Thus a high Bonsdorff and a high lymphocyte percentage are assets, and a high sedimentation reaction and high polymorph and monocyte percentages are liabilities. The formula, which I have previously described in detail⁴, is as follows:—

$$V.B. - [S.R. + (P + M - 2L)] = \text{Index.}$$

Eosinophils being regarded as assets are added to the lymphocyte percentage. The index ranges from zero in the worst cases to 300 in the best cases, and I regard any figure above 260 as within normal limits. This index has been in routine use at Colindale for the past five years, and I have no hesitation in saying that it gives an accurate indication of the pathological status of the patient at the time of making the test.

Prognosis

In the interpretation of the blood picture in prognosis I believe that considerable caution is necessary. As a means of ascertaining the precise condition of the patient at the moment, the method is invaluable, but it must be remembered that the exhibition of a good blood picture is no real guarantee against future relapse. One is certainly justified in drawing a satisfactory conclusion if in spite of the presence of infiltrated lungs the blood picture is not unduly depressed. If, on the other hand, when the x-ray reveals only a small early lesion the blood picture shows great all-round deterioration, the prognosis is undoubtedly a grave one. Compare, for example, the following cases:—

Case 4.		Case 5.	
Polymorphonuclears ..	52	Polymorphonuclears ...	70
Lymphocytes ...	39	Lymphocytes ...	22
Eosinophils ...	4	Eosinophils ...	0
Monocytes ...	5	Monocytes ...	8
Blood count ...	239	Blood count ...	211
Sedimentation rate ...	41	Sedimentation rate ...	35
Index ...	227	Index ...	42

Case 4.—A man, aged 38, afebrile, and with tubercle bacilli in the sputum, responded well to treatment. He put on 1 stone in weight, and returned to work. The blood picture though far from normal is so much better than the x-ray picture suggested, that it was safe to assume that he had considerable powers of resistance, that his disease was not of a very active type, and that he had it well under control.

Case 5.—A lad, aged 18 and afebrile, had no sputum at the time of blood test. Left artificial pneumothorax was induced, but the opposite lung broke down. The poor blood picture resulting from an early lesion, far less extensive than case 4, indicated a comparatively poor resistance and bad prognosis.

Case 6.—The blood picture of a member of the hospital staff who had a blood test as one of a series of normal individuals. Two years later he had a hæmoptysis, and a small acute lesion was found at one apex. The second blood picture indicates some toxæmia, but the sedimentation rate is still normal because the general condition has not yet deteriorated, and there is no appreciable constitutional disturbance. He has been back at work for over a year.

	17/3/32	15/1/34
Polymorphonuclears ...	57	71
Lymphocytes ...	36	23
Eosinophils ...	1	1
Monocytes ...	6	5
Blood count ...	274	237
Sedimentation rate ...	3	4
Index ...	282	205

So far as immediate prognosis is concerned it can be stated that of those patients admitted to hospital with a blood index of less than 120 (a purely arbitrary figure), 72 per cent. died, and of those who survived and passed out of the hospital 60 per cent. died within a few months of discharge.

Case 7.—An example of this type of case is a man, aged 26, with somewhat extensive disease of both lungs. He was on routine treatment at Colindale for ten months; he apparently did well, put on weight, and had consistently normal temperature. He performed the heaviest grade of work without any distress.

	14/2/33	8/12/33
Polymorphonuclears ...	68	67
Lymphocytes ...	25	29
Eosinophils ...	1	0
Monocytes ...	6	4
Blood count ...	179	157
Sedimentation rate ...	83	38
Index ...	74	106

In view of the very poor blood index on discharge, one was not surprised when he was re-admitted two months later in a dying condition.

With the kind co-operation of the tuberculosis officers of some of the London boroughs, I was able to follow up 107 patients of whose blood condition on discharge I had a record. Of those cases with an index above 180 on discharge, 84 per cent. were stated to be at work: of those with a figure below 180 and above 120, 24 per cent. were at work and 63 per cent. unfit; of those with an index below 120, 36 per cent. were unfit and 60 per cent. were dead. Apart, therefore, from our own observations on cases under treatment, the blood picture and index would seem to be of value in forecasting the patient's capacity for work and his immediate prospects on leaving hospital. A blood test taken during an acute exacerbation of the disease would of course give an unduly depressed blood picture. Acute pleurisy and acute pleural effusions depress all the features of the haemogram to an exaggerated extent, and blood tests taken at these times will produce unduly pessimistic figures. Such considerations are of obvious importance if the blood is to be used in prognosis.

The Blood Picture in Treatment

When a patient first comes under observation and his future treatment is under consideration, it is necessary to decide whether the disease is advancing, stationary, or

retrogressive, what is the degree of toxæmia or constitutional disturbance, and what margin of resistance the patient possesses. I believe that these questions can be answered more accurately by the blood reaction than by any other single factor. One cannot lay down any hard-and-fast rules, but the following observations may be of assistance in determining what line of treatment is to be adopted in a particular case.

Ordinary periods of routine sanatorium treatment do not tend to bring about great improvement in the blood picture. Patients who begin treatment with a comparatively high blood index (above 200) may return to normal standards by routine measures alone, but in the majority the improvement in the blood picture is but slight and is confined to improvement in the sedimentation rate. Those whose initial blood index is low are unlikely to show very great improvement in the index after routine treatment.

Following successful artificial pneumothorax treatment in unilateral disease, improvement in the blood picture is dramatic, and may within two or three months be completely normal. This, however, is no guarantee that the case will not relapse, but is an indication that for the moment auto-inoculation has been completely controlled. Subsequent deterioration in the picture will indicate reactivity. I have found that cases commencing artificial pneumothorax treatment with a very poor, toxic blood picture are more liable to subsequent relapse than those who had previously exhibited a fair measure of resistance. I believe, therefore, that it is often as well to delay intervention until the maximum improvement in the blood picture has been obtained by rest, even at the risk of the formation of adhesions in the interim. Decrease in the sedimentation rate alone is of little value in this connexion as a criterion of the establishment of resistance. If the patient fails to show improvement, possibly owing to massive infiltration, then one has no alternative to intervening. The same observations apply, perhaps more forcibly, to the application of thoracoplasty. If definite improvement in the blood picture has not occurred within six weeks of artificial pneumothorax induction, the operation is unlikely ultimately to be beneficial, unless a more satisfactory collapse can be obtained.

Patients in whom bronchitis is a prominent complication are notoriously unsatisfactory subjects for collapse therapy. They often become dyspnoeic and lose weight, and constitutional disturbance is so great that the treatment has to be abandoned. Such patients frequently give a typical blood picture, the chief feature of which is the wide discrepancy between the sedimentation rate and the Bonsdorff count.

Case 8.									
Polymorphonuclears	...	70	Monocytes	...	...	...	...	5	
Lymphocytes	...	22	Bonsdorff count	...	...	...	...	248	
Eosinophils	...	3	Sedimentation rate	...	...	...	...	52	
Index	...	...	...	...	...	...	...	171	

The explanation of this type of blood picture seems to me to lie, first, in the fact that such patients are usually suffering from a chronic fibroid type of disease with but little tuberculous toxæmia, and in consequence there is but little shift to the left of the neutrophils; and secondly that deficient aeration through fibroid and possibly emphysematous lungs has brought about profound changes in metabolism, with a consequently poor sedimentation rate. Finally, there being very little tendency either to activity of tuberculous processes or healing in the lungs, neither the monocytes nor the lymphocytes are increased in the differential count.

This "bronchitic blood picture" is not uncommonly met with in cases in which there is no apparent element of bronchitis. We have found, however, that such patients

frequently fare badly when artificial pneumothorax is induced. They lose weight and become dyspnoeic and generally distressed.

It must be remembered that the discrepancy between the Bonsdorff count and the sedimentation rate is only one of degree, and that indefinite blood pictures will occur. Artificial pneumothorax treatment would not of course be withheld in an otherwise suitable case on the strength of a bronchitic type of blood count alone, but one would certainly hesitate before recommending such a case for major surgery—or even for a permanent phrenic operation. Case 9 is of interest from the point of view of comparison with the foregoing type of blood picture. It shows the effect of a thoracoplastic operation on a unilateral lesion, in a man aged 42.

Case 9.									
Polymorphonuclears	...	61	Monocytes	...	...	...	...	5	
Lymphocytes	...	35	Bonsdorff count	...	...	...	...	255	
Eosinophils	...	1	Sedimentation rate	...	...	...	...	67	
Index	...	...	...	...	...	...	...	190	

The test was made six weeks after operation. The lung was well collapsed, the sputum was negative, and the temperature normal. He was inclined to be dyspnoeic, however, and recovery from the operation was rather slow. Hence, although there is no appreciable tuberculous auto-inoculation (Bonsdorff 255), the constitutional disturbance is reflected by the rapid sedimentation rate.

This case serves again to emphasize the view that a rapid sedimentation rate is often due to the remote effects of the illness rather than directly to tubercle formation and the spread of tuberculous disease. An ineffective or inadequate collapse of the diseased lung by thoracoplasty will be betrayed by failure of the Bonsdorff count to revert to normal. In a patient who has stood the operation well, the rate may quickly improve with bed rest, even though the pulmonary lesion is inadequately controlled.

When it is decided to re-expand the lung on the completion of artificial pneumothorax treatment, there should be no falling away in the blood index as the lung again comes into action. This would obviously indicate, in the absence of some other cause, a recrudescence of focal activity.

For the assessment of progress under treatment the blood index has an obvious application. An example of its value is a case in which phrenic evulsion has been performed as an alternative to artificial pneumothorax: if substantial improvement in the blood picture does not occur, further treatment will have to be considered. Considerable improvement in the haemogram frequently follows phrenic operations, presumably owing to limitation of auto-inoculation and promotion of healing by diminished movement. Sanocrysin may be of benefit to those patients who already have a reasonably good blood picture, but those with a toxic blood picture are liable to be made worse¹.

Conclusion

I submit that limitations in the value of the methods of blood assessment are largely technical. Blood counts take time (perhaps a quarter of an hour for each count), and although the technique is not difficult to acquire, some experience is necessary before consistent results can be obtained, particularly in the nuclear count. I consider, therefore, that every centre for the treatment of tuberculosis should have the services of a technician who is able regularly to devote part of his time to blood examinations. Casual blood counts undertaken by inexperienced observers probably have little or no value. The complete blood picture with the summarizing index is of infinitely greater value than any single method, but the nuclear count is probably the most reliable single criterion of tuberculous activity and toxæmia.

It has been suggested that the modern tendency in tuberculosis is to treat x-ray films. But, as Medlar¹⁵ has said, "the final outcome depends more upon the underlying pathological condition than it does upon the presence or absence of signs and symptoms. For the clinician, the nearest approach to the pathological status of tuberculosis is the leucocyte reaction."

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INHALATION THERAPY

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Inhalation therapy has been but little used in England. It is claimed that the tracheo-bronchial mucous membrane has great absorptive power and that drugs given by this method are rapidly absorbed into the blood stream. The experimental work has mainly been carried out in Germany; dogs, cats, and rabbits have been used: atomized liquids have been supplied to these animals, and the size of the droplet required for inhalation therapy has been determined on the basis of animal experiments.

Wolfgang Heubner,¹ in a paper on the inhalation of atomized liquids, dated 1919, gives an interesting account of this work. The earlier experiments consisted of injections of various solutions and suspensions into the trachea of an animal which was killed a few minutes later, the lungs immediately being fixed and examined. H. Nothnagel² allowed rabbits to aspirate their own blood; three and a half minutes later the animal was killed and the lungs were examined immediately. Red blood cells were found in the interstitial tissue of the lungs, in the lumen of the smaller bronchi with their long axes at right angles to the bronchial walls, and in the act of penetrating between the cells of the bronchial epithelium.

W. Fleiner³ found that the absorption of particles of Indian ink after tracheal injection was extremely rapid. He claims that carbon particles may reach the lymph nodes in twelve seconds. Sehrwald⁴ injected a solution of dye into the trachea of a rabbit and half a minute later caused the animal to inhale lycopodium; immediately afterwards the rabbit was killed and the lungs were examined. In the lumen of many small stained bronchi were unstained lycopodium granules. The dye solution must therefore have been very rapidly absorbed.

A further demonstration of the rapid absorption of solutions in oil or water is afforded by the experiments of Heubner. He injected a concentrated solution of malachite green into the lower part of the trachea of a cat and killed the animal by dividing both carotid arteries, while perfusing the vascular system through the jugulars to wash away as much blood as possible. The respiration stopped in two minutes and the heart in four minutes. On dissection the muscles were found to be

stained green, especially on the breast. The heart and liver were deeply stained; the intestines, kidney, bladder, urethra, and intima of large arteries were lightly stained. The spleen, peritoneum, pericardium, and urine were unstained. In the lungs the smaller bronchi were deeply stained; dye had reached many alveoli and had perfused outward. The pleura was unstained. He calculated that the maximum time for absorption had been sixteen minutes.

Atomized Liquids

A similar test, using an atomized liquid, was carried out. A twenty-minute inhalation of 20 per cent. potassium ferrocyanide was given through a Spiess-Dräger atomizer. After twenty minutes ferrocyanide was present in the urine. The mucous membrane of the trachea was deeply stained for a few centimetres below the cannula, that of the main bronchi very lightly stained, and that of smaller bronchi not at all. At the bifurcations of the branches heaped-up stain was found. He concludes that the absence of staining in the smaller bronchi resulted from the very rapid absorption of ferrocyanide.

Kaestle,⁵ using rabbits under chloroform anaesthesia, was able to stain the whole bronchial tree and the alveoli with ferrocyanide. Narcosis may have hindered absorption, and a different type of animal was used.

I. Sikorsky⁶ caused dogs and rabbits to die from asphyxia as a result of the aspiration of sodium indigo sulphate; the trachea was immediately filled with absolute alcohol to precipitate the dye. Granules of dye were found between the cells of the bronchial epithelium, and streaks of dye were found in the peribronchial tissues. The cells of the bronchial epithelium were unstained. Sinkosky produced similar evidence. Heubner, using Victoria blue dye in olive oil, showed that oil drops passed between the cells of the bronchial epithelium, and that dye was absorbed from the oil drops by the bronchial epithelial cells. The dye was introduced into the trachea; eight minutes later the animal was killed. The lungs were kept in formalin for three days and examined in frozen section.

These experiments show conclusively that very rapid absorption occurs from the tracheo-bronchial mucous membrane, both for aqueous solutions and for those in which oil is used as a solvent. The depth to which atomized liquids penetrate the bronchial tree is very difficult to determine because of this rapid absorption. Most of the experiments have been carried out with an intra-tracheal cannula, but Hofbauer⁷ allowed dogs to inhale through the nose and the findings were similar. Dye is found at the points of division of the bronchi, down to minute branches, and in some cases in the alveoli. In Heubner's tests the dyes used were malachite green and Victoria blue oil; the Spiess-Dräger apparatus and the Tancre apparatus were employed. The former apparatus produced the more dense vapour with larger drops and with it only were drops of dye found in the alveoli.

Clinical Investigation

Dr. L. S. T. Burrell was using a Collinson's inhaler in the wards of the Royal Free Hospital, and when I was his house-physician he asked me to carry out some experiments to show the degree and rate with which certain drugs were absorbed and also to give an analysis of the results of cases treated in the hospital. The effects of inhalation of pure oxygen were studied both on patients and on students. A gauge was used to determine the rate of flow of oxygen from a cylinder, and the dial controlling the supply of oxygen was set at different levels according to the amount of oxygen in the cylinder. If the oxygen were delivered at more than ten litres a minute there