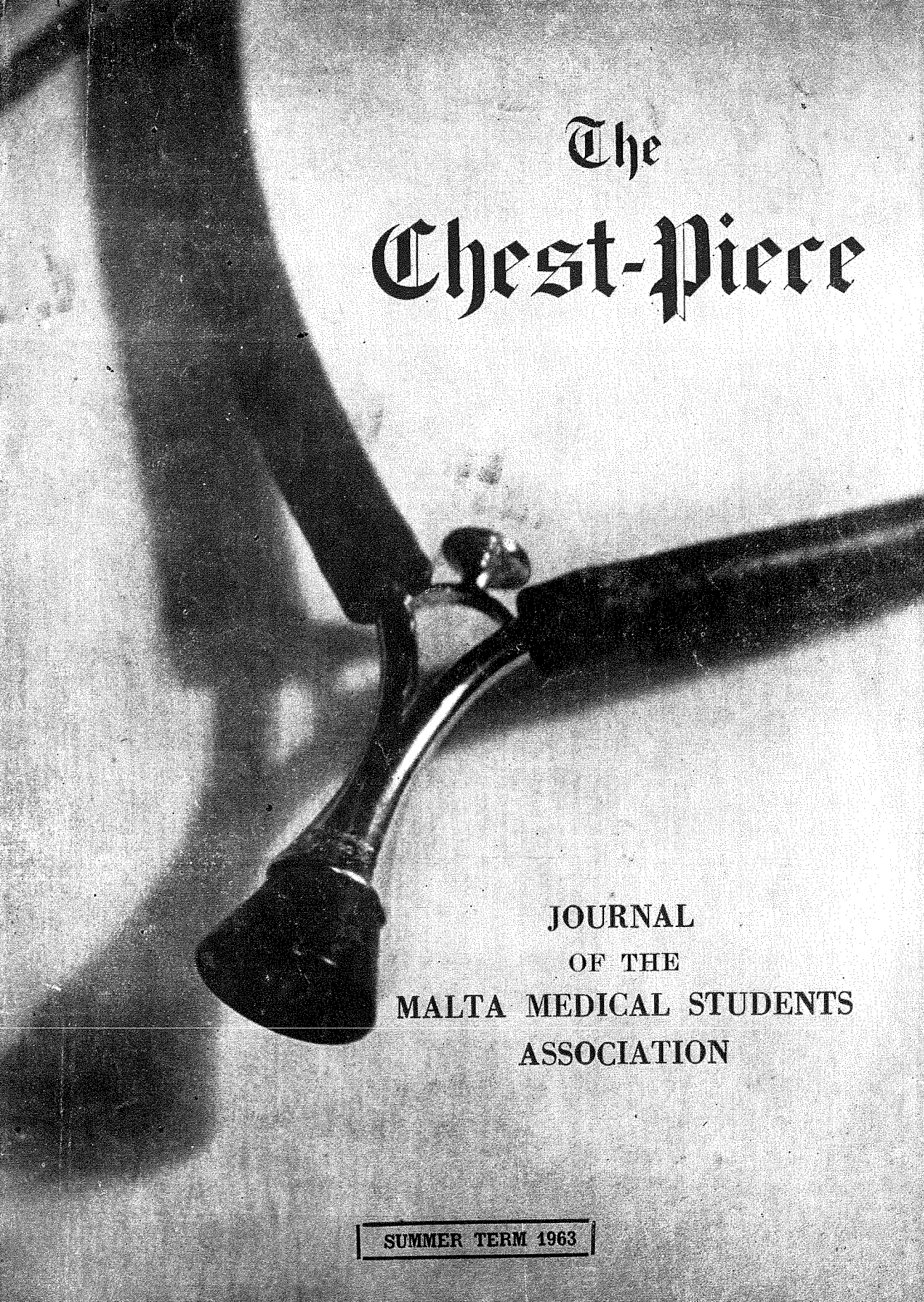

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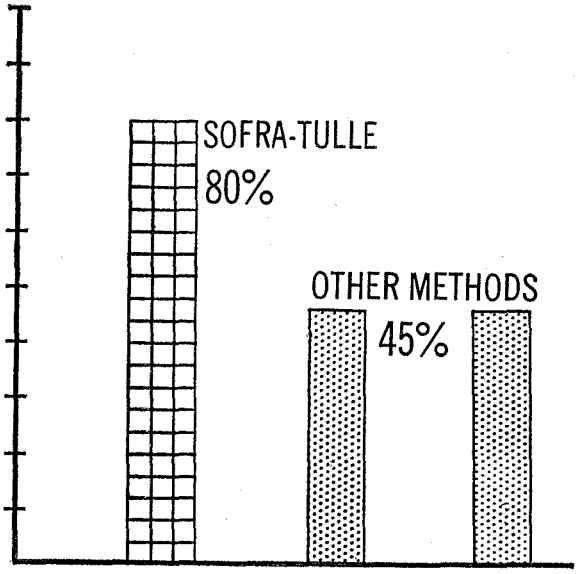

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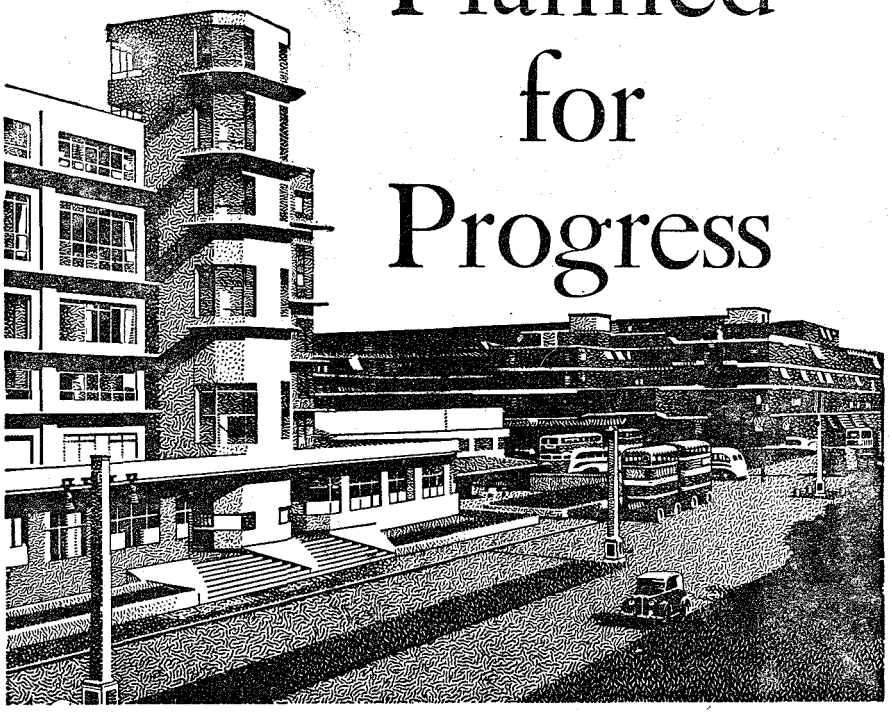

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The Chest-Piece

CONTENTS

EDITORIAL

Since the last publication of the CHESTPIECE in Summer 1959, there have been quite a few developments in the Faculty of Medicine and Surgery.

First of all we are now in a position to follow the developments in the system of the "Tests" which our predessors had, not without some good reason, opposed so rigorously. Contrary to what most optimistic people had hoped, some examiners missed completely the whole idea of a Test, and the number of failures, especially in one or two subjects, was astounding.

It was found out that the student was, out of fear of the Tests, stressing too much on the theoretical side while ignoring the wards altogether. The end result was going to be a batch of doctors full of volumes and volumes of material somehow stuffed in their minds, but with no idea as to how to face a commonplace case. The University Authorities, bitterly noticed their mistake, and so much so that earlier last year they revolutionised the system of the Tests.

First of all the final word in any Test was reserved to a Faculty Board, which besides the actual number of marks obtained by the student in any given subject, takes into consideration the results in the other subjects and above all, the attendance and diligence at practical work. To provide proper records of attendance, a system of signing after a practical demonstration was set up and this, although it makes it all look like a primary school, is to the student's advantage.

Moreover another step was taken, namely that there would only be two sessions — June and September. This at first was looked upon rather suspiciously by the students but once it was realised that the final word depended on a general assessment of the student's work during the past year, was accepted as being fair. In fact all the students in the Final course of Medicine and Surgery had passed their Tests by September last year — a very favourable contrast with the situation three years previously.

The present situation is therefore acceptable to both students and the University authorities and this was one of the main causes of the boosting up of morale in both teachers and students in the Faculty of Medicine this year. We sincerely hope that the present state of affairs will not be rudely shaken by any successor of the present authorities.

EXTERNAL EXAMINERS

In order to get assurance of recognition of the Maltese degree in the Commonwealth, the authorities have agreed that an examiner from the Commonwealth sent by the Inter-University Council would assess the general standard of knowledge in the various subjects. The first external examiner to be here in Malta under this scheme was Sir Stanley Alstead who said he was satisfied by the good standard reached by the majority of students in Therapeutics and Materia Medica.

CLERKSHIPS

Last year we have accepted fourteen foreign students as clerks in the summer months. Most of them came from Germany but we also had others from England, Italy, Canada and Austria. Unfortunately only three Maltese students went abroad on clerkships last summer — two to Berlin and one to Vienna. I take the opportunity to encourage the pre-clinical students to avail themselves of clerkships organized for them in some countries. For any information they should contact the local Exchange Officer Mr. George W. Vella, who will be very glad to help them.

I conclude by thanking the various agents who have published advertisements in this journal and without whose co-operation and public spirit we would not have been able to achieve our aim.

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DIABETES MELLITUS IN THE MALTESE ISLANDS

By WALTER GANADO B.Sc., M.D , B.Sc., (Lond), M.R.C.P. (Lond).
Departments of Medicine and of Physiology, Royal Univiersity of Malta

Is Diabetes Mellitus commoner in the Maltese Islands than elsewhere? If it is more common, why is it so common?

These questions call for an early answer because Diabetes Mellitus appears to be increasing in the Maltese Islands. This increase however does not appear to affect the young. Diabetes in the young does not appear to be more common in the Maltese Islands than elsewhere. During the period 1948-61 the writer met only eight diabetics between the age 8 and 20 years, but the number of diabetics at the age of 40 years and over have been a legion. The increase of Diabetes Mellitus in the Maltese Islands appears to be related to increase of the number of old persons. This has been brought about partly by the emigration drive affecting predominantly the young, and mainly by increased longevity. Crude death rate has in fact fallen from 12.2% in 1948 to 8.7% in 1961, and expectation of life at age one year which in 1948 was 64.8 years for males and 66.9 years for females has risen in 1961 to 68.4 years for males and 72.1 years for females. Hence the number of persons aged 40 years and over, which in 1948 stood at 89,262 and formed 28.5% of the total population, rose in 1961 to 96,691 forming 29.4% of the population; and the number of persons aged 60 years and over which in 1948 stood at 28,125 and formed 9.2% of the population, rose in 1961 to 35,515, forming 10.8% of the population (1). A small survey carried out in 1961 at an old age home in Malta showed that 16 out of 93 patients had glycosuria (2). The age distribution of these glycosurics was as follows:

60 - 64 years	4
65 - 69 years	5
70 - 74 years	5
75 - 79 years	2

Indeed, Diabetes Mellitus forms with Senility the major medico-social problem with which the Maltese Islands are faced at present.

Diabetes Mellitus is linked with senility not only because the incidence of Diabetes rises rapidly with advancing old age, but also because Diabetes accelebrates and aggravates the troubles of old age. Such complications as gangrene, heart attacks, kidney troubles, tuberculosis, other infections, paralysis and blindness are in fact much more common in diabetic than in non-diabetic patients of corresponding age. Thus a survey of blindness carried out in 1958 (3) has shown that of 638 blind persons, 92 persons or 15.9% of the blind had lost their eyesight because of Diabetes Mellitus. This percentage compares very unfavourably with the corresponding percentage of the United Kingdom. Whereas in the United Kingdom the percentage of total blindness is roughly equal to the percentage of total blindness in the Maltese Islands, the number of persons that are blind because of Diabetes Mellitus constitute in the United Kingdom only 6.9% of the total blind, when this percentage is 15.9% in the Maltese Islands. Of the 92 cases that were found blind because of

diabetes in the Maltese Islands 23 were males and 69 females.

A survey to assess the incidence of Diabetes Mellitus in the Maltese Islands and to establish its relationship to age, sex, occupation, genetics, fertility and diet, is very much indicated. This survey should not present great difficulties. The population is cooperative; Malta is just less than a hundred square miles and all its parts are accessible. Results should throw light also on theoretical aspects. This is a closed community numbering 328,854 persons in 1961 situated in the Central Mediterranean and consuming abundance of carbohydrate foods and fats. Is the Maltese diet related to the incidence of Diabetes?

Once that the incidence of Diabetes is firmly established for the total population, comparison with the incidence in special groups of this population may be indicated. A case in point would be to study the incidence of Diabetes in religious persons living in community. These are hundreds of these single persons of either sex in the Maltese Islands, consuming meals in common. This food consumption can be accurately estimated.

Is the incidence of Diabetes mellitus higher among descendants of first cousins who marry in the Maltese Islands than in the total population? The Maltese do not marry outside the Cathlic Church and this allows marriage between cousins only by dispensation. Hence a list of marriages between first cousins is available. It should be possible to trace down a large number of descendants from first cousins to compare the incidence of Diabetes mellitus of this group with the incidence in the total population.

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1. Data kindly supplied by Central Office of Statistics, Malta.
2. Survey on Old Age People in Malta by St. Anne Welfare Committee for the Old, Malta, 1961.
3. Dr. F. Damato, Br. J. Ophth., 1960, 44,164.

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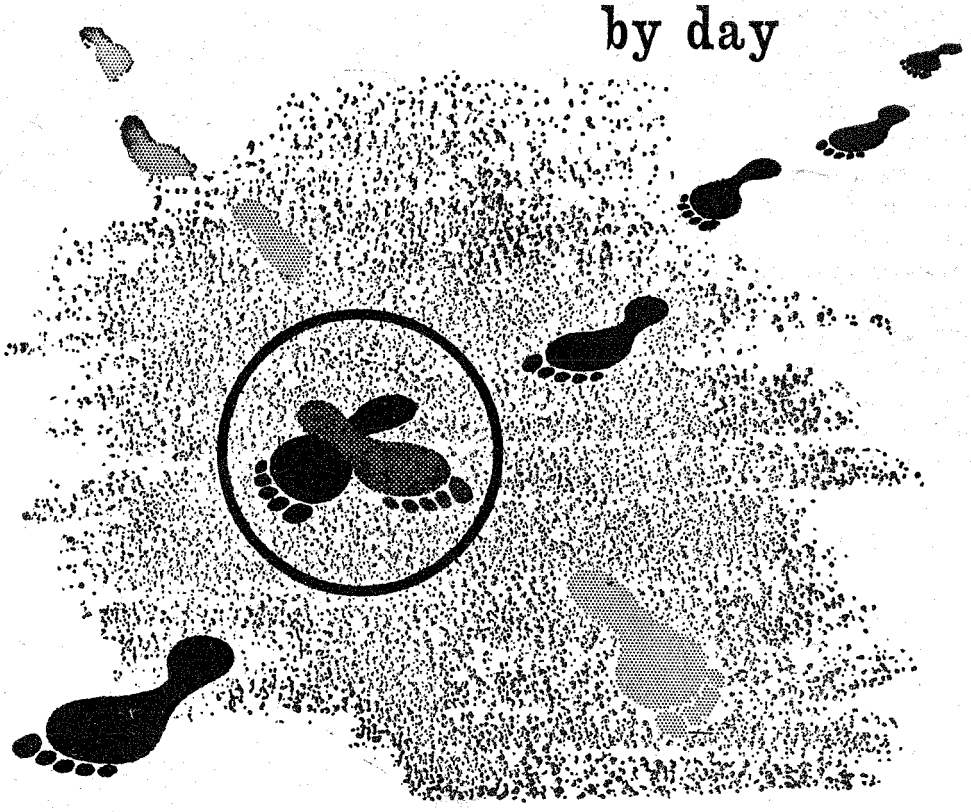

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DWARFISM

R.J. CAMPBELL, M.B, Ch.D.(L'Pool)

Department of Pathology, Royal University of Malta

While there can be no scientific explanation for either Gulliver's Lilliputians or for the "Little folk" so beloved by our Irish friends, the following is a brief account of the causes of stunted growth. As the subject is so extensive the account itself must be "dwarfed".

Dwarfism is defined as a stunting of skeletal growth and as such does not include failure of sexual development which is termed infantilism. However in clinical practice it is unusual to have to distinguish between the two as they frequently occur together.

One should have no difficulty in recognising the obvious dwarf such as an achondroplastic or a cretin but as the majority present as a borderline failure to grow, it is important to be aware of the less obvious causes.

The diagnosis must be made without undue delay so that any treatment needed can be started before the epiphyses close, after which no further gain in height is possible.

The commonest causes for being below average size are racial and constitutional, thus the Mongol races tend to be smaller than the Caucasoids and small parents tend to have small offspring.

Any chronic illness in infancy and childhood will stunt growth and if the condition lasts up to the time of epiphyseal closure a small adult will result. Illnesses often responsible are bronchietasis, megacolon, bony tuberculosis, polycystic kidneys and mucoviscidosis. Congenital heart disease has a rather special place in that, tissue hypoxia leads to impaired growth. Malnutrition, while uncommon in civilised countries, is still a major problem for many of the world's population and is responsible for many stunted children. Lack of sufficient food, chronic infection and parasitism often work hand in hand. Kala azar, malaria, intestinal worms together with deficiency states such as kwashiokor are all responsible for stunted growth.

Specific causes for dwarfism may be loosely classified under endocrine; metabolic, bone diseases and hereditary conditions.

ENDOCRINE CONDITIONS

The Lorain-Levi or "Peter Pan" type of dwarf is probably due to a pre-pubertal shortage of anterior pituitary growth. They are normally proportioned but rarely over 48 inches tall. They are usually of a bright mentality but exhibit infantilism. There is no apparent shortage of corticotrophin or thyrotrophic hormone.

The cause of the pituitary failure is not often clear but some cases are due to non-functioning pituitary growths and others to supra-sellar tumours.

Cretinism and juvenile myxoedema produce persons of short stature who show in addition the other features of hypo-thyroidism — coarse skin, low mentality, generalised slowing of body activities and constipation. Cretins also have a large tongue, retroussé nose with sunken bridge and trident shaped heads. Unlike the other endocrine type of dwarfism cretinism is cureable provided and only provided the diagnosis is made within a few months of birth. There is no place for hormone treatment in older cretins as they are not improved men-

tally or physically and are often made more difficult to manage.

Stunting or early arrest of growth may occur in children showing precocious sexual development either due to adrenal cortical hyperplasia or suprarenal tumour or due to a virilising granulosa cell tumour of the ovary. The short stature is due to premature closure of the epiphyseal plates. Removal of the adrenal or ovarian tumour or supression of the hyperplastic adrenal cortex with cortisione *may,* if performed early enough, result in normal growth.

Frohlich's syndrome, which appears to be due to decreased production of gonadotrophins by a pituitary which is directly affected by a hypothalamic disorder, produces children showing sexual infantilism and marked mental torpor. There is a feminine distribution of fat and atrophy of the skin and hair. This syndrome may be caused by a craniopharyngioma or by a chromophobe adenoma of the pituitary but in most cases the cause is not found. True Frohlich's syndrome is a rarity but the name is erroneously applied to many obese children who are simply slow to develop sexually.

A variation of this last syndrome is the extremely rare condition described by Laurence, Moon and Biedl which in addition to the features of Frohlich's shows polydactly, retinitis pigmentosa and marked mental deficiency. This condition has a marked familial tendency.

Progeria, another condition of extreme rarity and unknown aetiology, is believed to be due to pituitary dysfunction. These patients show grotesque wrinkling and ageing of the skin in addition to the infantile and stunted appearance.

METABOLIC CONDITIONS

Rickets due to a shortage of dietary calcium and vitamin D is uncommon now but was a potent cause of dwarfism. Children seen now with the features of rickets are usually suffering from one of the secondary forms.

Renal rickets, which is better called renal osteodystrophy is really a conglomerate collection of renal diseases which cause alterations in calcium and phosporus metabolism. Almost any renal disease can cause sufficient damage to drastically alter the metabolism of these elements in a growing child. Blockage anywhere in the lower urinary tract such as neuromuscular dysfunction of the bladder neck which may lead to bilateral hydronephrosis; chronic pyelonephritis and nephrocalcinosis may all be responsible. Glomerular rickets occurs when the glomerular damage is sufficient to impair the excretion of phosphorus. Damage to the tubules or congenital defects of tubular function leads to a variety of conditions, the best known being Fanconi's syndrome in which there is an inability to reabsorb phosphorus. This leads to a low serum phosphorus and the excretion of calcium via the gut. The net result is a shortage of both elements for bone production. Other varieties consist of an inability to reabsorb either glucose or aminoacids or bicarbonate ions so that in addition to the bony abnormalities the patient may show glycosuria, aminoaciduria or a metabolic acidosis or all these. A combination of glomerular and tubular deficiency is present in Butler—Albright's syndrome which consists of dwarfing due to "renal rickets", hypochloraemic acidosis, precocious sexual development and a patchy pigmentation of the skin.

Conditions in which there is intestinal malabsorption, especially coeliac disease may give rise to secondary renal rickets as well as stunting growth directly.

A rare metabolic disease which causes dwarfism is the glycogen storage dis-

order of Von Gierke. Children suffering from any of the lipoid storage diseases are small but the other features such as mental deficiency, splenomegally and anaemia are of greater importance.

HEREDITARY AND CONGENITAL CONDITIONS

Mucoviscidosis or cystic fibrosis of the pancreas as it was called leads to a small stature as well as an increased liability to infection and to malabsorption.

A group of conditins arousing particular interest at present are those in which chromosomal abnormalities can be demonstrated. Mongolism or as it is better called Down's syndrome, is one such disorder and it has now been confirmed that these children have an extra chromosome. Cells from a normal human have 46 chromosomes arranged in pairs and each can now be recognised by special microscopic techniques but cells taken from hundreds of cases of Down's syndrome have been shown to contain an extra chromosome either as a separate unit or attached to a normal chromosome. There is reported a mongol child without an additional chromosome but the significance of this is not yet known. Despite this exception analysis of the chromosome number is likely to be a useful diagnostic tool in the future. Using similar methods the sex chromosomes can be identified and it is now possible to correlate the anomalous chromatin found in some patients with aberrations of their sex chromosomes. Turner's syndrome in which the person is stunted and shows webbing of the neck and is physically female can be shown to have the nuclear sexing of a male, that is XY.

BONE CONDITIONS

Achondroplasia is the commonest bone disease responsible for dwarfism and is incidentally responsible for the majority of dwarfs. The condition is strongly familial and primarily affects bone ossified in cartilage. The long bones fail to increase in length and the basal skull bones do not grow normally. The epiphyses are enlarged and the diaphyses abnormally short giving the unfortunate sufferer the characteristic short arms and legs with a normal trunk. Achondroplastics are of normal intelligence, are often genial and of normal fertility.

Fragilitas ossium is a condition of abnormal ossification, the child often showing multiple fractures at birth. The stunting of growth is mainly due to multiple fractures and telescoping of the long bones. These children often show blue sclerotics and their parents may have otosclerosis.

Two other osteodystrophies are also uncommonly responsible for dwarfism -- diaphysial aclasia and Morquio's disease, both are exceedingly rare and are diagnosed by their radiological appearance.

To complete the list of causes mention may be made of lipochondrodystrophy or Hunter's syndrome, more commonly called Gargoylism due to the characteristic ugly appearance of these children.

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DIAGNOSTIC CYTOLOGY OF EFFUSION FLUIDS

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Cytological diagnosis is the science dealing with the examination of cells from the human body and their interpretation for diagnostic purposes. The cells may have been spontaneously exfoliated or removed by artificial means. The subject has assumed great importance in the last few decades, and the possibilities of this field of pathology seem to be by no means exhausted. The concept has been greatly influenced by the well known work of Papanicolaou on the cytological aspects of cancer in the female genital tract. Papanicolaou's methods in fact have proved instrumental in giving cytology the definite status of an approved laboratory procedure. Cytology has in fact ceased to be an adjunct to other methods of diagnosis, but has become a primary and important source of information in many fields of medicine. The competent cytologist should not only be able to suggest, but should be prepared to establish a diagnosis on the evidence at his disposal in much the same way as the morbid anatomist does on biological evidence.

This note is concerned with the cytological diagnosis of effusion fluids, i.e. "puncture fluids" from pleural, peritoneal, and pericardial body cavities. The anatomical and physiological properties of these are largely identical, with their parietal and visceral layers forming a virtual sack around the respective enclosed viscera, and containing a small quantity of fluid to lubricate the movements of the enclosed organs. Histologically, also, they are all lined by a single layer of flat cells, the mesothelium, supported by connective tissue and provided with appropriate vascular and nervous apparata.

History. Cytological examination of fluids is not in itself a novel procedure. Reports, however sporadic, appear in the literature of the late nineteenth century. These were mainly concerned with the search for malignant cells. Even cytodiagnosis as we understand it here, not limited, namely, to the investigation regarding possible malignancy, dates from the first decade of the present century. Its introduction appears to be due to Widal who in 1900, classified the differential cell-pictures of fluids into various diagnostic categories. Numerous workers in different countries followed suite, with resulting rapidly increasing numbers of publications on the subject. Lack of completely satisfactory results and the continuous search for suitable techniques of preparation and staining methods are apparent from these reports; a state of things which resulted in the introduction of the "cell-block" technique. This consists, of course, in making sections, after fixing, of the centrifuged deposit of the fluid. But again the results, if they could satisfy the histopathologist, were not what the cytologist was after. The former bases his diagnosis on cell-aggregates, the cytologist on cell-appearances. The two fields, though analogous, are not identical. The method, however, gained ground and became the standard one especially in America, until it was challenged by Papanicolaou's method. The latter has finally provided the cytologist not simply with the choice method but with the standard one. The next evolu-

tionary step, was the application of the Romanowski stains to specially prepared films from effusion fluids. The secret of the method lies in the latter technique: very thin films, that dry up almost immediately on spreading, are required (Spriggs, 1957). The method is the one we have been using for some years, with very satisfactory results.

The cells of Effusions

Under normal conditions the potential body cavities described contain a very small amount of lubricating fluid, so small that it cannot be tapped. Allegedly successful experimental tappings were reported as yielding a fluid of very low protein concentration and containing a few cells mainly monocytes, together with a few mesothelials and lymphocytes, in the region of 1500-2000 per c.mm. An amount of fluid that can be aspirated with more or less ease is in itself indicative of a pathological process, which is readily reflected in the altered cytology of the fluid. The presence of the effusion is in fact attended by the following changes.

(a) The mesothelial lining of the serous layers, now mechanically separated by the effused fluid, undergoes a slight hypertrophy, the mesothelial cells becoming rounded or cuboidal in shape and are ultimately shed into the fluid to be replaced by younger ones. This is what happens in the presence of uncomplicated transudates, the mechanically produced effusions accompanying the accumulation of fluid in the rest of the body tissues. (in cardiac, or, more often in cardio-renal disease; in liver cirrhosis; in hypoproteinaemia etc).

(b) The presence of an inflammatory process of any nature, whether primary or supervening on a transudate, brings about a greater disturbance of the mesothelial lining, which becomes greatly thickened and several layers deep. Desquamation of the cuboidal mesothelial cells and their multiplication in the effused fluid goes on and is more pronounced; but the picture here is changed through the presence of the cells characteristic of the underlying inflammatory condition. Unlike transudates, this is an active, *exudative* process, probably associated with damaged capillary endothelium. *All the circulating blood cells,* apart from accidental contamination, may be present in an exudate, including the erythrocytes themselves, which, there is reason to believe, are produced locally. It may here be noted that pure, uncomplicated transudates are rare, and when confronted with the least complicated cytological picture we are always dealing with an exudate of some sort.

(c) If, as a result of the inflammatory process the free mesothelial surfaces become covered with fibrinous exudate (purulent pleurisy, tuberculous pleurisy, fibrocaseous tuberculosis), the mesothelial cells can no longer be shed, and they are consequently absent from the fluid. This may prove an important differential diagnostic point.

Cell pictures and their interpretation

From what has been said above, it is clear that the *cytological set up* of an effusion fluid may be quite a complex affair; and elsewhere we have said that the cytologist bases his diagnosis on *individual cell appearances.* This latter statement may sound ill-equipment on the part of the cytologist when dealing with complex pictures. It is true that in some cases, notably in malignant effusions, that all important concern of the cytologist is the detection of a particular cell, in that case the malignant cell. But it is equally true that the task of the cytologist is not merely that of accurately naming each one of the cells in the material under examination, however exacting that task may some-

times prove to be. His familiarity with cell morphology and its variations must go hand in hand with that of the significance of cell groupings and their incidence, their mutual association or exclusion. In other words he must be familiar with *differential cell-picture and their significance.* For this reason a classification of the cytological findings in effusion fluids based on cell-pictures is more profitable than one based on underlying pathological states. We shall therefore consider the interpretation of the more common and significant conditions under the following headings:—

Mesothelial predominance.
Lymphocytic predominance.
Predominant neutrophil polymorphs.
Pleomorphic cell-picture.
Easinophilic pictures.
Presence of L.E. Cells.

Mesothelial predominance

This is characteristic of simple, uncomplicated transudates, especially of the pleural cavities. These fluids usually contain very few cells, often requiring the centrifuging of considerable quantities of material to bring them out. Large numbers of mesothelials probably never occur is uncomplicated transudates. When they are present one is likely to be dealing with an exudate.

Lymphocytic predominance

Lymphocytes are present in varying numbers in most effusions, including *transudates,* where they accompany, and in exceptional cases may outnumber, the mesothelials. They are found in all *serous* effusions. In some conditions to be mentioned presently they may predominate even to the exclusion of all other cells. We often refer to the picture in these cases as a "purely lymphocytic fluid". Predominantly lymphocytic pictures are seen in:—

(a) *Tuberculous effusions.* both the primary and the condition secondary to fibro-caseous tuberculosis of the lung (They are absent in empyema and in pneumothorax effusions, which are characterised by pus cells and eosinophils respectively). A varying percentage of neutrophils may be present in addition during the first few, say ten, days after the onset.

(b) *Some post-pneumonic effusions,* which are also purely lymphocytic, mesothelial-free fluids. Obviously the case history and the M. tuberculosis-negative culture are necessary for distinguishing such cases from specific pleurisy.

(c) *Pulmonary infarction,* probably more common than suspected, and possibly accounting for many of the pleural effusions occuring in *congestive heart failure* which yield an identical picture (closely resembling the post-pneumonic effusion, but for the presence of mesothelials, which, especially in pulmonary infarction may be rather numerous).

(d) *Carcinoma of the lung,* which, however, should never be invoked as the cause unless malignant cells are clearly present;

(e) Effusions complicating *lymphatic leukaemia* and the reticuloses.

Predominant neutrophil polymorphs

This picture is characteristic of the *purulent type exudate* of acute inflammation of the serous membranes with a positive culture of pyogenic organisms (a few lymphocytes and macrophages may also be present at the onset). Some of the neutrophils may show the phagocytosed responsible microorganisms which it is their purpose to eliminate (cultures soon become negative under favourable conditions). They ultimately assume the characters of *pus cell,* becoming fragile, easily smudged during film preparation, their number of scavenging macrophages results in the appearance of a *staining background*

of cellular debris: a distinguishing feature of purulent exudate. The significance of the presence or absence of mesothelials in these exudates must be mentioned once more. In the presence of the blocking fibrinous exudate in purulent pleurisy, exfoliation of mesothelials does not take place, and consequently they are absent from the fluid. Their presence in decidedly purulent exudate consequently indicates a very recent onset of the process. It is also noteworthy that at this stage the condition is still reversible, with the possibility of the purulent being turned into a serous effusion by antibiotic treatment. Otherwise the fluid remains purulent up to the complete absorption. Conversely the presence of mesothelial in doubtful *long-standing* cases will give up the fluid as non-purulent in nature.

Pleomorphic cell-pictures

These are given by the *non-purulent* type, culturally sterile exudates of acute inflammation (cf. preceding paragraph), with the presence of neutrophils, lymphocytes, macrophages, mesothelials, eosinophils and basophils, roughly in that order of frequency. They are met with chiefly in *penumonia, influenza, pulmonary collapse*. The neutrophils are here well preserved; they are not "pus cells". There is no staining background debris. The macrophages assume various, sometimes arresting shapes, mainly an expression of their accentuated phagocytic activity. The lymphocytes may be very numerous, especially in post-pneumonic cases, making the distinction from tuberculous pleurisy important (see above).

Eosinophilic pictures

In spite of the existance of an extensive literature on *pleural* and *peritoneal eosinophilia,* not much is definitely known about the condition. There is not even unanimity about what percentage constitutes eosinophilia. We shall take it to mean over 20 per cent of all the cells present. In the pleura, the condition most commonly associated with eosinophilia is *pneumothorax,* either artificial or spontaneous, whenever it is complicated by an effusion. A noteworthy exception are those cases in which the complication takes the form of a true tuberculous pleurisy, which (together with tuberculous effusion in general) is eosinophil-free. It follows that an eosinophilic effusion complicating pneumothorax is a good prognostic sign as far as the nature of the effusion goes. Large numbers of eosinophils impart a marked turbidity to a fluid.

Pleural eosinophilia is also frequently seen in *post-pneumonic* and infarct pleurisy.

There is much uncertainty regarding peritoneal eosinophilia.

Presence of L.E. Cells

Lupus erythematosus may present with a pleural effusion, in which case L.E. cells are found. There are not many cases described. We have seen an interesting case of an old woman with a long standing pleural effusion. All investigations to establish the cause proved repeatedly negative, until we detected typical L.E. cells. The accompanying picture was a highly cellular one with numerous lymphocytes, mesothelials, plasma cells, neutrophils and eosinophils. Unfortunately, no "post-mortem" could be made.

Malignant effusions

Nothing else need be stated about this type of effusion, besides the fact that they are characterised by the all-important presence of malignant cells. The detection of the latter is here the chief task of the cytologist. Malignant effusions present themselves with other characteristics, e.g. they are in general haemorrhagic (probably due to erosion

of the mesothelial blood vessels) and very often contain large numbers of lymphocytes. But, it is to be repeated, the only criterion for labeling an effusion as malignant is the presence of undoubtedly malignant cells. No report of malignancy should be given on a fluid with characters suggestive of malignancy, if there is the slightest possibility that the condition may be other than malignant. It is here that the cyologist, if called to make a diagnosis, should have at hand all the clinical particulars of the case in order to enable him to weight his expressed opinion against all the available evidence. The criteria of cell-malignancy can be definied and tabulated; but in actual practice it is often a question of "feeling". Abnormal mesothelial cells and macrophages may mimic malignant cells in appearance, giving rise to much difficulty of diagnosis even to the most experienced.

Malignant effusions are given only by secondary (metastatic) pleural tumours. Benign and primary ones never give rise to effusion, if not very exceptionally and indirectly (mechanically).

Conclusion

Cytodiagnosis is now recognised as an approved, well established laboratory method, rapidly growing into a separate branch of clinical pathology, analogous to that of morbid anatomy. Cytodiagnosis of effusion fluids, the subject of this annotation, is an important part of this science. By a special though simple technique, air-dried preparations can be made which stain well with the Romanowski stains, and yield results which are comparable for practical purposes with those obtained by Papanicalaou's method which remains the standard one. The constantly obtained differential cell-pictures are definitely diagnostic, with few exceptions, of the underlying morbid conditions.

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THE USE OF ANTIBACTERIAL AGENTS IN SURGERY

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The term antibacterial agents includes all the antibiotics, that is drugs produced by the metabolism of living organisms, as well as the sulphonamides and other chemotherapeutic agents. The subject is so vast that only the more common or important conditions will be discussed in relation to these agents. (The term "antibiotics" is used below instead of antibacterial agents for the sake of brevity).

General conditions

A number of important principles bear repetition as they are often transgressed. Perhaps because of the bewildering variety of anti-bacterial agents and the ease of administration of many of them, it is often the practice nowadays to prescribe them for almost anything, even to afebrile patients where a diagnosis has not yet been made. This is obviously wrong. Again, the mere presence of fever does not warrant the giving of antibiotics blindly. A fairly accurate diagnosis must first be made or the clinical picture may become quite confused. Mild illnesses and minor infections, boils for example, do not necessarily require antibiotics, even if accompanied by some temperature.

Once it has been decided to prescribe antibiotics, it is vitally important that they are given in adequate dosage, especially in the first 24 hours. Otherwise, not only will be response be less than maximal, but there is the grave danger of promoting the growth of antibiotic-resistant organisms. As a rule, antibiotics should be continued for several days after all signs of infection have disappeared. If there is no response to the antibiotics being given, or if there is a relapse after an initial response, then, provided dosage has been adequate in the first place, either the organisms are resistant to the antibiotic or an abscess has formed. In the first case, the antibiotic has to be changed, if possible, after the sensitivity of the organism has been ascertained. In the second case, it is very important that the presence of an abscess is recognised as early as possible for it must be drained to cure the patient. A lot of time and money is often wasted in trying to cure abscesses with antibiotics. It should also be remembered that antibiotics may sometimes mask the presence of an abscess.

The route of administration may depend on the pacticular antibiotic chosen, but most antibiotics nowadays can be given orally, intramuscularly and intravenously. In that event, the route of administration will depend on the severity of the infection. As to the choice of antibiotics, where more than one will serve the purpose, the cheapest should be use, consistent with the ease of administration and relative lack of toxicity. In certain severe or chronic infections, more than one antibiotic may need to be used. In this connexion, some antibiotics maintain that the action of penicillin and sulphonamides may be antagonised by that of the tetracyclines.

Infections of the skin and subcutaneous tissues; Specific infections; Burns

Furuncles, as already stated, do not require antibiotics as the vast majority

regress spontaneously provided they are left severely alone. In certain situations however, the nose for example, it may be necessary to give them. Multiple furunculosis is another relative indication. Antibiotics should be given for carbuncles as many of them can be cured and the remainder will need only minor surgery. Penicillin in high doses, at least one million units a day by intramuscular injection, should be tried first. If there is no response within 48 hours, a wide spectrum antibiotic should be used. Cellutis can very often be aborted by penicillin or sulphonamides.

Penicillin in doses of one million units a day should be given in cases of tetanus. Gas gangrene requires the exhibition of very large doses of penicillin: six to ten million units topically at the site of the infection. Erysipelas is rapidly cured by sulphadiazine in a dose of one gram four-hourly or by penicillin. Antibiotics should also be given in cases of burns, even if not apparently infected, as a prophylactic measure.

Intra-abdominal infections

In cases of peritonitis, it is best to give a wide-spectrum antibiotic, one of the tetracyclines for choice, if necessary intra-venously. The same applies to peritoneal abscesses, e.g. subphrenic abscesses, though drainage is often essential. An appendicular abscess often resolves if a tetracycline or chloramphenicol is given. The initial dose is usually two grams daily, but when the symptoms and signs have subsided this can be reduced to one gram daily for the last few days of treatment. It should be noted however that a combination of penicillin (one million units) and streptomycin (one gram daily) is often effective in the less severe types of these infections. These same drugs may be used for cases of acute diverticulitis; or a combination of oral streptomycin and sulphaguanidine (one gram and twelve grams daily respectively). A sulphonamide derivative is also being used in cases of patients for surgery on the small and large intestine, a five day course of sulphaguanidine or other insoluble sulphanamide is given. Other intestinal antiseptics like streptomycin or neomycin may be used instead.

Infections of the Genito-urinary system

It is of the greatest importance in cases of urinary infection to exclude the presence of an obstruction to the flow of urine. If any obstruction is present and is not removed, not only will the infection continue but the organisms very quickly become resistant to the antibacterial agent being used. The presence of calculi also makes for chronicity of urinary infections.

Penicillin is usually ineffective against the common Gram-negative organisms found in these infections. Streptomycin has the disadvantage that bacterial resistance develops rapidly to it even in the absence of obstruction to urinary flow. Sulphonamides, on the other hand, are not only cheap but also very effective against the all too prevalent coliform infections causing cystitis, pyelitis, or epididymitis. A dose of one gram every six hours is usually effective. Sulphadimidine is the one most soluble in acid or alkaline urine, so that it is the safest to give alone. Mixtures of three different sulphonamides in equal proportions are about equally safe for the same reason. Patients should be of course advised to drink fluids and the urine should be kept alkaline with potassium citrate mixture. If there is no definite response to the sulphonamides in 24 to 36 hours or if the infection is very severe, then recourse should be had to one of the wide-spectrum antibiotics. Streptomycin is probably more effective than the tetracyclines against Proteus and Pseudomonas infections.

As a percentage of urinary infections relapses if the drug which is being used is stopped too soon, it may be wise, after the acute stage has completely subsided, to give one of the long acting sulphonamides for some weeks in a dose of one tablet daily. Nitrofurantoin is a very useful drug as it has a wide range of antibacterial activity and is effective in a dose of 300 to 400 mg. daily. Mandelamine is also useful provided however the urine is quite acid. (pH less than 5.5). Patients who have to be catheterised should be protected by sulphonamides or other agent against infection.

Infections of the hand

These are some of the commonest of surgical infections and are responsible for a considerable loss of man-hours of work in any year. It is therefore essential that they are treated with the greatest efficiency. Surveys of cases referred to hospital have shown that the patients as a rule first attend 10 to 12 days after the onset of infection. By then, there is gross inflammation and pus is present usually under tension, in spite of the administration of antibiotics parenterally in adequate dosage, say one million units of penicillin daily. This is often the result of an attempt to cure the condition by antibiotics alone. Hence it is clear that the doctor should be careful to recognise the stage where antibiotics alone are no longer enough and surgery is consequently indicated. Infection, it should always be remembered, is one of the main causes of permanent deformity and disability of the hand.

Acute Mastitis

As in the condition just considered cases of acute mastitis are often referred to hospital late. This may be due to the fact that the doctor is called in late but sometimes it is due to an attempt to cure the condition with antibiotics. In many instances, as fluctuation is not elicited, it is thought that an abscess has not yet formed. But pus is practically always present as early as four to five days after onset and it must be evacuated if the patient is to be cured in the shortest possible time and without sustaining considerable destruction of the breast. In hospital practice, the staphylococcus is almost always resistant to penicillin, so that for maximum effect one of the wide-spectrum antibiotics should be used. In domiciliary practice, however, the staphylococcus is less often resistant to penicillin, so that this is the drug of first choice, preferably in a dose of 3 to 4 million units daily by intramuscular injection.

Acute Osteomyelitis and acute Arthritis

It is vital that all the measures used in the treatment of these two conditions be applied with the greatest efficiency from the onset. In the older child, two million units of penicillin and one gram of streptomycin daily, in divided doses, should be started at the slightest suspicion of the presence of either of these conditions. If the infection is severe and the patient quite toxic, it is wise to add a third wide-spectrum antibiotic, for example chloramphenicol one gram daily. If there is no response in 36 hours, or at the most in 48 hours, surgery is indicated as a matter of urgency. Any fluid obtained is cultured and the antibiotics are changed if the sensitivity tests warrant it. If there has been a response within 48 hours, then surgery is not often indicated but both the general and local condition of the patient are carefully observed in case exploration becomes necessary.

Though penicillin can be given in the same dose as above stated in the younger child, the dose of the other antibiotics should be reduced in propor-

tion to the age. Ideally, the antibiotics should be continued not only until general and local symptoms and signs have returned to normal but also until the X-Ray appearances are also well on the way to normality. In cases of arthritis, apart from giving antibiotics systemically, they can also be given intra-articularly after aspiration of the fluid in the joint. Penicillin in a dose of 100,000 to 500,000 units is excellent for this purpose. It should not be forgotten, of course, that antibiotics are only part, albeit a very important part, of the treatment of these conditions. If septicaemia supervenes, intravenous tetracycline is indicated.

Tuberculosis

It is common knowledge that the treatment of tuberculosis in all its protean manifestations, with modern drugs has greatly influenced the prognosis. Surgery not only can (and should) be carried out under antibiotic cover, but it is selective, that is, used particularly for the removal of the residual lesion. Very often, indeed, there is no residual lesion to remove. With the help of antibiotics a cure is obtained earlier and much more frequently, and it is also more likely to be permanent.

What is important to remember is that two, any two of the three chief drugs must be given simultaneously. Otherwise, resistance, especially to streptomycin, develops rapidly and the prognosis is then radically altered. The initial doses are: streptomycin one gram daily; isoniazid 200 to 300 mg. daily and PAS 12 to 18 grams daily. In the later stages of the recovery, streptomycin may be given only three times weekly and the doses of the other two drugs may be reduced to the stated lower level. In advanced cases of tuberculosis all three may need to be given at first. When can the drugs be stopped? This is still a matter of controsy but the following is a safe rule. They should be continued for at least six months after the disease has become quiescent, but in most cases for a total minimum period of two years anyway. Quiescence is denoted by general and local symptoms and signs and including the X-Ray appearances. This rule applies to most forms of tuberculosis: pulmonary, intestinal, genito-urinary, bone and joint. In cases of tutuberculous lymphadenitis, it is not always necessary to give these drugs, and even when they are given, a relatively short course lasting for some months is often enough.

It is usual in the treatment of tuberculosis to ring the changes every three to six months: first streptomycin and isoniazid; then PAS and isoniazid; etc. It is opportune here to mention a somewhat vexed question. As already stated previously, a combination of penicillin and streptomycin is often given in surgical infections other than tuberculosis. There is obviously the danger not only of masking, perhaps, tuberculosis in latent cases but also that of enhancing the growth of streptomycin-resistant tubercle bacilli in such cases: a tragedy. To obviate, at least in part, this danger, streptomycin should not be administered to cases under investigation for tuberculosis until the diagnosis is proved, or to those who are T.B. contacts. In special instances, where resistance has developed to the usual three drugs, certain other agents like viomycin and cycloserine may be given.

Other conditions

There are many other conditions for which antibacterial agents are an essential part of the treatment. Acute cervical lymphadenitis is a fairly common occurrence, especially in children. At the other end of the scale, diabetic cellulitis of the lower extremity often proceeding to gangrene is quite common in middle

to old age, especially in Malta. In this condition, generous incisions and wide excision of slough are often required to complement antibiotic therapy. This too may need to be continued for a long time finally to get the better of a chronic smouldering infection. In infections of the brain or meninges, following on compound fractures of the skull for example, the most effective antibiotics to give systemically, because they diffuse best through the blood-train barrier, are sulphadiazine and chloromycetin, and to a lesser extent the tetracyclines.

A practice which is rapidly becoming controversial is that of giving antibacterial agents preoperatively and postoperatively as a prophylactic measure. Recent surveys of this practice in "clean" surgical cases have tended to show that there is a higher incidence of postoperative sepsis in these cases than in controls, also "clean" cases, where no such agents have been given. It has also been stated that such a practice contributes to the emergence of resistant strains of organisms in surgical wards and therefore to all the evils of increased hospital sepsis and cross-infections. There is of course much less controversy as regards the use of antibiotics in "dirty" cases. The question of hospital sepsis is a serious one today and is due mainly to streptococci resistant to the usual antibacterial agents. These organisms then become difficult to control and eradicate. One of more important measures for their control used in many hospitals is that of keeping one or two of the latest powerful antibiotics, like the newer penicillins, in reserve throughout the hospital and using them only in special cases where the staphylococci cannot be otherwise controlled.

Conclusion

It is clear that antibacterial agents are powerful weapons in the hands of a doctor against a wide variety of surgical infections. It is equally clear that their limitations must be recognised. They are not the be-all end-all of the treatment of very many conditions, where they have to be supplemented by other measures whether the administration of fluids parenterally or the application of splints or what have you. Antibacterial agents do not confer a dispensation from surgery. Indeed quite often, it needs a fine judgement on the appropriate time for performing the required operation as already stated; and the masking effect has also been mentioned.

It should be remembered that no antibacterial agent can be said to be free of toxicity with the exception of penicillin, which however can give rise to allergic reactions of varying severity. All other agents may cause a wide variety of toxic effects which indeed may make the patient worse than ever and even cause his death. Hence the decision to prescribe an antibacterial agent and the choice of the appropriate one for a particular patient is a matter which requires careful thought and sound judgement.

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Long Term Results Of Drug - Treated Pulmonary Tuberculosis

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During the last decade, antibiotics and chemotherapeutic agents have changed completely the treatment and outlook of pulmonary tuberculosis. In the majority of cases, the immediate results have been gratifying to physician and patient alike, but in such a disease as tuberculosis the final assessment of any form of treatment should rest more on the relapse rate than on the immediate results. This paper deals with 60 patients, all women, who started treatment during 1953 and 1954, and who have been followed up to the end of 1961. They are all women as they happen to belong to a hospital division.

Selection of patients

The patients under review consist of all types of pulmonary tuberculosis; but, they are "selected" in a way in that

(a) all have been treated in the wards and out-patient department of a hospital;
(b) all started treatment in 1953 and 1954
(c) none had ever had any anti-tuberculosis drugs before.

The advantages of hospital treatment are obvious: treatment is carried out under supervision, patients are more likely to take the drugs, follow-up can be better controlled, and therefore, the evaluation of results is more reliable. Only patients who started treatment during 1953 and 1954 have been selected, as a follow-up of at least 5 years from the end of treatment would increase the significance of the relapse rate. The fact that none had had any drugs before is of major importance in assessing the value of the treatment concerned.

Classification of patients and extent of disease

Patients were classified into A or B depending on the absence or presence of tubercle bacilli in the sputum, exudates etc., but "grouping" into 1, 2 or 3, was based more on the radiological findings, as suggested by Foster-Carter (Foster-Carter et al, 1952, Hoyle C., Nicholson H., Dawson J., 1955).

Eleven patients belonged to Class A and 49 to Class B, grouped as follows:

A1	2	patients
A2	5	"
A3	3	"
B1	2	"
B2	23	"
B3	25	"

Age of patients on admission. Table I gives the age-group distribution in years.

Duration of illness. This is very difficult to postulate with anything like certainty in pulmonary tuberculosis, as the disease may have been smouldering for a long time without producing any overt symptoms. This insidiousness of onset was again emphasized in the present patients by the fact that, in spite of the extent of the radiological findings, no less than 31 started to complain of any symptoms not earlier than six months before admission to hospital; 6 patients had no symptoms at all and were discovered on routine X-Ray examination -3 as prospective emigrants and 3 as contacts. Ten, 9 and 3 patients

had been feeling unwell for one, two and five years respectively; one was first diagnosed as having tuberculosis thirty years ago and the present illness was a relapse.

Complications on admission. Sixteen patients had a complicating condition or another disease; of these 9 had Diabetes Mellitus complicated by another condition as follows:—

Diabetic Coma, purpura	1
Arteriosclerosis	1
Hypertension	2
Nephrosclerosis	1
Ischaemic heart disease, Cerebral thrombosis	1
Ischaemic heart disease, Duodenal ulcer	1
Spontaneous hydropneumothorax	1
Undulant fever (Brucella Melitensis)	1

The other seven patients had

Disseminated Tuberculosis (lungs, ulna, five lumbar vertebrae, bilateral psoas abscess)	1
Undulant fever	1
Chronic nephritis	1
Third degree uterine prolapse severe microcytic anaemia	1
Squamous cell carcinoma of face	1
Mental deficiency	1

Three other patients were in the early months of pregnancy.

Methods of assessing progress

The traditional investigations — temperature taking, weight, E.S.R. bacteriology of the sputum and/or of the gastric contents, serial X-Ray — were carried out in every case, but final assessment was entirely guided by the last two objective criteria, i.e. bacteriological conversion and radiological improvement.

Fever. The absence of fever does not rule out active or extensive tuberculosis, and temperature taking has now very little value in following the progress of the disease, except during the acute phase of the illness; the following are the highest temperatures recorded on admission in the 60 patients:

98.4° F.	21 patients
99° F.	13 "
100° F.	6 "
102° F.	9 "
103° F.	7 "
104° F.	4 "

Weight. Patients were weighed on admission and again at weekly intervals. With very few exceptions, their weight was found to be below the average local normal standard.

E.S.R. This was estimated by the Westergren method and was read after one hour. It was repeated monthly and was found to be a good index of the activity, extent and progress of the disease. In fact only 3 patients had an E.S.R. below 10mm. on admission — classification A1, B1 and A2 respectively.

E.S.R. (1st. hour) of 60 patients on admission.

Below 10mm.	in 3 patients.
Between 10 — 19mm.	in 11 patients
20 — 39mm.	in 18 "
40 — 59mm.	in 20 "
60 — 79mm.	in 4 "
80 — 99mm.	in 2 "
100 — 120mm.	in 2 "

Sputum. Direct (Ziehl-Nielsen) bacteriological examination of the sputum, including counts per field, was done on admission and repeated monthly thereafter. Culture and/or guineapig inoculation (sputum or gastric contents) were carried out if smears turned out negative on repeated examination. Tubercle bacilli were found in 48 patients, as follows:

Sputum, direct, in 38.

Gastric contents, culture, in 6.

Gastric contents, guineapig, in 1.

Gastric contents, culture and guineapig, in 2.

Pleural fluid, culture, in 1.

Radiological Findings. A postero-anterior X-Ray was carried out routinely, repeated monthly, or more frequently in special cases. A "lateral" or tomogram was done when considered necessary.

Of the 60 patients, 4 had only one zone in one lung involved, 32 had unilateral or bilateral lesions in two or three zones, and 24 patients had bilateral disease involving four or more zones. 42 patients had cavities, 20, 11, 4, 1, and 6 having one, two, three, four and multiple cavities respectively.

Cavities were graded into small (1cm. or less), medium (1cm. to 2cm.), or large (2cm. to 6cm.), according to the size of their largest diameter: 10, 15, and 17 patients had small, medium and large covities respectively.

The total number of cavities present in the 42 patients was 70, 38 in the right lung and 32 in the left, the majority being in the upper zones (right upper zone 22, middle zone 16; left upper zone 24, middle zone 8). In the present series no cavities were present in the lower zone.

Treatment

Bed Rest. All patients were kept in bed at least for the first six months, being allowed up only to wash and for toilet purposes, whenever their physical condition permitted. When cavities were present, rest in bed was enforced as long as the covities remained open and for a further 3 months after their closure.

Drugs. One of the three possible combinations of the three anti-tuberculosis drugs — Streptomycin, PAS and INAH — was given continuously from one to two years, except in one patient when treatment had to be stopped after six months because of side effects and in two others who died five and six months after admission to hospital. Table II gives the duration of treatment in months in the 60 patients.

The routine procedure was to give Streptomycin 1G coupled with PAS 12-15G or INAH 200 mgm. daily for at least six months or until sputum conversion and/or cavity closure, whichever was the longer period. During the next three months, Streptomycin was reduced to 1G three times weekly, and reduced further to 1G. twice weekly for the following three months. In those patients who received more than one year of the drug, treatment was continued with PAS 10-12G. and INAH 200 mgm. daily either as in- or as out-patients.

During in-patient treatment the Streptomycin-PAS combination was used on 28, the Streptomycin-INAH on 39, and the PAS-INAH combination on 19 occasions.

Ir the older age groups this schedule had to be somewhat modified because of their greater tendency to Streptomycin neurotoxicity. Streptomycin, therefore, was only given daily during the acute phase of the illness, say for a month or two, and then it was reduced to three times weekly. Since March 1953 whenever Streptomycin had to be given intermittently, in the presence of a positive sputum and/or an open cavity it was always coupled with PAS and not with INAH to lessen the danger of emergence of resistant strains of bacilli. (M.R.C. 1953., Editorial B.M.J., 1953).

Triple drug therapy was never used; it must be remembered however, that these patients were receiving the drugs for the first time, and in 1953 and 1954 the local incidence of primary drug resistance in untreated patients was not yet of any significance.

Toxic reactions and side-effects. It was not found necessary to withold permanently drug therapy because of side-effects, toxic reaction, or for any other reason, except in one patient. Even when these appeared, it was always possible to continue treatment with a different combination of drugs. The only

patient in whom treatment had to be abandoned altogether had chronic seborrheic alopecia and showed skin sensitivity reactions to all the three drugs. Desensitization in this patient was not attempted as she was below average intelligence and uncooperative. Desensitization to Streptomycin, however, was carried out successfully in another patient who became allergic (swelling, pain and erythema at the site of injection) to this drug, and who had already exhibited allergy to PAS, in the form of fever, cervical adenopathy and a rash. Ten other patients showed reactions to Streptomycin: 5 headache, 3 paraesthesias around the mouth, 2 vertigo. Headache and vertigo usually appeared when treatment had been going on for some months and was more frequent in the older age groups; in all these patients streptomycin was substituted by PAS or INAH. In one patient vertigo was permanent. Paraesthesias around the mouth, in the form of pins and needles, appeared in younger patients early on in treatment and usually following immediately after the injection; the drug was continued and the complaints disappeared as treatment went on. Three others had pruritus and an erythematous rash due to PAS and in each case the drug was replaced. In the dosage used, 12-15G. daily, gastrointestinal complaints after PAS were remarkably uncommon and mild, and they could be controlled either by giving the mixture after meals or by replacing it with cachets. Except the one patient already mentioned, none had any toxic reactions or side-effects attributed to INAH.

Examination of urine, blood count and picture and liver function tests were done periodically; no alterations due to drugs were noted.

Other treatment. Other treatment beside rest in bed and drugs was found necessary in 7 patients: artificial pneumothorax. 2; thoracoplasty, 2; phrenic crush, 1; aspiration of psoas abscess and immobilization in a plaster bed, 1; aspiration of a spontaneous hydropneumothorax, 1.

The patients who had Undulant Fever were given orthodox chlortetracyclin therapy in addition to the other drugs.

RESULTS OF IN-PATIENT TREATMENT. Fever subsided rapidly and was down to normal after a few days; it never took longer than three weeks to settle down. Cough and sputum likewise disappeared very quickly, even when cavity remained large.

With two exceptions, one of whom had a carcinoma of the face, all gained weight rapidly even those who eventually died.

The E.S.R. improved concurrently with the disappearance of the toxaemia and with the radiological improvement.

Progressive decrease in the number of bacilli per field was noted almost weekly; in some cases, sputum conversion occurred after the first three months of treatment.

Radiological improvement was fairly rapid, and as would be expected, the "soft" shadows produced by the exudative lesions were the first to disappear, clearing up completely by the end of the third month. Cavity closure, in the majority of cases, took longer. Whether a cavity closes or not with drugs alone, depends to a great extent, apart from the state of the bronchus, on the amount of lung-tissue destroyed and of the structure of its walls; one thing is certain, to prognosticate about the fate of a cavity before anti-bacterial treatment is well under way may lead to surprises, pleasant and unpleasant. A giant tension cavity will very often close in no time with drugs and rest in bed, while a small fibrotic one will not close at all. In the present series one such tension cavity, and in the apex of the lower lobe of the left lung, vanished after only

three weeks of treatment. "Calcification" of the nodular shadows perhaps appeared earlier than formerly, and miliary shadows, more often than not, disappeared completely. Healing was more frequently by resolution than by fibrosis unless there was extensive disease.

The three pregnant women had normal deliveries and healthy babies, and the pregnancies did not effect their pulmonary condition. The two patients who had Undulant Fever did well and there was no relapse.

Duration of stay in hospital. The average stay in hospital was 15 months, the extremes being 6 and 24 months. Patients were kept in hospital from 4 to 5 months after being allowed out of bed, sending them home for the week-ends and on public holidays. This had the double purpose of getting them acclimatized to Sanatorium regime when up and about, and of observing the reaction of their disease to increased activity.

Deaths. Five patients all belonging to Class B 3 died while in hospital. Their ages at the time were, 41, 54, 59, 67, 71 years. In only one patient was death directly attributable to pulmonary tuberculosis, an old "chronic" who had an associated cor pulmonale. In two others, both diabetics, the tuberculosis had reached the quiescent stage and they were due for discharge: one died of a second attack of coronary thrombosis and the other of cerebral haemorrhage. In the other two the tuberculosis had improved, but one died of an inoperable carcinoma of the face, and the other, who had diabetes, ischaemic heart disease and cerebral thrombosis died in congestive heart failure.

Condition of survivals at time of discharge (55 patients)

Weight. With only one exception, who maintained the same weight throughout, all patients had gained from 2 to 5 stones in weight.

E.S.R. This was normal in 48 patients; in six it was above 20mm. and in one, above 80mm. Of the six who had an E.S.R. above 20mm. all were sputum negative, but two had only had 8 months of the drugs and were discharged partly at request continuing treatment as out-patients, one had had extensive bilateral disease and the lesions were not yet fully calcified, and another had had only 6 months treatment, when this had to be stopped because of allergic skin manifestations. The single patient who had an E.S.R. above 80mm. had active disease, an open cavity and positive sputum.

Sputum Conversion.

Bacteriological tests carried out before discharge from hospital consisted of repeated culture of, and/or guineapig inoculation with, the gastric contents as very few had any available sputum at that time.

Of the 55 patients discharged, 45 had positive bacteriological findings on admission, and of these only one had a positive sputum when she left hospital.

Cavity closure. Of the survivals, 38 had cavities on admission. In 32 patients the cavities closed with rest in bed and drugs; 5 had to have collapse measures (2 artificial pneumothorax, 2 thoracoplasty, 1 phrenic crush) all with successful results. One left hospital at request with an open cavity and a positive sputum. Cavity closure was controlled by tomograms in every case. There were no "open negative" cases.

Out-patients follow-up of 55 patients

50 of the 55 patients discharged have been followed up for about 5 to 6 years after the termination of treatment; of these, 48 have remained well and 2 have had a radiological relapse, but both

responded well to a second course of the drugs. Three died, two in ureamia following chronic renal disease 5 and 3 years after they left hospital with no evidence of reactivation of the tuberculosis, and the other one, aged 54 years, of pulmonary tuberculosis; she was the one who left hospital at request with an open cavity and a positive sputum.

Two patients never attended the clinic after leaving hospital and could not be traced

End results

Of the 60 patients who started treatment during 1953 and 1954 and who were having anti-tuberculosis drugs for the first time, 50 are now living and well (end of 1961); 8 died, 2 from pulmonary tuberculosis, 6 from other causes; two could not be traced, but had left hospital with their disease in the quiescent stage.

Comment

Relapses. The two patients who relapsed had had bilateral disease involving three or more lung zones with cavities in the upper lobes and a positive sputum on direct smear. One had had 12 and the other 15 months of continuous drugs while still in hospital; in one the relapse occurred one year and in the other 4 months after stopping treatment. No tubercle bacilli could be discovered either in the sputum or in the gastric contents, on smear and culture, and in both the relapse was radiological, at the site of the original lesion and consisting of "softening" of the nodular shadow which had undergone "hardening." In one, the relapse occurred during the fifth month of pregnancy and in the other it followed an abortion. Both were re-treated as outpatients and responded promptly to PAS and Isoniazid. These patients were insufficiently treated; considering the extent of their original lesions, both should have had at least 18 months of the drugs from the start.

Hospital stay. A stay in hospital for 15 months may appear long by present day standards. Even in Ross's series, which consisted mainly of advanced and far advanced cases (B.2 and B.3 in the present series), the average stay in hospital was only ten months (Ross et al, 1958). At the same time, one cannot but agree that the longer the hospital stay the shorter the period of "self medication" with all its drawbacks (Dixon et al 1957; Lancet, E., 1958; Ireland, 1960; Luntz and Austin, 1960).

Perhaps the point at issue today would not be the duration of hospital stay, but whether hospitalisation is really necessary. It is readily granted that present-day treatment permits a more liberal approach to tuberculosis; at the same time, however, one should remember that drug-resistance is practically non existent in hospital treated patients. "In avoiding resistance to drugs it was important to see that the regimes laid down were understood and carried out by the patients, who varied considerably in intelligence. There was a danger that treatment might be regarded too lightly and admission to hospital was desireable in the first instance." (Scadding J.G. 1958)

Tuberculosis is *still* an infectious disease. Although some workers have shown that the results of domiciliary and hospital treatment may not differ very much where the patient is concerned, yet the risk to contacts of those treated at home is relatively high, especially among the young. As the International Union against Tuberculosis puts it *"institutional treatment is desireable in all sputum positive cases,* mainly to ensure that the patient takes his chemotherapy and to decrease the danger to others." (XV International Tuberculosis Conference 1959). Inspite of growing tendency to a shorter hos-

pital stay and to domiciliary treatment, it is still the practice of the writer to extend hospitalization to one year, thus making sure that patients have had at least on year of proper drug treatment. Although many more factors bearing on the relapse rate of tuberculosis have yet to be established, sufficient evidence has now accumulated to prove that as regards drug treatment the relapse rate is inversely proportional to its duration (Low, 1956; Crofton, 1959).

Rest in bed. In some of the present patients, this may have been prolonged unduly. Recent controlled trials have shown that patients with "mild" pulmonary tuberculosis (sputum negative on direct smear, cavity not more than 2 cm. in diameter) may be treated at work with good results (Tuberculosis Society of Scotland, 1960). However, it is also a fact that cavities close earlier with rest (Ross & Kay, 1956); the earlier the cavity closes the more rapid is sputum conversion and the emergence of drug-resistance is less likely. Weir, Schless O'Connor & Weiser who treated 105 patients in hospital conclude that control of physical activity is not necessary for successful treatment of pulmonary tuberculosis which includes adequate chemotherapy. But out of 46 of their patients with cavities, 24 had to undergo resectional surgery for residual cavities after 5 to 11 months of treatment (Weir et al, 1961). In the present series, out of 39 of the 42 patients with cavities (excluding the one patient who left hospital at request and the two who died in the early phase of treatment — all three considered as unsuitable for any kind of surgery), only 5 had to have other treatment for the closure of cavities, besides drugs and rest in bed. It is felt that rest in bed must have contributed to the high rate of cavity closure by conservative measures in these patients.

Treatment. In the present series, the duration of drug treatment, from one to two years, is compatible with modern ideas, except that today, even in the less severe case, one is more inclined towards the longer period. In all other respects, during the last years, treatment has been modified to conform to accepted standards. Since 1955 drug sensitivity tests have been carried out routinely in *all* our patients before and during treatment, all the three standard drugs have been given until the results of these tests were available, and Isoniazid always formed part of the drug combination.

It is unjustifiable, especially today, to speak of the drug treatment of tuberculosis and to draw any conclusions thereon without including bacterial sensitivity. In the patients under review sensitivity tests were not done regularly enough to warrant inclusion in this report; however, as already stated, in 1953 and 1954 the local incidence of primary drug resistance was not yet of any significance, and from the response to treatment and the results obtained in the present series one is justified to assume that the bacilli remained sensitive throughout treatment. The 2 patients who died of tuberculosis would have done so irrespective of the drug sensitivity of their bacteria.

Summary

Sixty women suffering from Pulmonary Tuberculosis started treatment between January 1953 and December 1954.

All were treated in hospital (some continuing treatment as out-patients) with a combination of two of the three standard drugs (Streptomycin plus P.A.S. or Isoniazid, or P.A.S. plus Isoniazid), and rest in bed; all were having the drugs for the first time.

Fifty-seven patients completed from one to two years of treatment; two died within six months of admission to hos-

pital, one from malignant disease, the other from chronic pulmonary tuberculosis and cor pulmonale; in another patient treatment had to be suspended after six months because of drug allergy.

Forty-two patients had cavities, three being unsuitable for any kind of active treatment; in thirty-four, the covities closed by conservative measures only (i.e. drugs and rest in bed), in the other five collapse therapy had to be used, with successful results.

By the end of 1961, of the 57 patients who had completed from one to two years of treatment, 50 were alive and well, including 2 who had relapsed but who did well on re-treatment; one other patient in whom treatment had to be suspended after six months because of allergic reactions was also alive and well. Six had died, one from pulmonary tuberculosis (this patient had left hospital against advice), 5 from other causes. Two others could not be traced, but at the time of their discharge from hospital their disease was in the quiescent stage.

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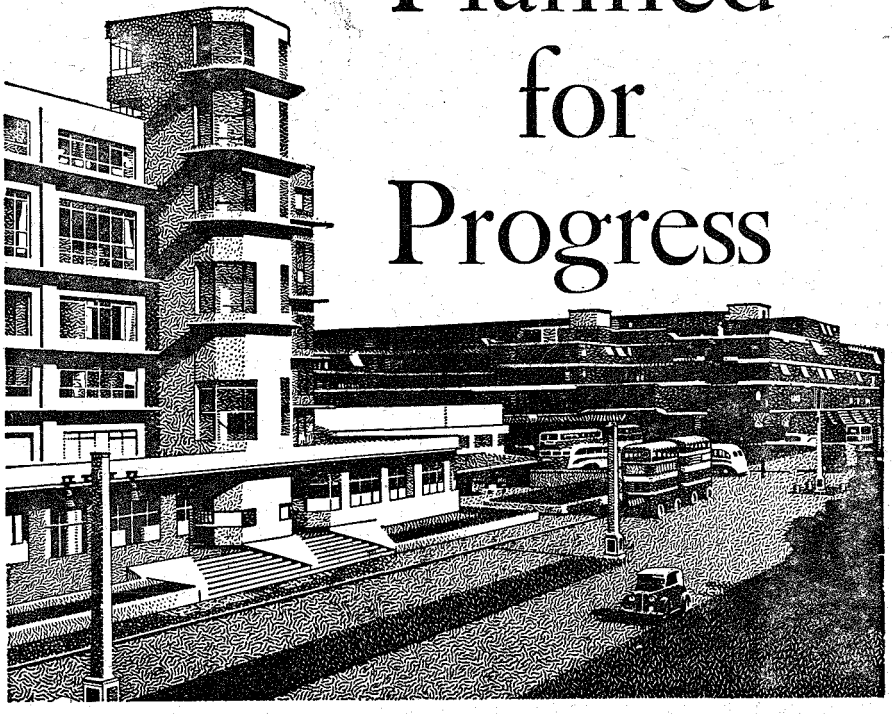

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