and men. In medical phraseology we would designate men like Mr. Bernard Shaw not only experimenters but vivisectors in the cause of social reform. He inflicts pain, I am sure quite unconsciously, on account of his enthusiasm, very real pain, upon the sensorium of those he criticizes adversely or dissects in the open theatre of the public press. Has he been called names by the medical profession for performing a vivisector's experiment without an anaesthetic upon the Chancellor of the Exchequer? There exists no more justification for hurling back at Mr. Shaw's head offensive but painful criticism than there is for him to fling poisoned darts at the honour of the profession.

We want to restore the profession to the proud position it was in years ago, and it will be done if it is left in the hands of family doctors who understand the inward history of progress of our science and art.

The State and the Need for Further Organization to Meet the Requirements of the Country Doctor.

This society will be able to do much good by helping to place the medical service in country districts in a better position than it is at present with regard to the treatment of medical and surgical emergencies.

When I was apprenticed the medical profession had not discovered the methods which should be adopted in acute abdominal emergencies. The public to-day require to be informed that it is not possible for any doctor to treat certain medical and surgical cases under conditions now existing in such districts as this. Many cases in their early stages require frequent visits from the doctor and constant observation by a trained nurse before a decision to take action can be reached; hospitals are too far away to take patients to for prompt surgical action, the homes are hopelessly unfit and unsuitable; operating in them is unthinkable, and patients naturally do not like to be turned out of their own homes when suddenly taken seriously ill, and placed under strange doctors far away. They will not hear of it, notwithstanding that prompt action may be the only means of saving life. What, then, can be done in your district to meet the demand and to improve existing conditions?

Patients' homes are often far away from you, almost inaccessible, telephonic communication does not exist, suitable ambulances are not to be had, nurses for the homes are not available, women or the folks at home have not yet been taught how to assist by taking the pulse and temperature and to report. Rapid and decisive action cannot be undertaken. Patients are every moment in the firing line, but the country is not yet properly organized to meet these casualties, and loss of life is inevitable. You have the knowledge but not the means to meet the situation.

The public through the State has since my days of apprenticeship thrown new responsibilities upon you; county and district councils have been instituted, and probably it will be indirectly through these bodies that you will be able to get some of the essentials necessary for raising the standard of treating people living in the country to that level which now exists in big cities.

You have gone a long way towards the solution of the difficult problem of how to render the best medical service in country districts by adopting a river valley as the unit of co-operation. With the aid of motor cars, motor ambulances, "a nursing home" for medical and surgical emergencies, and an efficient telephone system, I see no very great difficulty before your society in making the vale of the river Teifi your future unit of administration. The State has quite recently shown its great concern in the medical service by voting funds for the provision of nurses.

I propounded last year a scheme for the organization of voluntary aid in connexion with nursing in Wales, at the annual meeting of the South Wales Nursing Association, taking as my subject "the trained nurse, the village nurse, and nursing in the home." Your President is taking a very active part in the organization of Red Cross voluntary aid detachments, and I feel certain that, with your hearty co-operation, it will be possible to train the men and the women of the voluntary aid detachments to be of great value to your medical service in rendering aid in stretcher and other methods of transport work, and in carrying out intelligently your orders in the homes.

In conclusion, I thank you sincerely for giving me an opportunity to express views which were in the realms of imagination in the days of my apprenticeship, but are to-day realizable, thanks to experiment, which, unfortunately, has not been unassociated with loss of human lives.

[The meeting passed resolutions that steps be immediately taken to approach the proper authorities to provide a nursing home and a suitable motor ambulance for medical service in the Vale of Teifi.]

SPRUE.

BY

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(From the London School of Tropical Medicine.)

THE researches upon which this paper is founded were conducted in Ceylon, where sprue has been especially prevalent in the European planting community during recent years, and has occasioned considerable inconvenience and loss of valuable lives.

The expenses of this work on which I have been engaged for the last two years were met by a combined grant from the Ceylon Government and from the Ceylon Planters' Association.

Since the classical clinical studies of Van der Burg and Manson in 1881 it may be said that no serious or systematic attempt has been made to make a thorough study of the etiology of this disease; I need, therefore, offer no apology for presenting the following communication, which may be regarded as a preliminary to a more detailed study which will be published shortly.

Physical Features of Ceylon.

It is necessary that I should briefly describe the physical features of Ceylon in so far as they have a bearing on the epidemiology of sprue. It has been rightly said that no tropical island possesses such a variety of climatic conditions in so confined an area; four-fifths of it consist of an undulating plain surrounding a mountainous zone, in which the temperature and rainfall are subject to considerable fluctuations, the former ranging from an average of under 60° F. in Nuwara Eliya (6,200 ft.), the sanatorium of the colony, to an average of over 80° F. in Colombo and the low country. The rainfall also varies considerably, from an average of under 75 inches in the north and east—the dry zone—to over 200 inches in the elevated tea-bearing provinces.

Definition of Sprue.

Sprue is a chronic and particularly fatal tropical disease characterized by diarrhoea, progressive emaciation and anaemia, by a specific denudation of the buccal mucosa, and by symptoms suggesting atrophy of the organs subserving digestion. The diarrhoea is of a peculiar kind: the stools, which are large, pale, and frothy, are generally passed in the early morning, and are accompanied by much flatulence. At the same time there is a grave flatulent dyspepsia which becomes particularly severe towards the later hours of the day, and which is only relieved by the passage of stool. In the early stages there is a specific inflammation of the tongue, involving especially the fungiform papillae on the anterior portion and on the edges. At times small, painful, and evanescent aphthous ulcers make their appearance on the tongue itself, the fraenum, and especially on the buccal mucosa in the vicinity of the opening of Stenson's duct. After repeated attacks of the specific inflammation the tongue becomes glazed and superficially fissured, and the papillae are entirely destroyed. Dysphagia, suggesting an involvement of the oesophagus, is often a terminal symptom. Persistence of these symptoms leads to an atrophy of all the organs of the body, and eventually to a fatal termination.

General Geographical Distribution of Sprue.

Recent evidence suggests that sprue has probably a world-wide tropical and subtropical distribution. It is encountered, in this country, in its most virulent form in Europeans hailing from Eastern seaports. It has been

reported from the following countries: India, Burma, Siam, Malaya, Cochin China, China, Japan, Java, Sumatra, Celebes, Macassar, Borneo, Ceylon, the Philippines, Fiji, Porto Rico, Haiti, West Indies, Mexico, South America, Gold Coast, Upper Congo, and Morocco. The scanty records from tropical Africa are of doubtful value.

I made extensive inquiries amongst the European community in Ceylon with the object of ascertaining whether the incidence of sprue were greater in any particular region or district, but I was unable to ascertain any strictly topographical limitation. Cases were found in which the first symptoms occurred in Nuwara Eliya, as also in Colombo, where the mean average temperature is 22° F. higher.

Sprue in Native Races.

All authors who have so far written on the subject are agreed that sprue is pre-eminently a disease of the European in the tropics, and that the native is only occasionally, if ever, attacked. I do not consider this statement to represent the true facts of the case. It is more than probable that it is extremely common amongst the indigenous natives, and that in this respect it conforms to other tropical diseases of known specific origin. I need hardly say that there are certain real difficulties in diagnosing a disease of such an ill-defined nature as sprue in natives, who are so liable to ankylostomiasis and malaria. I managed, however, to obtain notes of eleven cases in natives, members of all the principal races—Moors, Cingalese, and Tamils—inhabiting Ceylon, in whom there could be no reasonable doubt about a correct diagnosis. Five were seen shortly before death; in only one instance was a complete *post-mortem* examination obtained.

Amongst the Europeans, the majority (19) of my 36 cases occurred in females, a figure which, taking into account the disproportion (two to one) of the European males to females in Ceylon, denotes a special liability of the female sex to the disease. Though sprue generally occurs in adults, age is apparently no bar to infection. The youngest case I saw was in a Eurasian boy of 13, the oldest in a Ceylon burgher of over 70 years of age.

Predisposing Causes.

Features in the immediate environment of each case—such as housing, water supply, and food—were each made the subject of a separate investigation. The question of food and water supply being in any way concerned in the production of sprue could easily be ruled out. There is, however, a popular idea in Ceylon that the “dry rot” which infests nearly every wooden tea estate bungalow is in some manner directly connected with the occurrence of sprue cases in “dry rot” bungalows which are considered to be unhealthy. This is not invariably the case, for I found a number of planters in whom symptoms had first commenced in bungalows built entirely of stone or of brick.

A previous attack of some intestinal disease, as dysentery, may be regarded as a most important but not as an essential etiological factor; in one half of my cases no history of such an illness was obtainable. There are ample grounds for regarding sprue as a primary disease, but any depressing influence, such as debilitating disease or unhealthy surroundings, may lower the vital resistance, and thus render the alimentary canal more liable to attack by the specific sprue germ.

Is Sprue Communicable from Man to Man?

The occurrence of sprue in all classes of the community in Ceylon, irrespective of age, race, sex, or environment, suggests that either it is caused by exposure to similar surroundings, or that it is a directly communicable disease. The latter suggestion received support from my discovery of six instances in which one or more members of the same family were simultaneously affected. In one case more or less reliable evidence of direct infection was forthcoming. This was a boy of 13, in whom symptoms commenced while he was living in close association with his mother, who eventually died of the disease.

The Symptoms of Sprue regarded from an Etiological Standpoint.

The symptoms of sprue and the manifestations of the specific desquamation of the epithelium of different por-

tions of the alimentary tract vary so considerably that I concluded that the only possible clinical classification was one which had as its basis a hypothesis that the disease affects the various regions of the alimentary tract to a varying degree, thus giving rise to symptoms according as one or other portion is specially affected.

As *typical or complete sprue* I have included all the cases in my series exhibiting the two cardinal symptoms—the characteristic tongue and stools—but even in this type I have notes of cases in my series which I feel I am justified in regarding as acute, mild, and chronic manifestations of the same disease.

As *incomplete sprue* I classified a number of cases which exhibited the typical intestinal symptoms and the pale and frothy stools, but in which there was—for a period of some years in some instances—no involvement of the tongue and mouth whatever, and also a series of diarrhoea cases with massive bilious and frothy stools accompanied by emaciation, flatulence, and dyspepsia, without any involvement of the mouth, and which I regarded as early cases of sprue, involving especially the intestinal tract.

Finally, I found a number of cases, both in Europeans and in natives, in whom the disease had apparently attacked the buccal cavity alone. The tongue showed the lesions—destruction of the filiform papillae and superficial fissures—which are typical of the sprue tongue. As further evidence in favour of this assumption I may mention that I found four cases in which these tongue symptoms developed during the time the patients were living in close association with typical cases of the disease. These tongues, which appear to be etiologically related to sprue, and cannot be regarded in any way as a local manifestation of syphilis, I have termed for convenience and for the purposes of description “tongue sprue.” Although I am inclined to regard tongue sprue as being a distinct affection produced by the same agency as complete sprue, yet it must be borne in mind that an atrophy of the lingual papillae is found in other diseases characterized by general nutritional changes and anaemia, such as chlorosis, pernicious anaemia, ankylostomiasis, and chronic malaria. The clinical evidence I have collected on this point seems to suggest that the loss of the filiform papillae in sprue is the result of some active destructive process, while that in the other diseases I have enumerated is the result of some passive process dependent possibly on a lack of nutrition.

Pathology of Sprue.

(a) *Stools.*—The pale colour of the sprue stools is probably due to several causes—first, to the farinaceous or milk diet with which the patients are generally dieted; secondly, to the presence of a colourless reduction product of hydrobilirubin, the normal faecal pigment, which is known as leucourobilin; and, thirdly, to the abnormal proportion of undigested fat they contain. The reduction of hydrobilirubin to leucourobilin is said to take place in the absence of the normal pancreatic juice, and may occur, according to Mayo Robson, in malignant disease or in chronic inflammation of the pancreas in which the glandular secretion is deficient in amount or is prevented from entering the duodenum. The reoxidation of this colourless compound—leucourobilin—to hydrobilirubin takes place with great ease outside the body, an alcoholic extract of a sprue stool, which is at first colourless, soon becomes converted to a brown colour when exposed to direct sunlight. There can be little doubt that normal bile is secreted in sprue, and as such enters the intestinal canal. In six autopsies which I performed I found in all unaltered biliverdin and bilirubin in the gall bladder, so that any change in the chemical composition of the biliary pigments must take place during the passage of faecal matter through the intestinal canal. The fat absorption was found to be reduced in my cases, and was from 70 to 90 per cent., whereas in milk-fed normal subjects it is said to be over 95 per cent. I regret that I was unable, owing to the lack of suitable apparatus, to perform more elaborate analyses on the process of fat splitting in these cases. The reaction of sprue stools was found to be—almost invariably—acid, and was due to the presence of lactic and of butyric acids.

The complete absence of trypsin, which is said to be present in the majority of normal stools, appears to be a further peculiarity of the sprue stool.

(b) *Urine*.—The quantity of urine passed by sprue patients appears to be normal, and the urea excretion, on the whole, to be purely of exogenous origin—that is to say, proportionate in amount to the proteins ingested in the food. Indicanuria and urobilinuria were observed during the acute as well as the terminal stages of the disease; the excretion of the former substance is dependent probably on the amount of intestinal putrefaction, the latter on the degree of blood destruction at the time. I found that the excretion of these substances ceased immediately the stools became normal, and the patient reacted to the appropriate treatment. Cammidge's reaction, though performed in twenty-seven cases, was invariably negative.

(c) *Saliva*.—The saliva was found invariably acid to litmus paper; this was especially the case in cases with acute tongue lesions and those in the terminal stages of the disease and those whose mouths were overgrown with the thrush fungus.

(d) *Blood*.—In the early stages of the disease no alteration in the structure or number of the red cells, the leucocytes, or in their relative numbers was noted, but in two fatal cases a poikilocytosis, polychromatophilia, and normoblasts were present. In fact, the blood picture in these cases resembled, save for the absence of megalo-blasts, that of pernicious anaemia. It is probable that the exact degree of anaemia is dependent, as in other anaemias, on certain factors, such as the duration and severity of the intestinal symptoms, the amount of toxin absorbed, and the individual susceptibility of the patient.

Morbid Anatomy and Pathology of Sprue.

Conclusions from *post-mortem* examinations in the tropics are open to the obvious objection. Tissue destruction takes place with great rapidity; this is especially the case in such a delicate structure as the intestinal mucosa. It is possible that the gross tissue changes which have been described as being pathognomonic of sprue are really in great measure the result of *post-mortem* decomposition.

The following account is based upon two autopsies I was able to perform—both in Europeans—within two hours of death. The tissues were immediately fixed in 4 per cent. formalin.

The bodies presented all the external appearances of a chronic starvation: there was a complete absence of fat; all the muscles were dark in colour; the heart small, dark, and atrophied; all the organs exhibited a proportional degree of wasting, and weighed less than half the normal. The liver was yellow and fatty—bile-stained in one case, the gall bladder was full of bile. The most noticeable feature was the transparent and distended ileum. The whole of the intestinal mucosa was covered with ropy mucus. The tongue and oesophagus were overgrown by a white film composed principally of the thrush fungus. The bone-marrow was dark in colour, and exhibited no peculiar macroscopical or microscopical features.

In microscopic sections desquamation of the epithelial coats of the tongue and of the oesophagus and a superficial infiltration with yeast cells and mycelial threads penetrating into the deeper tissues were the most noticeable features. The mucus lining the intestinal canal was overgrown by these organisms in a similar manner, though I could obtain no evidence that any actual invasion of the intestinal mucosa had taken place. In smears from the liver in one *post-mortem* examination these organisms were also sparsely noted. They were cultivated in glucose broth from every part of the intestinal canal, from the liver and spleen in one case, and from the kidneys in the other, but not from heart blood.

Sections made of various portions of the intestinal canal from stomach to rectum exhibit chronic inflammatory changes; the columnar surface epithelium is mostly preserved. It is possible that a certain amount of epithelial destruction took place previous to death. In sections of the liver the hepatic cells have undergone fatty changes, and contain a few granules of free iron, though this reaction is by no means so positive as in pernicious anaemia. In sections of every organ such as the tongue, the stomach, duodenum, ileum, caecum, sigmoid and rectum, the heart, suprarenals, mesenteric lymphatic glands, bone marrow, and spleen, numbers of Gram-positive, acid-fast, hyaline and spherical bodies, which I consider identical with Russell's "fuchsine bodies," were found in abundance.

The endothelial cells of the smaller veins in the trabecular tissue of the spleen were filled with minute hyaline bodies of a similar nature—that is to say, they are Gram-positive, though they differ in not being acid-fast. These bodies are a striking feature in all the six sprue spleens I have examined, and I have failed to find them in forty-three spleens from tropical cases which I examined as controls. (In twenty-two of these cases the immediate cause of death was diarrhoea; amongst them were 4 cases of amoebic dysentery, 10 cases of ankylostomiasis; in the remaining 8 the exciting cause of the diarrhoea could not be ascertained. The controls also included 3 cases of malaria, 2 of kala-azar, 2 of pernicious anaemia, 2 of ankylostomiasis without diarrhoea, 3 cases of tuberculosis without diarrhoea, 1 case each of lymphatic and spleno-medullary leucocythaemia, trypanosomiasis, pellagra, pneumonia, uraemia, lymphosarcoma, filariasis, bacillary dysentery, etc.) I am inclined to regard these bodies as being of a degenerative nature, and as possibly characteristic of sprue. Their homogeneous structure and the lack of surrounding tissue reaction negatives their parasitic origin.

Microscopical sections from a case of "tongue sprue"—that is, from a native who exhibited tongue symptoms only during life—show the same desquamation of the surface epithelium and infiltration with yeast cells as the true sprue tongue. The microscopical structure of these tongues does not differ in any important particular from those of two infants which were overgrown with thrush during life, and with which they have been compared.

Etiology of Sprue.

Several investigators during recent years have favoured the fungoid origin of sprue. Kohlbrugge¹ in 1901 found in the intestinal mucus, in the lymphoid patches of the intestinal canal, and in the epithelial covering of the tongue and of the oesophagus great numbers of yeast cells, which he regarded as being the causative organism, and resembling *Monilia (oidium) albicans*. His results have been partially confirmed by Le Dantec.² In favour of this theory I can only bring forward as a result of my work the following evidence:

1. Yeast cells and mycelial elements are found *intracellularly* in scrapings of the tongue lesions at an early stage of the disease, and cannot be found in scrapings made from the former site of the lesion at a later stage when symptoms have subsided.

2. Yeasts are the only organisms found in the deeper layers of the tongue in microscopical sections. The evidence that the infection is not one of recent date receives support from the chronic inflammatory changes in the epidermis and corium of the papillae.

3. The desquamation of the epithelial cells accompanied by a subacute inflammation of the tongue and of the oesophagus are changes such as would be expected from a study of the mode of growth of the fungus and of its low order of virulence.

4. A general infection of the intestinal mucus with yeasts was found in sprue autopsies, but no such general infection was found in other chronic wasting diarrhoeas. Yeasts were also the most abundant organisms in the stools and saliva of victims of the disease, especially during the acute and during the terminal stages.

5. The stools of sprue, their frothy and gaseous character, are such as one would expect in a blastomycotic infection of the intestinal canal.

6. The relapsing nature, the chronicity and latency of the disease, are symptoms such as one would expect from a knowledge of the life-history of the blastomycetes, their periods of attenuated growth and of sudden recrudescence.

7. There is no evidence in favour of the sprue yeast fungus being otherwise than identical with the thrush fungus *Monilia albicans*—an organism possessing a very low pathogenic power; but it is possible that under certain unknown conditions, more or less peculiar to the tropics, this power may become greatly augmented. In support of this view I may add that it is a well-recognized fact that there are endless varieties of yeasts employed in the brewing of beer and the making of wine, and the predominance of a variety in certain districts imparts, presumably, to the local wine much of its characteristic flavour. These yeasts, though differing widely from each other in their powers of growth and fermentation, yet

resemble each other minutely in their morphological and cultural characters. May it not be that the pathogenic yeasts can be altered similarly by local conditions? It is possible that these fungi, though normally non-pathogenic, can, as in the case of the pneumococcus and diphtheria bacillus, assume at times a pathogenic rôle.

A minute study of the microscopical sections of the tongue and oesophagus in sprue shows that there is a considerable reaction on the part of the host to the invasion of the superficial tissues by this fungus, and there can be little doubt that these fungi in their downward growth are capable of exposing the taste buds and nerve terminals and of causing the very lesions which the lingual and oesophageal symptoms of sprue suggest.

8. Wasting and anaemia—both symptoms of sprue—can be produced in rabbits by continuous intravenous injections of small doses of a broth culture of a pathogenic yeast.

9. Diarrhoea, atrophy of the lingual papillae as in sprue, digestive disturbances, and aphthous ulceration of the mouth are commonly found in children the subjects of a thrush infection in temperate zones.

10. It is possible that obscure alimentary diseases of children in temperate zones—such as Gee's coeliac diarrhoea—are of the same nature as sprue in the tropics. A hypothesis of this sort would explain the occurrence of sporadic cases of sprue in temperate zones.

11. The local affection of different portions of the digestive tract with this fungus would best explain the varying clinical manifestations of sprue.

12. To maintain such a hypothesis it is necessary to stipulate for a third factor, a predisposing cause which may exist in local tropical conditions—conditions which favour a more precocious and luxuriant growth of all fungi, a matter of common observation to laboratory workers in the tropics.

GENERAL CONCLUSIONS.

Finally, as a result of my investigations I am able to put forward the following conclusions:

1. Sprue is a specific disease of tropical and subtropical countries, though it is possible that cases occasionally originate in temperate zones.

2. It is a prevalent disease in Ceylon, especially amongst the Europeans. Contrary to the opinion hitherto held, it occurs amongst the natives irrespective of race or mode of life.

3. This fact, together with the occurrence of the disease in people closely associated with one another, suggests some local influence or some communication of the specific cause from man to man.

4. Sprue is a variable disease. It may occur in a mild or in a particularly virulent form, and, in common with many other serious diseases, is prone to sudden exacerbations, remissions, and periods of latency.

5. There is evidence that the disease may occur as distinct clinical forms, according to the portion of the alimentary canal attacked.

6. Researches in the composition of the stools point either to a complete absence or inadequacy of the intestinal digestive ferments.

7. Researches on the blood and on the urine suggest that certain of the more important clinical features of sprue are dependent on an alimentary toxæmia.

8. The pathological findings are also in favour of such a conclusion, and, if anything, point to an invasion with the thrush fungus (*Monilia albicans*) as being concerned in their production.

REFERENCES.

¹ Kohlbrugge: *Ned. Tijdschr. v. Geneesk.*, 1901, ii, No. 16; and *Mense's Archiv*, 1901, vol. v, No. 12, p. 394. ² Le Dantec: *Compt. rend. de la Soc. de Biol.*, 1908, lxiiv, No. 21, p. 1066.

THE report presented to the annual meeting of the Automobile Association and Motor Union shows that it has 86,402 members. In addition to ordinary members, there are light car members who pay an annual subscription of 1 guinea and 32,000 motor cyclist members paying half a guinea. Mr. Joynson-Hicks, in moving the adoption of the report, said that proposals for the further taxation of motorists should be resisted. He believed that a properly made road was not damaged by motor traffic, and that, as ratepayers and taxpayers, motor users were entitled to demand that roads should be up to sufficient strength to carry the heaviest form of traffic.

THE "CONTROLLED" USE OF NEW TUBERCULIN IN THE TREATMENT OF PULMONARY TUBERCULOSIS.

BY

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AND

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LATE HOUSE-PHYSICIANS AT THE HOSPITAL FOR CONSUMPTION AND
DISEASES OF THE CHEST, BROMPTON.

It is obviously absurd to say that tuberculin is of value because two or three patients have improved under it, just as the converse is equally absurd. What we have done here is to attempt to work on some fair system by which to prove the efficacy or otherwise of tuberculin, and the system we adopted was one of controls. As many cases as possible of pulmonary tuberculosis (the criterion for which was the presence of tubercle bacilli in the sputum) were collected and paired off in such a way that a febrile patient was paired with another febrile, whilst an afebrile was paired with an afebrile. Then by lot it was decided which should be given tuberculin, so that there should be no suggestion as to picking cases, for if tuberculin is to be given with any idea of proving its value, it is, of course, useless to administer it only in cases in which the prognosis is distinctly favourable. Further, as fresh patients were admitted into the hospital, it was decided by lot which should be given tuberculin and which should act as controls.

Although we admit that it is practically impossible to select two cases precisely similar in degree and extent, yet we think that if a sufficiently large number of cases is observed on this plan this difficulty is to a great extent abolished.

The period over which the treatment should extend was decided as three months. This, unfortunately, is too short, yet we find that it is a period commonly chosen for tuberculin treatment in private practice, and the difficulty of keeping several patients in hospital for a longer period was very great.

The cases were classified into three groups:

1. *Afebrile cases.*

2. *Intermittently febrile cases*—that is, using the term "intermittent" in the sense that after a day or two rise the temperature would fall to normal, and then a further rise would be recorded.

3. *Febrile cases.*

A temperature of 99° F. was our standard; anything over that was considered to be febrile, and the patients were consequently kept in bed. If, however, at the end of the second day following this the temperature was below 99° F. they were allowed up for two hours, this period being gradually increased day by day as long as there was absence of fever. Many of the patients remained febrile as long as a month, and then would pass into an intermittently febrile or afebrile condition, but to overcome this difficulty the original classification was adhered to. Such cases as were severely ill, and those complicated with pleural effusion which masked the signs, by severe recent hæmoptysis so that they could not be examined fairly, and extensive laryngitis which obscured the pulmonary sounds, were not included in our series.

Method of Administration.

The tuberculin selected to be used was the new tuberculin T.R., and it was decided to give minute doses, increasing the doses gradually every second or third day at first and later at longer intervals in the case of the afebrile patients, while the febrile patients received a dose every fifth or seventh day. The initial dose in the former case was 1 one hundred thousandth milligram, and was increased to 2, 3, 5, 8 and 12 one hundred thousandths milligram, and then again about three-fourths as much again every dose. In the febrile cases the original dose was 1 two hundred thousandths milligram T.R. The object was to work up to the strength of T.R. the patient would take without producing a reaction. When a reaction did occur the patient was kept quiet, and after a few days the same dose was repeated, and if no reaction followed the treatment was continued as before. If, however, a reaction occurred a second time, then a further