FIG. 1.—Case I, tuberculosis. Before thoracoplasty.

FIG. 3.—Case II, bronchiectasis. Before thoracoplasty; lipiodol injections demarcating cavities in the right lung.

FIG. 2.—Case I. After thoracoplasty. (Sides reversed in photograph.)

FIG. 4.—Case II. After thoracoplasty; lipiodol injection showing collapse and flattening of peripheral and central cavities; those near the mediastinum are only partially collapsed.

W. E. COOKE: THE MACROPOLYCYTE.

FIG. 1.—Normal polymorph. ($\times 1000$.) FIG. 2.—Macropolycyte from a case of staphylococcal osteomyelitis. ($\times 1000$.) FIG. 3.—Macropolycyte from a case of streptococcal septicaemia. ($\times 1000$.) FIG. 4.—Macropolycyte from a case of pernicious anaemia, showing hypersegmentation of nucleus. ($\times 1000$.) FIG. 5.—Macropolycytes of the megakaryocyte type in pernicious anaemia. ($\times 1000$.) FIG. 6.—Macropolycyte of the megakaryocyte type showing large granules in the cytoplasm. ($\times 1000$.) FIG. 7.—Macropolycytes of the megakaryocyte type in pernicious anaemia. ($\times 1000$.)

THE SURGICAL TREATMENT OF PHTHISIS AND BRONCHIECTASIS.*

(With Special Plate.)

BY

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IN most European countries, and to an increasing extent in America, operative treatment of certain classes of cases of phthisis and bronchiectasis has been widely accepted. In this country—chiefly, in my opinion, as a result of lack of knowledge of the results obtainable and of the more suitable types to submit to operation—progress has been very slow. Operative mortality has been very considerably reduced; and whereas formerly it has been so high that only the most hopeless cases were submitted to operation, a stage has now been reached where operation can be recommended with reasonable certainty that the immediate post-operative period will be safely passed.

The two conditions—bronchiectasis and phthisis—offer very many similarities, and as their cure is dependent in many instances upon the same factors I shall consider them together, pointing out various minor differences as occasion offers. In both diseases the evolution of surgical treatment has developed along similar lines. Both diseases occur at a comparatively early period in life and both have a very high mortality. In third-stage tuberculosis the mortality is probably in the neighbourhood of 80 per cent. in the course of five years, and Powell and Hartley state that "bronchiectasis, owing to its anatomical character, is not a disease from which we may expect recovery. At the best, all that we may hope for is that, by preventing decomposition of the sputum, we may be able to arrest its further progress. In nearly all cases, in spite of treatment, the disease gradually advances."

The object of the surgeon is to prevent the evil results of the contraction of fibrous tissue on the important pulmonary structures, either by allowing the rigid thoracic wall to fall in, or, by interposition of either solid or gaseous buffers between the chest wall and lung, to allow localized or generalized pulmonary collapse. In this way cavity walls are brought into apposition and healing is aided, in addition to which the lung is given adequate rest.

METHODS OF TREATMENT..

Division of Adhesions.

These operations are used in cases where artificial pneumothorax treatment is only partially successful owing to the presence of localized adhesions between parietal and visceral pleurae, which prevent full pulmonary collapse. Only comparatively narrow bands offer any hope of successful division. These bands are commonly found overlying cavities in the lung; their deleterious effects are shown by the figures of Sangman and Gravesen. In 211 pneumothorax cases the proportion of patients able to work after three to thirteen years was only one-half as many in those with adhesions as compared with those free from adhesions. Open thoracotomy with ligature and division of the adhesions has been tried, and resulted in some cases in widespread infection of the pleura or eventual intractable fistula. It has therefore been abandoned. The method of choice is the cauterization of adhesions under the control of thoroscopic vision, as devised by Jacobaeus of Stockholm.

The operation, performed under local anaesthesia, consists in the introduction of a trocar and cannula through a convenient intercostal space, the telescope with its terminal light replacing the trocar. After perforation of the pleura any adhesions present are examined with a view to their division. If this is considered possible, a finer trocar and cannula is introduced in such a position as to bring the cautery as nearly as possible at right angles to the adhesions to be divided. The current required to cause a strong red glow in the cautery is estimated before intro-

duction and is controlled, advisably, by a foot switch. Gentle pressure will result in gradual division of the adhesion. When this is complete the ends retract and should be examined for any bleeding points, which, if present, can be retouched.

When doubt exists as to the presence of a prolongation of a cavity into the pulmonary end of the adhesion cauterization should be done as near the parietal pleura as possible. Smoke may temporarily obscure the field, but is rarely a serious inconvenience. A slight degree of surgical emphysema is a common sequel, but the main complication has been severe empyema, either early or late, and has resulted in death in 7 to 8 per cent. of cases. A small effusion, the result of irritation, is fairly common, but reabsorbs in the majority of cases within a short time. One case of fatal haemorrhage has been recorded.

The indications for this procedure depend upon x-ray appearances in conjunction with the amount and character of the sputum, the temperature, and the pulse. Thus, during artificial pneumothorax treatment, when a definite cavity is held uncollapsed by a fine adhesion, and the temperature, pulse rate, and sputum are increased, the operation is advisable. The operation should not be attempted in the presence of pleurisy nor with bands of greater thickness than one centimetre. Within these limits this auxiliary method of treatment appears to have a limited but definite field of usefulness in tuberculosis.

In my series of fifteen patients thoroscoped with a view to cauterization the complete operation was only possible in four, of whom two have done well eventually.

Pneumolysis.

The object of this operation is to produce a localized collapse of the lung in order to compress cavities. The operation consists in the separation of the lung, with the visceral and parietal pleurae (being adherent), from the chest wall, the line of cleavage being underneath the endothoracic fascia. It may be performed anteriorly, in the axilla, or posteriorly. The latter site is usually chosen where the operation is combined with thoracoplasty. Various media have been used for filling this space between pleura and chest wall. Tuffier uses fat from the abdominal wall, lipomata, or omentum. Baer uses paraffin wax with a small proportion of bismuth carbonate and iodoform. The objection to this fill is that it acts as a foreign body, and may be discharged following sinus formation. Archibald has used a portion of the pectoral muscle, and Sauerbruch occasionally uses a gauze pack, repacking the space repeatedly, with the result that granulation tissue is formed over which the superficial structures are subsequently allowed to fall in.

Pneumolysis may be used as an independent or a supplementary procedure. In the former case results have been disappointing, the reasons being that the procedure is too localized. Tuberculosis is very rarely localized to the apex of the lung, and for bronchiectasis enormous fills would be required to bring about any noteworthy compression of the base. As a supplementary operation to pneumothorax some quite satisfactory results have been recorded. The best results have been obtained in apicolysis secondary to thoracoplasty, in which a residual cavity has remained at the apex.

I have operated on two cases by this method—one in order to collapse the apical portion of the lung, following incomplete artificial pneumothorax, the other as supplementary to a previous thoracoplasty with a partially collapsed apical cavity. In each case fat was used as the filling medium, and both cases healed by first intention. The ultimate benefit, however, was only slight, and it is doubtful if the operation justifies a wider field.

Phrenicotomy.

Paralysis of the diaphragm resulting from division of the phrenic nerve will cause diminution of the hemithorax and consequent collapse of cavities in the base of the lung, and even some decrease in size of cavities higher in the lung. Simple division of the phrenic nerve in the neck, however, is not always followed by diaphragmatic paralysis, complete and permanent. This is due to the presence of accessory phrenic fibres which join the main

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stem after its entrance into the thorax. When present, they join the main phrenic in the thorax within two inches of the clavicle, and are stated to occur in from 30 to 40 per cent. of cases. The original operation of simple division has therefore been modified.

Radical Phrenicotomy (Local Anaesthesia).—A small incision is made parallel with the posterior border of the sterno-mastoid muscle in its lower half. The fascia is incised and the muscle drawn forwards. The phrenic nerve is exposed beneath the fascia overlying the scalenus anticus. The nerve is anaesthetized, divided, and the lower end seized in artery forceps. The nerve, carefully freed from surrounding structures, is slowly twisted around the forceps, and gradually withdrawn from the thorax. Often the nerve can be completely extracted, in other cases it may require division when a sufficient portion is withdrawn. Some dragging pain in the chest is common, and spasmodic movement of the diaphragm may occur. The only noteworthy complication has been haemorrhage, from which death has been reported in one case out of several hundred recorded. The average raising of the diaphragm after operation was stated by Felix to be 7 cm. at the end of inspiration and 3 cm. at the end of expiration, and it is said that the lung volume is reduced by 400 to 800 c.cm. The indication for this operation in tuberculosis is when the disease is subacute and the patient too ill for major proceedings, or when the disease in the better lung appears too extensive for artificial pneumothorax treatment. It can be used as an indication of the condition of the so-called "better lung" preliminary to thoracoplasty. When basal adhesions limit the value of pneumothorax treatment it is of value, and has been advised as a routine to prevent mediastinal displacement and reopening of cavities after pneumothorax treatment has been concluded. In bronchiectasis great improvement has followed radical phrenicotomy, but the cure is rarely complete. It has also proved valuable in haemoptysis in this disease.

My series of cases numbers 17, 5 being supplementary to thoracoplasty, 3 to pneumothorax treatment. In 8 of these simple division of the phrenic nerve was performed, and in those cases in which no other operation was done proved disappointing. The last 9 cases, however, have had radical phrenicotomy performed, and the results have proved much more satisfactory. (Since the above I have carried out the operation a further thirty times, making a total of 47 cases, without complication and in practically every case some definite improvement.) The diaphragm has become raised in every case and the chest capacity has been obviously reduced, with improvement of symptoms.

Thoracoplasty.

The following are the indications for thoracoplasty in tuberculosis: fibrotic disease with mediastinal displacement; cases in which artificial pneumothorax has been successfully carried out but in which reactivation results when the treatment is given up (in these cases pleural adhesions generally prevent further pneumothorax treatment); certain cases of long-standing disease with more extensive cavitation; pleural effusions, recurrent in spite of other treatment; true tuberculous empyemata, unassociated with secondary infection; recurrent haemoptysis resistant to other forms of treatment. The important factor in all cases is that the disease must be mainly unilateral. There should be no signs of recent activity in the "better" lung unless they are minimal and considered to be the result of spread from the worse lung. Cavitation in the better lung negatives operation. In general, there should have been no spread of disease in the better lung as shown by physical signs or x-ray examination during the three months preceding operation.

Thoracoplasty is, as a general rule, inadvisable under 14 years of age, as in the contracting fibrotic type of disease the chest wall naturally tends to fall in. In adults over 45 years of age the cardiac condition is not so satisfactory and the chest wall and costal cartilages are rigid. The general condition must be taken into consideration, although wasting is not a contraindication in itself. Advanced lesions of the cardio-vascular system will contraindicate except where cardiac embarrassment is due to

mediastinal displacement. Moderate laryngeal lesions are permissible, but tuberculous lesions in other parts—especially intestine, kidneys, and bones and joints—are generally accepted as contraindications.

In bronchiectasis it has not yet been definitely determined which are the types of disease to give the best results from thoracoplasty, but the disease must be unilateral. Physical signs are often absent or indefinite even in advanced disease, and x-ray evidence may be very doubtful. The introduction of substances opaque to x rays—such as lipiodol, an oily solution of iodine—into the bronchi has proved of very great value and will generally show whether the disease is unilateral or bilateral. The substance is introduced into the trachea under local anaesthesia; the patient is tilted to the side required, and the chest x-rayed about ten minutes later. The two lungs are examined in this manner at seven days' interval.

Partial thoracoplasty, done either in the upper or lower part of the chest in combination with artificial pneumothorax or as a sole method, has proved unsatisfactory in the majority of cases, being too localized and preventing the full value of the rest factor.

The Operation of Thoracoplasty.

Apart from my first eight cases, which were done under local anaesthesia alone, all thoracoplasties have been done under the combination of gas and oxygen with local anaesthesia. The usual antishock treatment with glucose saline is undertaken for forty-eight hours. One hour before operation the patient is urged to empty the cavities of all secretions by coughing and changes of posture.

In my own series the two-stage operation has been done as a routine, owing to diminution in shock and to the lessened absorption of toxins into the circulation from the more gradual compression of the lung. The interval between the stages is as near as possible three weeks.

The operation itself is performed with the patient in the semi-sitting posture, the vertebral column being made convex towards the affected side by means of an axillary cushion. The incision commences from the level of the spine of the scapula and passes downwards in the space between the scapula and the vertebral column, turning outwards along the tenth rib, to the posterior axillary line. The muscles are divided in the same line, and the skin edges clipped off with towels. The ribs are exposed by raising the scapula, and each intercostal nerve from the eleventh to the fourth infiltrated with a few cubic centimetres of 1 per cent. novocain. The periosteum is rapidly stripped off each rib and the small back muscles off the posterior ends. The ribs from the eleventh to the fifth are then divided posteriorly as near the transverse processes as possible and anteriorly as far as is required for each individual rib. This is variable, but generally about $4\frac{1}{2}$ to 5 inches is removed from the fifth to the tenth and only a small portion of the eleventh. The wound is closed in layers with drainage for twenty-four to twenty-eight hours and firm strapping applied over the dressing to fix the involved hemithorax, but allowing the tube to be withdrawn without disturbing the main dressing. The main point in after-treatment is the insistence on the expectoration of sputum. Pain can be prevented by omnopon, and coughing assisted by firm hand pressure on the affected side during the effort. Sputum rapidly increases in quantity after the first three days, diminishing later. The temperature and pulse rates reach their maximum on the third day, owing probably to some retention of sputum and to increasing absorption into the circulation from the collapsing lung.

The second stage, comprising removal of portions of the first four ribs, is performed through an incision from the upper trapezius and following the inner border of the scapula to its inferior angle. The further steps are similar to the first operation, the first rib only offering difficulty. It is often advisable to complete the removal of the second rib before any attempt is made to expose the first. Only half an inch need be removed, but care must be taken not to damage the dome of the pleura, or the vascular and nervous structures in the near neighbourhood.

The after-treatment is similar to that of the first stage. A compression splint is worn, after the wound has healed,

for several months until the bone union is firm. Sanatorium treatment is advisable for several months after operation, especially for tuberculosis.

The complications are: death from shock; death from pulmonary embolus; aspiration pneumonia of the better lung, the most common complication leading to early death; infection in the wound arising from spread through the pleura; later deaths generally resulting from spread of the disease in the sound lung; one fatal case of haemorrhage has been recorded from erosion of the subclavian artery by the first rib (Brunner).

Alexander has collected all the results of thoracoplasties for tuberculosis published in the period 1918 to 1925. There were 1,159 operations, by fifty-three surgeons, and 57 per cent. of the patients showed improvement or were cured. All these were far advanced and were becoming worse in spite of sanatorium methods of treatment. So far I have done the operation of thoracoplasty on 33 patients. Of these, 33 per cent. have been apparently cured or greatly improved; 21 per cent. have improved; in 20 per cent. there has been slight or no change; 20 per cent. have died later from tuberculosis; and 6 per cent. have died within three weeks of the date of operation.

ILLUSTRATIVE CASES.

CASE I.—*Tuberculosis.*

A woman, aged 31, with a history of having had pleurisy in 1918 and again in 1921. Under Dr. Vere Pearson at Mundesley Sanatorium artificial pneumothorax was started on the right side and continued for eighteen months. It was abandoned owing to pain and contraction of the pneumothorax cavity. In June, 1924, she had haemoptysis with the return of tubercle bacilli in the sputum and evidence of slight activity of the left apex. The sputum amounted to 1 to 2 ounces daily. There were signs of activity and excavation in the right upper lobe with generalized signs over the middle and lower lobes. (Fig. 1.)

On September 3rd, 1924, under gas and oxygen and local anaesthesia, thoracoplasty (first stage) was performed. Portions of the fifth to the eleventh ribs (inclusive) were removed—total 38½ in. = 96.5 cm. There was only slight reaction to operation. On September 26th, under the same anaesthesia, the second stage of the operation was carried out, portions of the first to the fourth ribs being removed; these offered some difficulty owing to close approximation. Length removed at second stage 11½ in. = 29.5 cm.; total removed at both stages 50½ in. = 126 cm. There was no noteworthy post-operative reaction.

After-History.—The sputum rapidly disappeared and the temperature became normal. Within three weeks the sputum was free from tubercle bacilli. The patient has kept quite well during the last eighteen months and is apparently cured. Seen recently, there was no cough or sputum; the only complaint was that she was putting on too much weight. (Fig. 2.)

CASE II.—*Bronchiectasis.*

A woman, aged 33, was admitted to Brompton Hospital in December, 1923, for bronchopneumonia, which was followed by pulmonary abscess formation in the right lower lobe. This abscess burst into a localized area in the pleural cavity. The empyema and abscess were drained by me early in 1924, the narrow opening between being dilated. Healing occurred in spite of the presence of the bronchial fistula, and the patient left the hospital well in every way.

In August, 1925, she returned to hospital on account of cough, copious blood-stained sputum of offensive odour, and night sweats; the amount of sputum was 10 ounces daily. Tubercle bacilli were found on one occasion. Lipiodol, administered intratracheally, showed large cavities in the right lung; the left lung showed emphysema. (Fig. 3.)

Thoracoplasty (first stage) was performed on August 29th, portions of the fourth to the eleventh ribs being removed—25 inches in all. The patient's condition after the operation was especially good. The second stage of the operation was carried out on September 16th, when portions were removed from the first to the third ribs—8 inches in all; the total removed at the two stages was 33 inches. Except for a post-operative rise the sputum steadily diminished in quantity, and six weeks later, when she was transferred for convalescence, the sputum amounted to only 1 ounce. There was also a gain in weight at this stage of 3 lb. She has since gained a stone in weight and the sputum is less than 1 ounce daily, being mucoid in type. (Fig. 4.)

CASE III.—*Bronchiectasis.* (See Chart.)

A male, aged 20, was admitted to hospital with bronchiectasis. He had had pneumonia two and a half years previously. He was well until August, 1923, when he suffered from cough and expectoration. From June to October, 1924, he had right artificial pneumothorax treatment; this reduced the sputum from 10 to 12 down to 3 ounces daily. Later there was an increase to 8 ounces daily and pleural effusion developed. From October the sputum increased to 14 or 15 ounces daily.

The first stage of thoracoplasty was performed on January 28th, 1925, under gas and oxygen and local anaesthesia, a total amount of 25 inches being removed from the eleventh to the sixth ribs

inclusive. At the second stage, on February 18th, the first to the fifth ribs were partially resected, 14 inches being removed. The total resection amounted to 39 inches. By March 23rd the sputum was reduced to 6 ounces daily; the patient had gained 9½ lb. in hospital.

After-History.—Within four months of leaving hospital the sputum was nil. He is now doing a full day's work as chauffeur.

CASE III, bronchiectasis. Chart showing changes in sputum following the two stages of thoracoplasty, and the gradual disappearance of the sputum in the ensuing weeks.

SUMMARY.

1. Thoracoscopy and cauterization of adhesions is a valuable aid to artificial pneumothorax treatment, especially in cases where cavities are prevented from collapsing by adhesions of the band-like or string-like type, not thicker than 1 cm. The number of cases is comparatively small.
2. Pneumolysis can be used as an independent procedure or as supplementary to other operations; it is of no use in bronchiectasis, where basal collapse is required and there is no point of counter-pressure. It is most valuable for uncollapsed apical cavities following thoracoplasty for tuberculosis. Fat appears to be the ideal medium if enough can be obtained. As an independent procedure the results are not satisfactory as the collapse is too localized.
3. Phrenicotomy, or rather radical phrenicotomy, is of value, as an independent procedure, occasionally in the more acute forms of phthisis, where major operations are contraindicated, and in early and, on the worse side, in bilateral bronchiectasis. It is of value as a test of the activity of tuberculous disease in the so-called "better" lung previous to thoracoplasty. As a supplementary procedure it is useful in cases treated by artificial pneumothorax, either where diaphragmatic adhesions are present, or, by reducing the capacity of the hemithorax, it may prevent reopening of cavities when the lung is allowed to expand at the end of pneumothorax treatment. Supplementary to thoracoplasty, it is of much value where the compression of the major operation is found to be insufficient. Haemoptysis from basal cavities can sometimes be controlled by this operation.
4. Thoracoplasty offers considerable hope of amelioration or actual cure in chiefly unilateral tuberculous disease of the lung, where artificial pneumothorax treatment is impossible or unsatisfactory, and where the disease is progressing in spite of careful medical treatment. It is of use also in cases of tuberculous empyema without secondary infection. In the septic tuberculous empyemata the results are not good, but the disease is otherwise almost invariably fatal. Considerable improvement, amounting to cure in some cases, can be obtained by thoracoplasty in unilateral bronchiectasis, but this operation will not collapse the larger bronchi near the hilum, and in some cases a non-odorous mucoid sputum remains after the operation.
5. Pneumotomy should be reserved for localized tuberculous abscesses which are not draining well through the bronchus, and in cases in which the generalized tuberculous process appears to be inactive. In bronchiectasis it should only be used in those cases of large localized abscess formation, and not in the diffuse variety.
6. Bronchostomy is occasionally of great value following drainage of large abscesses; a partial plastic operation on the chest wall should be performed subsequently.

7. Pneumectomy appears to be almost totally contra-indicated in phthisis. In bronchiectasis, although apparently the ideal procedure, it is followed at present by an almost prohibitive mortality (50 per cent.). Further improvements in the technique may eventually make it the operation of choice. The more recent cautery pneumectomy, as practised by Graham in America, has been followed by a much lower mortality than any other lobectomy operation, and offers reasonable hope of eradication of the septic lobe.

My thanks are due to my medical colleagues of the staff of the Brompton Hospital for the opportunities afforded me in this work, and to Dr. Stanley Melville for the very excellent skiagrams, a few only of which are reproduced here.

THE MACROPOLYCYTE.

(With Special Plate.)

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DEFINITION.

THE diameter of a normal polymorph in stained films is from 10 to 12 microns. The term "giant" polymorph or macropolycyte—a name suggested by Sir Humphry Rolleston—may be applied to those polymorphs having a diameter of more than 14 microns. Fig. 1 represents a normal polymorph with five nuclear segments. This has a diameter of 11.5 μ .

ETIOLOGY.

The macropolycyte is found in two widely different conditions—such opposite conditions, in fact, as to make one doubt whether the causation can be the same in the two cases.

The first is in the acute pyogenic infections. Fig. 2 illustrates a macropolycyte from a case of staphylococcal osteomyelitis showing the following blood picture:

Total leucocytes	...	...	18,000	per c.mm.
Polymorphs	...	...	84	per cent.
Lymphocytes	...	...	12	"
Large mononuclears	...	...	3.5	"
Myelocytes	...	...	0.5	"

Polynuclear count:

I.	II.	III.	IV.	V.
41	43	15	1	0 per cent.

Fig. 3 illustrates a "giant" in a case of streptococcal septicaemia.

Total leucocytes	...	...	26,000	per c.mm.
Polymorphs	...	...	79	per cent.
Lymphocytes	...	...	13	"
Large mononuclears...	...	...	7.5	"
Myelocytes	...	...	0.5	"

Polynuclear count:

I.	II.	III.	IV.	V.
34	43	21	2	0 per cent.

The staining reactions of the nucleus and cytoplasm are identical with those of other polymorphs in the films. They are rare—encountered perhaps twice or three times a year by anyone constantly examining blood films—and seem always to be associated with a polymorphic leucocytosis and the presence of myelocytes in the peripheral blood. They are, I think, "sports."

The other condition in which macropolycytes occur is pernicious anaemia, and in this disease they are frequently seen. They measure 16 to 21 microns in diameter and are of two distinct types. The first type of macropolycyte is similar in nuclear structure and cytoplasm to the other polymorphs, but the cell is larger, and the nucleus is frequently hypersegmented, as shown in Fig. 4, which illustrates this type. In the second pernicious anaemia type the total bulk of the nucleus is great, absolutely and relatively to the amount of cytoplasm. The nucleus may be of the band form, or have one, two, or as many as fourteen divisions. The basi-chromatin is not so densely massed as in the normal cell, and the cytoplasm contains larger granules, which are neutrophile in reaction. Figs. 5, 6, and 7 illustrate this type. These cells look very like megakaryocytes.

The etiology of the macropolycyte in pernicious anaemia is probably that of the disease itself. The polymorph, even in the absence of the "giant," behaves in a curious manner.¹

The normal polynuclear count may be taken to lie between the following values:

	I.	II.	III.	IV.	V.
(1) ² :	11	25	47	15	2 per cent.
or (2) ³ :	5	35	41	17	2 per cent.

which give readings of 36 and 40 in the left-hand columns and 64 and 60 in the right.

In infections the count moves to the left, as in the cases of osteomyelitis and septicaemia quoted above:

I.	II.	III.	IV.	V.
41	43	15	1	0 per cent.
34	43	21	2	0 "

In pernicious anaemia frequently, possibly in all uncomplicated cases at some period of the disease, the polynuclear count shows an increase of the cells of Classes 4 and 5, as in the following examples:

	I.	II.	III.	IV.	V.
Case 1 ...	8	20	39	22	11 per cent.
Case 2 ...	6	27	40	22	5 "
Case 3 ...	7	20	44	24	5 "
Case 4 ...	7	16	29	39	9 "
Case 5 ...	12	34	26	20	8 "
Case 6 ...	10	15	38	24	13 "
Average...	8	22	36	25	9 "

The left-hand columns give an average of 30 and the right 70. The count is actually right-handed. As far as my experience goes, this does not occur in any other disease.

We have, then, at the outset in pernicious anaemia some factor producing a dysleucopoiesis, and accentuation of this may lead to the production of the macropolycyte.

Some recent papers on the transformation of monocytes in frog's blood, and cells of lymph nodes, into giant cells are suggestive. M. R. Lewis⁴ states that giant cells are formed from monocytes in hanging drop preparations of frog's blood. E. Barta,⁵ working on tissue cultures of lymph nodes, finds that giant-cell formation takes place at some distance from the surface, and ascribes this to deficiency of oxygen. The addition of embryonic extracts greatly diminishes the effects of oxygen want, and cells in the deeper layers then behave like those with a sufficient oxygen supply. There are many more factors in experimental conditions than simple oxygen want. Alteration in pH, gaseous diffusion, surface tension, saline ratios, and lipid changes must take place and also influence cell metabolism.

Anoxaemia is not the only state responsible for the production of macropolycytes in pernicious anaemia, but whatever the primary general state in this disease is, the marrow seems to take control in the later stages. In addition to the behaviour of the polynuclear count, and the presence of macropolycytes and ichthyoid cells, there is direct proof of this local influence. Walterhöfer and Schramm⁶ have scraped and irrigated the medullary cavities of long bones in cases of pernicious anaemia that were apparently moribund. The alteration of the local chemical state effected produced surprisingly good results. That the results may be only temporary does not affect the argument.

These considerations lead to the conclusion that the macropolycytes and pernicious anaemia may be due, either to a primary defect in the chemical composition of the blood, the marrow changes completing the vicious circle, or to a congenital or an acquired condition of the haemocyto-blast itself leading to defective haemopoiesis and local biochemical abnormalities, with, later, general effects.

PROGNOSTIC IMPORT.

The first type of macropolycyte, that found in pyogenic infections in association with myelocytes, is, I think, an "accident" and has no prognostic value, except, perhaps, as signs of marrow "stress." Of the second type, the first subdivision, an exaggerated form of the polymorph frequently found in pernicious anaemia, is present at the crises of the disease, and is an index, I think, of local urgency in the haemopoietic tissues, which may or may