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LUPUS VULGARIS WITH SPECIAL REFERENCE

TO ITS TREATMENT WITH TUBERCULIN.

Thesis for the Degree of M.D.

by

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LUPUS VULGARIS WITH SPECIAL REFERENCE TO

ITS TREATMENT WITH TUBERCULIN.

Lupus is a chronic inflammation of the skin, of a tuberculous character. It is characterised by its slow growth, and its progressive nature. It terminates in ulceration and scar formation, but sometimes in absorption and atrophy.

<u>AETIOLOGY.</u> Lupus is now known to be due to the invasion of the skin by the tubercle bacillus. We have no definite knowledge of the way in which the skin becomes infected in most cases, but according to Leloir¹, it probably takes place in one of the following ways:-

- (1) Direct inoculation from without.
- (2) Indirect inoculation by continuity from deep tuberculous foci.
- (3) Inoculation by way of the lymphatics or the veins passing through a tuberculous focus more or less remote.

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- (4) Infection of haematic origin.
- (5) Infection by inheritance.

It is most likely, however, that the first two are the usual means of infection.

That direct inoculation does occur, may be shown by the fact that it occasionally occurs after tattooing. Jonathan Hutchinson² mentions a case of this nature, where the moisture used to dissolve the paint was the saliva of a brother dying of phthisis. Lupus is also known to follow circumcision, where the operator has been phthisical.

Grossman/

Grossman reports the case of a boy who developed lupus as the result of direct inoculation. His mother pierced the lobe of his ear so that he might wear an earring. The neighbour who assisted at the operation, wetted the needle with her saliva to facilitate its introduction. The wound developed lupus vulgaris. The neighbour soon after the operation died of tuberculosis of the lungs.

Williams" records a case of lupus developing in vaccination scars. The history showed that the mother had applied a cow dung poultice to the arm after the vesicles had formed, without the knowledge of the doctor.

Though cases of direct inoculation do occur, yet they are not very common.

<u>PATHOLOGY</u>. It is doubtless probable that weakened tissues and regions disposed to circulatory disturbance show less resistance to invasion. The "flushing" parts such as the nose and cheeks and parts where the circulation is sluggish are most vulnerable. It has a tendency to appear at the site of injuries or in scar tissue. Walsh⁵ describes a case of lupus which developed in symmetrical seton scars and it has been known to appear on a leech bite.

The Histopathology of lupus resembles that of tubercle elsewhere. Owing to anatomical reasons, however, there are modifications. As a rule, too, the tubercle bacilli/

bacilli are present in the skin in relatively small numbers, and this leads to a slight amount of caseation as they do not produce sufficient toxins to cause much destruction of tissue. The disease starts in the lower part of the corium and progresses upwards. In general, the lesion consists of a collection of tubercles with the epithelioid cells, the round cells, and the giant cells. As the disease progresses the newly formed cells degenerate, and a certain amount of caseation takes place. Along with this degeneration, there sets in a reparative process and fibrous tissue is pro-In this manner is produced the lupoid scar duced. which Unna considers quite different from the ordinary scar tissue. Sometimes this fibrous tissue formation is excessive, and the hypertrophic type of disease results. Sometimes a diffuse infiltration occurs and may spread along the hair follicles into the deeper parts of the cutis. This explains why so often relapses occur, the deeper parts not being touched by the remedies ordinarily applied, only the superficial part of the lesion being destroyed.

<u>SYMPTOMS</u>. The most common site for lupus is the face, especially the nasal region. The malady begins by the appearance of small brownish-red spots. These spots are situated in the true skin and are completely covered with epithelium. On pressure they become pale yellow and have been likened to apple jelly. These/ These spots are rather softer than normal tissue and a probe generally can penetrate a short distance into them. As the disease progresses, the several nodules run together and a slightly raised patch results. This patch slowly and insidiously spreads, doubtless by the bacilli or their products spreading either in the perivascular spaces or along the lymphatic channels. New nodules appear in this way a short distance from the main patch, but gradually the intervening space is filled up, and the whole area becomes continuous. After having attained some size, the patch may for a time remain stationary and then begin to show retrogressive or degenerative changes, the nodules disintegrate and ulceration results. These ulcers are shallow and rounded, as a rule they are sharply demarcated at the margins which, however, are sometimes undermined. The ulcers present a granulating surface from which a variable amount of secretion exudes. As the patch increases these ulcers tend to heal up and are finally replaced by fibrous tissue.

A typically developed patch of lupus shows several conditions. One notices the characteristic apple jelly nodule, small ulcers, cicatricial tissue and, at the edges, one can often see isolated tubercles.

Sometimes the patch shows an excessive growth of one element compared with another. The granulations may be more pronounced and to this type of lupus, the name lupus hypertrophicus is given. In another, the fibrous/

fibrous tissue seems to be produced in excess, and this is known as fibroid lupus. This is usually seen on the limbs and is uncommon on the face. On the hands and feet a horny type is seen, and this is known as lupus verrucosus. Various other names have been used to describe the condition such as lupus mutilans, lupus nodosus, lupus serpiginosus, lupus tumidus and so on, but these are self explanatory.

Considerable deformity may be caused by lupus in some situations. If near the eye, the cicatricial contraction leads to ectropion. In the case of the nose, the deformity may be considerable. The tissue becomes destroyed, the nostrils become narrowed, and the tip of the nose thin and pointed. In other cases, the cicatricial tissue may tend to distend the nostrils. In the case of the mouth, there may be considerable distortion or the orifice may be inconveniently narrowed. When the lupus is situated near a joint the resulting contraction may lead to a great restriction of movement.

As before stated, the face is the most common, and in most cases the only, seat of the disease. In an analysis of 310 cases from the Skin Department of the Royal Infirmary, I found that the face was affected in 238 or 77%. In a few of these cases, there was a lesion on some other part of the body as well. Of the 238 cases, the nose was the site in 73, one or other cheek in 82, the nose and cheek in 24, and the nose and both cheeks in 31.

These face cases do not include patients who had patches/

patches on various parts of the neck; these numbered 30.

47 patients had the disease on the upper extremity, but of these a good many had it on other parts as well, as had also some of the 29 who had it on the lower extremity.

As a rule, lupus is not manifest in many parts of the body of the same patient, but some cases show evidence of wide-spread disease. One patient had it on the buttock, wrists, elbow, thigh, knee, and feet. Another had his neck, cheeks, shoulder, back, arms and thigh affected. On one patient to be referred to later, I counted nine patches on various parts of the body. Another boy, under the care of Dr. Gardiner, had as many as fifteen patches on his body. Jonathan Hutchinson⁶ believes that when lupus is multiple, the dissemination must have taken place in the earliest stages, and that later there comes a tendency to diminish multiplicity rather than to increase it.

In 21 of the cases, the mucous membrane of the mouth was affected in some way, either the lips, gums, or palate, while one of them had laryngeal trouble. Unfortunately, I can bring forward no figures showing the frequency with which the nasal mucous membrane is attacked, but of the cases I have been more in touch with, where the nose has been involved, the mucous membrane was also affected in most instances. This is very important from the point of view of treatment and/ and gives greater force to Dr. Norman Walker's advice that no lupus patient should be allowed to depart before the mucous membranes are examined. In a great many cases the mucous membrane seems to be the starting place of the disease. According to Finsen, 70-80% of the patients at his Light Institute had some membrane involved. Stellwagon thinks this a percentage above the usual. Other authorities do not place the percentage so high as Finsen, e.g. Bender, who gives it at 45%. There is no doubt, however, that many patients have some mucous membrane involved.

The course of lupus has to some extent been stated It is always an extremely chronic disease, above. progressing insidiously from month to month. Very occasionally it disappears spontaneously. Sometimes it develops rapidly, but at other times it appears to remain stationary. Occasionally it even seems to retrogress, but on the whole it gradually extends. It is a pity that it is not painful, as the want of discomfort frequently causes the patient to neglect it and not to seek advice when it would be of most value. Dr. Walker mentions a case in which the disease had lasted from thirty-five to forty years before the woman sought advice. This patient had lived all her life in Edinburgh, had had several children, and, although the disease was extensive, had not thought it of sufficient importance to mention to the doctor who attended her in her confinements. The general health of the individual. is/

is, as a rule, good and is not disturbed by the malady. Enlarged glands sometimes result and a general tuberculous infection may eventually ensue. Later in life, carcinoma develops on the lupus in some cases and it is apt to be a rapid involvement. Sequeira⁹ believes that epithelioma occurs in about 2% of the cases of lupus.

<u>INCIDENCE OF LUPUS.</u> Lupus is much more common in some countries than in others. It is fairly common in this country but, according to Stellwagon¹⁰, it is relatively infrequent in America. Why this should be is not very clear but Stellwagon believes that it is partly to be accounted for by the different methods of living and the character of the food supply. Though this may be partly the reason, yet it cannot altogether account for the difference.

Lupus is more common in females than in males. Since 1892 there have been 1054 cases of lupus treated at the Skin Department of the Royal Infirmary. Of these, 655 have occurred in females and 399 in males. This makes it about twice as common in females, but some authorities place it as high as three times.

Lupus usually begins in childhood or early adolescence. Cases which begin after middle age are seen, but are not very common. In an analysis of 294 cases during the last seven years, I find that the period 5 - 10 years shows the greatest number, no less than 73, or almost 25%, occurring during that time. Before the/ the age of 5 years, 45 cases occur and of these a good many began during the first year of life. Several of these latter began when the child was about eight months old, and generally after some illness, e.g. measles. The period 10 - 15 years accounts for 50 cases. Thus we see that more than half the cases begin during the school life of the child. Forty cases occur between 15 - 20, and 48 between 20 - 30. We then see a diminution, only 18 occurring between **50** - 40. Thirteen are found between 40 - 50 and six between 50 - 60, while one patient had passed her sixtieth birthday before the lupus appeared.

We find too, and this strengthens the evidence that lupus is a tuberculous disease, that most of the patients have a family history of tuberculosis or themselves show other signs of tubercle, e.g. some have had glands removed. Numerous cases could be brought forward in this connection, but I will only mention one. A young woman, referred to by Walsh¹¹, had lupus upon the face and other tuberculous symptoms; her father died of phthisis, her mother of bronchitis, and eight or nine brothers of pulmonary tuberculosis. In some cases, of course, a negative history is obtained.

Lupus has recently become of more importance in that it is now compulsorily notifiable. In England, the notification of lupus came into force on 1st February 1913; in Scotland it was rather later, 1st July 1914 being the date.

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I have tried to get some idea as to the prevalence of lupus in areas throughout the country and as to whether the notification order were enforced. I wrote to various Medical Officers of Health and asked them if they could furnish me with the number of cases of lupus which had been notified in their districts. I should like here to express my indebtedness to these gentlemen for their readiness in giving me such useful information. The results of the inquiry are as follows:-

In Sheffield there were 7 cases of lupus notified in 1914. In Liverpool " " 34 " and in addition 9 cases stated to be tuberculosis of the face, etc.

- In Bristol 17 cases were notified from 1st February 1913 to the end of that year. Of these 9 were males and 8 females. 4 cases were notified in 1914; 2 of these males and 2 females.
- In Cardiff 5 cases were notified in 1913. All of these were females and 4 of them had it on the face and nose. No cases were notified in 1914.

In Newcastle 4 cases were notified in 1913. 3 " " " " 1914.

Coming to Scotland, we find the following: -

In the county of Forfar only 1 case was notified.

Dumfries (County) 2 cases.

Argyll l case.

Roxburgh. No case was notified but the Medical Officer of Health found one unnotified case during the last week of 1914.

Fife. 7 cases, of which 5 were on the face, 1 on the arm and in the other the site was not stated.

Midlothian/

Midlothian. 5 cases.

Linlithgow. 8 cases.

Peebles (county) shows only one notification and that from the burgh of Innerleithen.

These figures for the counties do not include the burghs situated therein, as these have separate Medical Officers.

I will now take some of the Scottish cities:-

In Leith no case was notified.

Inverness 1 case (intra-nasal).

Glasgow 53 cases.

Edinburgh 42 cases. Of these 19 were from the city and 23 from country districts. Of the 42 cases, the Skin Department notified 41, 23 from country districts and 18 from the city. That means that only 1 case of lupus was notified during six months in the city of Edinburgh outside of the Skin Department.

Dr. Bolam of Newcastle has kindly furnished me with the number of cases seen at his clinic at the Royal Victoria Infirmary. These figures are as follows:-

In	1909	there	were	46	cases	•
	1910	<u>11</u>	11	53	11	
	1911	#	11	45	11	
	1912	#	#	56	F1	
	1913		11	72	11	
	1914	**		61	11	

In the Skin Department in Edinburgh, the following are

the figures:-

In	1908	there	were	64	cases.
	1909	#	**	48	#
	1910	11	11	46	ff
	1911	**	11	42	. 11
	1912	11	11	47	11
	1913	"	11	35	
	1914	#1	11	33	11

Since October 1912, Dr. Gardiner's figures, with which he/

he has kindly supplied me, must be added. These are:-

1912 1 1913 8 1914 10

That would bring the totals to 48, 43, and 43 for these years.

Obviously this state of affairs is very unsatisfactory. Lupus is a disease notifiable "under pains and penalties" as one Medical Officer expressed it. We see, however, that notification is far from complete. It is almost incredible that a city like Cardiff should have not a single case of lupus during a whole year. Even allowing for doctors not being quite accustomed to the Order, that state ought to have passed off by this time in England, where the notification has been in force for two years. Though I have mentioned Cardiff, it is not the only delinquent. The other districts show the same deplorable state of affairs.

It is not only as regards actual numbers that conditions are unsatisfactory. In one large English city, tuberculosis is notified as referring to various organs or limbs, and many notifications do not state whether it is the skin or other part of the limb that is affected. One Scottish city is even worse, as the Medical Officer states that lupus **is** not notifiable in that city.

Something is wanted to remedy this. Even though the notification were complete, more requires to be done. Patients frequently disappear for years at a time/

time, and when they return the disease is almost invariably worse. So much valuable time has thus been lost, and it is this which makes people think that lupus is an incurable disease. Provided the case is taken early, and treated thoroughly with the intelligent co-operation of the patient, there is nothing to prevent the disease being cured. That this is the case is shown by the fact that extensive lupus is not seen in the better classes. People in these circumstances seek advice early, and carry out the instructions given with the result that they become cured. It is desirable that the authorities should have some power to keep a hold of lupus patients once these present themselves. We might then be able to prevent these cases that one too frequently sees, of the whole face being covered with lupus and its horrible disfigurement.

To show that this control is required from the point of view of public health, to say nothing of the patient, I may mention a case which was seen in the Skin Department early in 1914, i.e. before notification was in force. This was a patient who had a considerable patch of lupus on her right hand. She kept a dairy and sold the milk therein every day. It is not too much to say that it is highly probable that she has occasionally infected the milk she cells. I may add that, to my knowledge, this patient has not returned to the Skin Department since the date of her original visit. Had the authorities had some power, they might have been able/

able to prevent such a person selling milk, even though they could not compel her to attend for treatment.

With regard to deaths from lupus, no very satisfactory evidence can be got. Lupus is not, as a rule, a disease that kills, and statistics do not throw much light on the subject. Thus, from the years 1892-1904 there were 33 deaths from lupus registered in Scotland. Of these, three occurred between the ages of 5 and 20, seventeen between 20 and 60, while the remaining thirteen cases died after they had reached the age of 60. The statistics, however, do not say whether the lupus was of the larynx, or had led to a general tuberculous infection or not.

<u>DIAGNOSIS.</u> The diagnosis of lupus vulgaris is as a rule easy. The apple jelly nodule, easily penetrated by a probe, is very characteristic. The diseases with which it is usually confounded are syphilis and rodent ulcer. Lupus erythematosus and acne rosacea as a rule give less trouble in diagnosis.

Syphilis sometimes bears a striking resemblance to lupus, and occasionally even the trained eye may be at first puzzled. Generally speaking, however, there are points of difference which enable one to decide. This manifestation of syphilis usually occurs at a later age than lupus, and progresses very much more rapidly. The eruption of syphilis will attain dimensions in a few months that it would take lupus years to attain. The colour/

colour sometimes helps as syphilis is a coppery-red, while lupus is yellowish-red or brownish-red. In syphilis crescentic and serpiginous outlines are usual, while they are uncommon in lupus. The common site of lupus is the face, and though it may appear on other parts, yet it is usually associated with a lesion on the former region. While syphilis also occurs on the face, it occurs on almost any part independently. In ulcerating syphilis, the ulcers may either be shallow or deep, while in lupus they are almost always shallow.

More difficulty occurs in the non-ulcerating forms of syphilis, but again there are various facts which aid one. The history is sometimes valuable. A patient may come of a tuberculous stock or present other manifestations of tuberculosis. On the other hand, in syphilis careful inquiry and examination may elicit the history or evidence of other manifestations.

At times, however, one meets with cases which give no such assistance. Here help may be got from a Wassermann reaction, but even though a positive reaction were got, that does not exclude the possibility of the patient having lupus as well as syphilis. To my mind, a much more delicate and reliable test is the local application of Old Tuberculin in the form of an ointment. This is applied daily for five days, and if the condition is tuberculous, a reaction occurs which will be described more fully in the tuberculin section.

As to rodent ulcer, it is found to differ from lupus/

lupus in the following particulars; it is usually single, begins late in life, and has a pearly roll-like edge. It frequently arises from some pre-existing mole, and when ulceration begins, it almost invariably does so at one point and is often somewhat deep.

Lupus erythematosus differs in the absence of nodules but presents yellowish-gray adherent scales.

Acne rosacea has a different history and course and shows dilated vessels and acne lesions. These are, as a rule, sufficient to establish the diagnosis.

PROGNOSIS. The prognosis of lupus is rather a difficult question. Much depends upon the age of the patient, the duration and extent of the disease, and the care with which the treatment is carried out. It is always a chronic disease and relapses are not uncommon. The social condition of the patient has rather an important bearing as the poorer classes have the disadvantages of want, home conditions, etc. Stellwagon gives it as his experience that small commencing areas of the disease, especially in the young, are readily curable and that, even in more extensive lesions, the final result is satisfactory if treatment is persisted in. One must always be ready for small recurrences at the edges but if these are treated vigorously, they will disappear. The prognosis must be somewhat guarded as some cases are stubborn, no matter what is done. With perseverence, however, great benefit may be obtained and the disease kept in abeyance. One danger must be borne/

borne in mind, and that is that these cases are always liable to a general infection. In some cases death from tuberculosis of the lungs results.

The treatment of lupus is both general and TREATMENT. The local treatment is by far the most importlocal. ant, but the general treatment is by no means to be neglected. The patient must have plenty of fresh air and good nourishing food. He must take plenty of out-door exercise and expose himself as much as possible Medicinal treatment is useful only in so to sunshine. far as it improves the general condition of the patient and enables him more successfully to cope with the existing disease, and prevent the extension of it. Of these remedies I will mention a few. Cod liver oil in moderate doses seems to be by general opinion the This must be given for a prolonged period. best. Other remedies have been praised, such as the hypophosphites, syrup of the iodide of iron, arsenic, creosote, and potassium iodide. One other internal remedy I must mention and that is thyroid extract. Byrom Bramwell was the first to introduce this treatment and got excellent results from it. One patient, who will afterwards be mentioned, derived great benefit from thyroid treatment and various other observers have praised it, Pringle stating that in cases where the hyperaemic or inflammatory element is marked, the result is little short of marvellous.

Of far greater importance is the local treatment, and/

and in this connection various factors must be taken into consideration. Such are the time at the disposal of, and the social status of the patient; but broadly speaking, for lupus of the face and other exposed surfaces, these methods are chosen which inflict least mutilation. The local treatment may be divided into operative and non-operative. Of the operative measures, excision may be first mentioned. This method has been warmly advocated by Lang of Vienna, but has not been generally adopted. To be successful, it must be very thoroughly done, the excision going wide of the apparent disease, and the dissection deep. Obviously this has only a limited application and must be used only with lupus of small extent and on a covered part. The raw surface left after excision may be covered with skin grafts. Excision with skin grafting has been favoured by Nelaton, Brocq and Sabouraud. It has been suggested that an injection of Old Tuberculin be given beforehand to map out the limits of the disease.

Instead of being excised, the part may be scraped. It is only in certain types of lupus that this method is of use, and the catarrhal form of lupus offers the best chance of treatment by this method. The sharp spoon gets rid of the diseased tissue and also the micro-organisms which cause the catarrh. Fibroid lupus is not successfully treated by this method, as the fibrous tissue is too tough to be scraped away. It must be recognised that scraping of itself is not curative/

curative. To lessen the chance of recurrence, the raw surface must be treated. This may be done in several ways. It may be sponged over with zinc chloride to which a little hydrochloric acid is added. Afterwards a dressing of pyrogallic acid in vaseline of the strength of 1 in 4 is applied for four days and then boric compresses. Another way is to cauterise the raw surface with caustic potash in stick or strong solution. In the Royal Infirmary, Dr. Norman Walker has had good results by applying uranium nitrate powder to the raw surface. This is left on till the scab falls off when the result is found to be excellent. In treating lupus by scraping, it must be remembered that the hair follicles sometimes extend deeply, and disease there is not removed and so recurrence frequently takes place.

Linear scarification is a method which has many advocates who say that it is the remedy where mutilation and scarring are to be avoided. It is painful, however, and requires the administration of a general anaesthetic, and it must be repeated at intervals. The lupus patch is covered with close parallel incisions, reaching through the diseased tissue, and then the area is crosstracked in the same way. This latter procedure is thought unnecessary by some, notably Stopford Taylor¹², who believes that by doing so, the epidermis is liable to be torn off, and suppuration ensue. Umna and others object to this method of treatment on the ground that auto-infection is possible, but this does not seem to be/ 20.

be supported by facts.

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Electrolysis may be used in the treatment of lupus and it is said to give excellent results. It is comparatively painless, there is no blood to frighten the patient, and it does not interfere with his work. The sound skin is hardly, if at all affected. The strength of the current is about 7 milliamperes and it is allowed to pass for seven or eight minutes.

The non-operative methods are very numerous and the same substances have been employed in many varied ways to try and cure this disease. The non-operative methods may be divided into the directly destructive and the indirect or mild and stimulating. Of the stronger remedies, among the best is arsenic. This drug has a selective action, i.e. it acts on the diseased tissue, while the normal skin is hardly affected unless the application be continued too long. This remedy is best applied in the form of a paste as recommended by Dr. Walker.

> Acidi Arseniosi grs X Hydrarg.Bisulph.rubr. grs.XXX Ung. Rosae 36

This is spread on cloth and applied night and morning for 5 - 7 days. It causes the diseased part to slough out, and the raw surface left is healed up under a mild ointment. The disadvantage of this method is its pain, which is so great that morphine may have to be administered. Hebra recommends the following: R Acidi Arseniosi grs. XX Cinnabar 3 N Cold Cream

In/

In order to diminish the pain, 5-10 grs. of cocaine muriate may be added.

Various other caustics may be used, such as fuming nitric acid, zinc chloride, and acid nitrate of mercury. Silver nitrate is less satisfactory than the cautery, the caustic action being so superficial that the remnants of the disease are almost invariably left behind and lead to recurrence. Similar in action but not quite so actively destructive are other drugs such as salicylic acid, resorcin, and pyrogallic acid.

Salicylic acid may be prescribed in several ways, but the best way to employ it is in the form of a plaster. Unna's salicylic creosote plaster is excellent for this purpose, the creosote lessening the pain of the application. It is made in several strengths and the strongest that the patient can stand ought to be employed. The plasters are changed night and morning and soon the nodules slough out. After this is accomplished, Dr. Walker recommends the continued application of the . plaster till the part heals under it, as in this way the result is much more thorough and lasting. Many patients, however, cannot bear this and more soothing remedies must be employed, but the longer the surface is kept open, the better the result is.

Other ways of prescribing salicylic acid are in collodion, 30-60 grs. to the ounce; mixed with sufficient glycerine to make a paste; or in ointment form in the strength of 2-3 drachms to the ounce.

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Resorcin is generally used in ointment form, and as/

as a rule, the application is not painful.

Pyrogallol may be employed as an ointment: 10% is the strength usually recommended, but Stellwagon believes that it must be used at least 25% to secure an effective result. It may also be used as a guttapercha plaster as recommended by Unna, or in ethereal solution as a spray, the powdery deposit being immediately covered with a coating of Liquor Gutta Percha.

Carbolic acid may be used as a destructive agent. A dentist's burr or a wooden match sharpened is dipped into pure carbolic and then forced into the nodule. This is done repeatedly with the individual nodules, until all have disappeared, but a watch must be kept on the patient, to attack any fresh nodules which may appear. Instead of carbolic acid, the acid nitrate of mercury may be used.

Another excellent remedy is trichloracetic acid. It should be painted on lightly and re-applied in about a week's time when the crust has disappeared.

Dr. Walker¹³ for some time used uranium oxide in the treatment of lupus. This was made into a plaster and applied at night, being removed in the morning. The results were distinctly encouraging. More recently, however, he has used the nitrate. The best results seem to be obtained when it is applied to an open surface, such as that left after scraping, after treatment with salicylic creosote plaster, or after the application of tuberculin ointment. The powder is applied and a crust forms which is allowed gradually to/ to come off. It is possible that, in addition to the caustic action, there may be some radio-activity which helps to give the excellent results. The milder remedies are used with a view to exciting a reaction, and it is this reaction that destroys the lupus. Of these remedies oleate of mercury has a leading place. The formula used in the Skin Department is a modification of Brooke's and is as follows:-

R	
Hydrarg. Oleatis	grs. XXX
Ichthyolis	m XXX
Acid Salicyl.	grs. XX
Vaselini	38
Lanolini	ad Rit
	34

This is known in the Department as the brown ointment and will be referred to frequently later. The patient is instructed to rub it into the part for half an hour night and morning.

Mercury in other forms may be used also. It may be employed in the form of corrosive sublimate in the form of an ointment 1%, gutta percha plaster 1%, a lotion 1%, or an injection. In the latter, the sublimate is injected in the strength of a $\frac{1}{2}$ - 1% solution, and the results are said to be good. Calomel has also been used in lupus. Scarenzia¹⁴ injected 10 cgr. into the buttock for lupus of the face. 5 cgr. were given twenty days later with marked benefit.

Potassium permanganate has been used both indirectly and directly. Butte¹⁵ of Paris uses compresses of a 2% solution of potassium permanganate applied for 10-15 minutes every day for a fortnight. Hall Edwards¹⁶ uses/ uses a saturated solution either alone or with X-rays and finds it useful. He paints the active parts again and again till they disappear. Isolated nodules may be treated in the following way¹⁷. Novocain and adrenalin are first injected into the area. A hard wooden pointed skewer is then driven into the part by a rotatory motion. The hole left by the skewer is packed lightly from the bottom with potassium permanganate, and a drop of water is applied to the surface. This has a caustic action. A few hours later the surface should again be wetted. The plug of permanganate sloughs away in the course of a week or two, and the spot rapidly heals.

Kachanovsky¹⁸ of Petrograd employs powdered potassium permanganate. The powder, freshly prepared from dehydrated dried crystals, is applied in a layer 3 - 5 mm. thick over the whole surface of the lupus and the suspected portions of the surrounding tissue. In the case of deep ulcerations, the powder is applied after curetting two or three times to level the uneven surfaces.

Carbolic acid when painted on the surface is placed by Unna in the front rank of remedies for lupus. It may be used also as a plaster or as an ointment in the strength of 1 - 15 or 1 - 20. The usual carbolic precautions must be employed, treat small areas, never cover with gutta percha tissue, watch urine, etc.

Liquor Antimonii Chloridi is also useful. After a/

a few days, the part becomes so painful that the treatment must be stopped. It is specially valuable in the fibroid form as it removes the complication and the disease. Ortho, meta, and para kresole act like carbolic, but with no special advantage over it. Coal tar creosote and beech tar creosote are similar. Zérénene¹⁹ used the beechwood product with good results. He employed it pure in compresses, or in a 10-30% solution in oil or glycerine.

Aniline oil may be used as it renders the surface of the lupus transparent. Individual nodules can then be treated, e.g. with a fine pointed cautery. It tends to neutralise the pain of the carbolic application. It is useful as an anodyne addition to those caustics which are not covered with an impervious dressing. Oil of cloves is sometimes used in covered compresses. The nodules thus treated finally suppurate, the lupus tissue at the same time breaking down painlessly. Camphor is excellent for healing the surfaces after the application of the phenols or clove oil. It has, according to Unna²⁰, a powerful keratoplastic effect, and appears in its concentrated form to develop a directly destructive action on the lupus. It prevents and removes inflammation, cleansing the nodules broken down by other remedies; it possesses anodyne properties. Unna used it rubbed down with oil of cloves into a paste, as a salve mull, and combined with chloral/

chloral.

Hardy²¹, the successor of Bazin at the St. Louis Hospital, made the observation that facial lupus disappeared after an attack of erysipelas. He tried to produce a severe local artificial inflammation by using an ointment of the biniodide of mercury in various strengths. This plan was soon discarded on account of the uncertainty of the result which would be produced.

Dreuw²² mentions a treatment of lupus used in Unna's clinic. The patch is frozen with ethyl chloride and then crude hydrochloric acid is forcibly rubbed into the frozen surface by means of a swab. This makes the surface whitish gray. As soon as the patient complains of burning pain the patch is frozen again and the acid reapplied. Single nodules can be bored into by a sharpened stick dipped in the acid after freezing. The patch is dressed with a dusting powder and covered with a bandage. A crust forms in two to four days and falls off in eight to fourteen days. In three to four weeks it is said that there is a smooth surface. Any nodules left can be treated as above.

Good results²³ are said to follow the treatment of lupus by local subcutaneous injections of a 1-2% aqueous solution of gold chloride, and of a similar solution of potassium cyanide, the dose of the former varying from $\frac{1}{1000} - \frac{1}{100}$ gr., and of the latter from $\frac{1}{1000} - \frac{1}{200}$ gr. The/

The injections were given daily or every other day; ulcers healed, pain ceased, and discharge lessened. Sulphurous acid has been used in the treatment of lupus, but opinions vary as to its value.

MacKie²⁴ of Elgin used bismuth subiodate with apparently good results. The crusts and scabs were first removed, and the surface then irrigated with a solution of iodic acid, strength 1-500, and while still wet, the subiodate of bismuth is dusted on.

Moreau²⁵ of Toulouse used subcutaneous injections of guaiacol and thymol, or guaiacol and aristol. The latter is more painful.

Hollander²⁶ employed air heated to 300°C. in the treatment of lupus. He also tried steam, but the patients were unable to stand a temperature sufficiently high to affect the diseased tissues. The latter method cannot be easily controlled.

Injections of thiosinamin have been recommended by Hebra Jr.²⁷ using a 15% alcoholic solution of which the initial dose is m iv increasing to m xv. An injection is administered every two or three days.

Pfannenstill²⁸ of Sweden introduced the treatment of lupus by nascent iodine. He gave sodium iodide internally, and surrounded the patient with an atmosphere of ozone. Later he substituted a solution of hydrogen peroxide for ozone. This treatment applies chiefly to nasal and laryngeal lupus. This method was also applied to the skin, but it was by electrolysis and not by hydrogen peroxide that the iodine was produced.

Sequeira/

Sequeira²⁹ also uses this treatment. He gives 45 grs. of sodium iodide per diem and a tampon is put into the nasal cavity and kept moist with hydrogen peroxide. Ulcers usually heal in two to three weeks. Recently it has been suggested that the patient should have an exposure to radium after taking the iodide. This produces the iodine and this method is available for cutaneous lupus.

Albert Carless³⁰ of London used Colley's fluid to treat lupus. This was injected into the neighbourhood of the disease, but also into the healthy tissue around. The results were said to be beneficial.

Zinc ionisation has been used by Stopford Taylor³¹ with apparently good results.

Scatchard³² reports a case of lupus which was treated by painting the parts with a solution of formalin and glycerine in equal parts, having dusted orthoform powder on the parts about an hour before to lessen the pain.

Lupus has also been treated by freezing the part with ethyl chloride without previous scraping. During the first week of treatment, the freezing was done daily, later every second or third day. After each freezing there occurred serous effusion which soon died up into a scab. This was removed before the next freezing. After ten weeks, the ulceration was healed, the lupus nodules had disappeared, and the whole was covered with smooth skin of almost normal appearance. Freezing/ Freezing may be done with CO₂ snow. Opinions seem to vary as to the value of this treatment, but Dr. Cranston Low⁵⁵ thinks the results encouraging. He applies the snow with considerable pressure for 30 - 45 seconds, and for 60 seconds in cases which have not been X-rayed. I shall mention later a case which was treated in this way with good results.

When lupus is confined to the limbs, Bier's congestion may be used with beneficial results.

Recently an article appeared in which it was stated that it had been found possible to combine two of our best antiseptics, iodine and oxygen, in a stable form as a powder called "Ulsarin". Ulsarin is a nonpoisonous bright yellow powder, hygroscopic, and when placed on the open palm it immediately becomes brown and emits a strong odour of iodine. It splits up, if in contact with any moisture, into iodine and nascent oxygen. Leonard has tried this powder in a very obstinate case of lupus vulgaris. The patient, a woman of 29, had suffered from lupus of the right cheek and latterly of the nose for sixteen years. She had been treated by most of the accredited methods - scraping, Finsen light, pyrogallic acid, cauterisation, etc. -. with temporary improvement but constant relapses. She was somewhat ill-nourished and pale. The lupus consisted of nodules, patches and ulcerations. He treated the spots and ulcers by applying the powder daily. The parts to which it was applied assumed a dusky brown colour. The disease disappeared in shreds, as if wiped away/

away. After two months the further use of the ulsarin was abandoned, but a few remaining miliary nodules were destroyed with the galvano-cautery. Two injections of old tuberculin gave no reaction, and to appearance the patient seemed cured. The treatment was begun in August and it was then October. The remedy appears worth further trial.

The treatment of lupus of the mucous membranes has to a certain extent been touched upon in the foregoing remarks. There is one remedy, however, which has not been mentioned and which is very effective; that is, lactic acid. When the lips or the gums are affected, this should be painted on every day and the results are very gratifying.

Towards the end of last century, Finsen introduced that treatment of lupus which bears his name. This treatment is based upon the properties of the chemical rays of light, blue, violet and ultraviolet, and especially the two latter. These rays have a bactericidal property, have the power of producing inflammation of the skin, and have the power of penetrating the skin. It is only when sunlight is concentrated in such a manner that it contains as many chemical rays as possible, that Widmark³⁵ it has this powerful bactericidal property. of Stockholm was the first to demonstrate the power of these rays to produce an inflammation of the skin, though even in 1859 Charcot had expressed the opinion that erythema solare was due to the violet and ultraviolet/

violet chemical rays. Widmark concentrated electric light into parallel rays by means of a quartz lens, and applied them to the skin after either passing through a layer of distilled water which absorbs the heat rays, or through a glass plate which absorbs a large part of the ultra-violet rays. It did not matter whether the heat rays were present or not; on the other hand no inflammation appeared when the ultra-violet rays were absorbed.

Godmeff and Finsen³⁶ investigated the penetration of these rays. Godneff placed under the skin of dogs and cats small sealed glass tubes containing muriate of silver. Some of the animals were exposed to direct sunlight, while the rest were kept in the dark. After an hour, he took out the tubes. It was found that the muriate of silver was blackened in these animals exposed to the sun, but not in these kept in the dark.

Finsen proved that they penetrate far more easily in bloodless tissues than in these filled with blood. He placed a piece of sensitised paper on one side of a man's ear, and concentrated the blue and violet rays of the sun by means of his apparatus on the other side of the ear. After five minutes this paper was not affected; on the other hand, the paper was distinctly blackened in twenty seconds, if all the blood were pressed out of the ear between two glass plates.

Finsen utilised these properties in the treatment of lupus. For treatment by sunlight, he used a special lens. This had a plain glass side and a curved one. These/ These were framed in a brass ring, and between them was placed a bright blue weak ammoniacal solution of copper sulphate. This absorbs the heat rays but lets the chemical rays through almost unimpaired. He also used arc lamps of 50 - 80 amperes. The rays from these lamps were concentrated by a special apparatus. Briefly, this was a telescope, the large end of which was placed next the lamp, having lenses made of quartz or rock crystal, which itself can absorb heat rays. Between two such lenses was a length of tube filled with distilled water, and around this, cold tap water was made to circulate.

These rays, after leaving either apparatus, are still too warm to be applied to the skin. They are, therefore, made to pass through a small lens with a plain and a curved surface. Between these surfaces a stream of water is kept flowing. This lens is pressed against the skin and so renders the part anaemic, thus letting the rays penetrate more readily.

Using such apparatus, Finsen treated lupus with such success, that patients went to him from all over Europe. The treatment was given for one hour daily, using fifty amperes. The results were excellent, the scar being pliant and good. The following statistics³⁷ show how successful this treatment was. They refer to cases treated at the Finsen Institute and relate to 804 patients in whom the average duration of the disease was eleven years:-

Cured/

Cured - 412; very nearly cured - 192;

Under treatment - 117; treatment stopped - 83. Of these cases, 695, or 94%, were favourably influenced by the treatment. Where small areas were diseased, cures were obtained in 73%, whereas in extensive cases, there were only 23% cures.

The best cases for the Finsen treatment are those in which the disease is not spreading, is limited to a small area, is superficial, where there is little pigmentation, and where it has not undergone any previous treatment, especially operative.

The drawbacks to the Finsen method were the long duration of treatment and the cost. With regard to the former, the average duration of treatment was estimated at four months with an hour's sitting every day, while Morris states that a year is required to treat an extensive case.

Following the success of Finsen, this treatment was adopted in various places, and various modifications were made in the lamp used, such as the Finsen-Reyn, Genoux-lortet, the London Hospital, Bang, Dermo, Foveau, and Trouvet.

Various other modifications of the treatment were introduced, chiefly with the intention of intensifying the rays, or allowing them to penetrate more easily. ' Thus Dr. Allan Jamieson³⁸ used a solution of adrenalin to blanch the skin and so allow the light to act better. Sequeira³⁹, who believes that phototherapy is much superior/ superior to X_rays, sensitised the tissue by painting the part with a 1% solution of erythrosin. Graham of Shadwell⁴⁰ used aesculin in addition to the Finsen light. He injected 1-5 minims of a 5% solution immediately under the spot to be treated. The reaction lasts from four in to seven days instead of being over/three days as is usual with the Finsen treatment. Aesculin is a fluorescent substance and Graham suggested that its action is purely physical. It absorbs ultra-violet rays and gives them off again in the wave lengths corresponding to the violet and blue, and, by causing a local excess of concentration of these rays at the time the light is applied, and by its prolonged fluorescence in the tissues afterwards, clears up the nodules more rapidly than the arc light alone.

The use of a pyrogallic ointment in addition to the Finsen is recommended. A 5% ointment has been used for a week, and then the part is allowed to heal before the light applications are begun. By this means the thickening is reduced and the light can penetrate more easily.

For some time past, Dr. Walker has been using the Kromayer mercury vapour lamp, and the results obtained have been very satisfactory. The lamp is pressed against the part to render it anaemic and a current of five amperes is allowed to flow for ten minutes. The patient does not experience any pain during the application. As a rule, a blister is raised and this is dressed with a weak/
weak ammoniated mercury paste till it heals. Opinions differ as to the painlessness of the Finsen treatment, but with the Kromayer lamp no complaint has been made; a certain feeling of fulness prevails, but no patient has had any pain. So pleased are the patients with the result of the treatment, that they ask if it cannot be extended to other parts. One patient, to be referred to later, had lupus on both sides of the face; she was receiving tuberculin injections, and the lamp was applied to one side only. Though the general improvement of the condition was great, the side which was lamped showed a more striking improvement, so much so that the girl's parents wished the lamp applied to the other side also. The photographs here shown illustrate







January 9, 1915.

well the result of treatment with the lamp. This patient/

patient, a girl of 14, had the disease for thirteen years. It got steadily worse in spite of all treatment till in January 1914 the condition was that shown in the first photograph. It remained about the same till May when the lamp was applied for ten minutes to two areas at the posterior part. She returned in June and the note made on the card was that the face was better where the lamp was applied. Since then she has come up regularly once a month to have the face lamped. In the intervals, she uses the brown ointment after the reaction caused by the lamp passes off. The present condition is shown in the second photograph, and there can be no doubt that there has been a striking improvement. These photographs incidentally show the difficulty of attacking places where the ordinary front of the lamp is unavailable, e.g. close to the nose. To overcome this, accessory parts may be fitted to the These have smaller areas but the time these lamp. have to be applied is longer, extending to about twenty minutes to obtain the same reaction.

Direct exposure to the sun's rays is excellent, where the sun is available. This method of treatment was mentioned at the Congress on Tuberculosis held at Paris in 1905, but it has not much scope in this country. Tomkinson⁴¹ of Glasgow mentions a case very successfully treated by exposure to the Egyptian sun for five hours nearly every day for four months. Williams⁴² treated a case by constantly painting the face with eosin, and exposing it to the sun for about two hours. In a month/

month there was distinct improvement.

With regard to the permanency of the treatment, some think that recurrence is more frequent than after X-rays because the Finsen rays have less penetrating power, but this opinion is not held by all, e.g. Jacobi, who believes that the Finsen treatment gives the best result both from the cosmetic and actually curative points of view.

When X-rays were introduced into medicine, various observers used them in the treatment of lupus. The results of such tentative treatment were excellent, and the rays were then extensively used. X-rays diminish oedema and lessen the thickening, while ulcers heal up rapidly. So striking were the results, that X-rays, along with the Finsen light were almost exclusively used in the treatment of lupus in the early part of this century. Observers differ in the dose they recommend; some say that the dose should be such that a moderate Stellwagon⁴³ and continuous reaction is brought about. goes so far as to say that it is sometimes necessary to produce a dermatitis of the second degree - vesiculation or serous exudation - before an impression is made on the disease. Other observers only bring about a reaction where the disease is limited, and where it is extensive, the case should be kept just below the level of reaction. One thing all are agreed about, and that is the need for great caution in X-ray treatment. There seems to be little room for doubt that, since X-rays were used in the treatment of lupus, the development of carcinoma/

carcinoma has become much more common. It is true that carcinoma develops on lupus which has never been subjected to X-ray treatment, and I append a photograph of such



Margaret D. Lupus Carcinoma.

a case. While that is admitted, it seems that we must also admit that it is more frequent in cases which have had considerable X-ray treatment. Among the cases of lupus treated in the Skin Department, there have been 22 cases of lupus carcinoma and at least six have died. Five of the twenty-two had no X-ray treatment, while the remainder had, some of them very prolonged, ray treatment. I show a photograph of such a case. This girl had prolonged X-ray treatment in a hospital in another town and the photograph shows the condition when she first came to the Royal Infirmary. Incidentally the/



Grace Y. X-ray Carcinoma.

the photograph shows another disadvantage of this treatment, viz. the telangiectasis which so often results.

The advantages of X-ray treatment over the Finsen light are as follows. A large surface can be treated at one time. Ulcerating surfaces can also be treated to which it would be inadvisable to apply the Finsen light. Another great advantage is that it can also be applied to the mucous membranes.

Before passing to the treatment of lupus with Tuberculin, it may be of interest to show the history and vicissitudes of that remedy.

At the International Congress of 1890, Koch mentioned that he hoped soon to announce a remedy for tuberculosis. All waited eagerly for the news, but it was not till November of that year, that Koch made his discovery public. In his famous address⁴⁴, he said that he had a substance to which all tuberculous persons were extremely sensitive/

sensitive, though a healthy person could stand a large dose without any result. This remedy was of the nature of a fluid which was injected into the patient. The following description of the fluid and its action is quoted verbatim from Koch's address. The fluid is brown and transparent, and does not require special care to prevent decomposition. For use, however, the fluid has to be diluted, and the dilutions are liable to decomposition if prepared with distilled water; bacterial growths soon develop in them, they become turbid and are then unfit for use. To prevent this, the diluted fluid must be sterilised by heat, and preserved under a cotton wool stopper, or, more conveniently, prepared with a 1/2 solution of phenol.

Koch stated that .01 c.c. of the fluid or 1 c.c. of a 100th dilution was the smallest dose requisite to produce a reaction in a healthy person. When this dose was injected into a tuberculous person, a severe general reaction, as well as a local one, followed. The general reaction consists in an attack of fever, which, generally beginning with rigors, raises the temperature above 103, often up to 104 and even 105. This is accompanied by pain in the limbs, coughing, great fatigue, often sickness and vomiting. The attack usually begins 4 - 5 hours after the injection and lasts 12 - 15 hours. Occasionally it begins later and then runs its course with less intensity. The patients are very little affected by the attack, and as soon as it is over, feel comparatively well, generally/

generally better than before it.

The local reaction can best be observed in cases where the tuberculous affection is visible, e.g. lupus. A few hours after an injection into the back, that is, in a spot far removed from the diseased part, the lupus spots begin to swell and redden, and this they generally do before the initial rigor. During the fever, the swelling and redness increase and may finally reach a high degree, so that the lupus tissue becomes brownish and necrotic in places. Where the lupus is sharply defined, we sometimes find a much swollen and brownish spot, surrounded by a whitish edge, almost a centimetre wide, which again is surrounded by a broad band of bright red.

After the subsidence of the fever, the swelling of the lupus tissue gradually decreases and disappears in about 2 - 3 days. The lupus spots themselves are then covered with a crust of serum, which filters outwards and dries in the air; they change to crusts which fall off after 2 - 3 weeks and which sometimes after one injection only leave a clean red cicatrix behind. These changes are exactly confined to the parts of the skin affected with lupus, though even the smallest nodules go through the process. Similar changes occur in tuberculosis of other tissues.

After this epoch-making announcement, medical men from all over the world, and patients suffering from tuberculosis, flocked in great numbers to Berlin. So great was the number of the latter that they became a danger/ danger to the public. Enthusiasm ran high and all were in great hopes that a remedy for the white scourge had at last been found. Physicians and surgeons all wanted some of the precious fluid in order that they could test it. A few of Koch's friends were able to obtain it, Koch only giving it to such men as could be relied upon to test it thoroughly.

This unbounded enthusiasm continued for some weeks and then doubts began to be expressed. Reports of deaths under the treatment began to be circulated, and even before the end of November the enthusiasm began to give way to uncertainty. About that time medical journals began to express surprise at the moderate and somewhat vague terms in which the remedy was spoken of, compared with the more enthusiastic language first held, and before the middle of December the opinion was formed that discouragement was taking the place of enthusiasm, and that the remedy had not fulfilled all the qualities claimed for it. From that time the enthusiasm waned and the remarks of Professor Gairdner in the Spring of 1891 describe the situation. "Few would be disposed to deny," he said, "that they were in the very trough of a wave of reaction or rather of discouragement from the hopes and expectations entertained in November last." After the first few months of 1891, tuberculin treatment was almost entirely given up, and its name was almost forgotten.

It was not without considerable opposition that Koch's remedy was tried. Not only the authorities in some/ some places, but even the medical men, objected to its use on the ground that it was a secret remedy. In the province of Milan⁴⁶, a domiciliary visit was paid to all the persons who possessed the lymph, the object being to confiscate it. This visit was unsuccessful and all those whose names were advertised as possessing it, were summoned to surrender it. In Russia also, the same objection was held, and even in this country some men refused to use it because the composition and nature of the fluid had not been made public.

With regard to the efficacy of Koch's treatment, there was a great difference of opinion. Koch's immediate followers and assistants reported cures of all kinds of tuberculosis, including lupus, one case of the latter being, it was said, cured in five days. Other observers, too, quoted cures of lupus in some cases, and improvement in others. In this connection, the remarks of Piffard⁴⁷ of New York are not uninteresting. He said that the cases of lupus at first treated with tuberculin were treated almost exclusively by those whose experience lay with pulmonary rather than with cutaneous tuberculosis, and that few, if any, of these cases were really cured. Jonathan Hutchinson⁴⁸, in an address on lupus, stated with regard to the tuberculin treatment, that all his friends reported that where the lupus patch was made to inflame, the results were definitely good, but no one ventured to report a cure. He did not think that prolonged periods of treatment would/

would be of more use than short ones. Unna is numbered among the supporters. He said he did not have the exaggerated ideas of what tuberculin would do for lupus, and he admits that his slight expectations have not only been fulfilled but even surpassed.

Virchow was perhaps the leader of the opposition. He stated that he had performed necropsies on patients who had died as the result of the injections. According to him, old tubercles were left entirely unaffected by the treatment, while new ones sprang into existence. He admitted, however, that some would have died without the injections. No case of lupus occurred among the necropsies. Lichman⁴⁹ of Trieste said that after one or two injections, the blood of phthisical patients contained tubercle bacilli where none formerly existed. The Physicians of the St. Louis Hospital appointed a commission to report on tuberculin and this report was adverse. Leslie Philips⁵⁰ of birmingham criticised this report on the ground that the Physicians did not persevere sufficiently with tuberculin.

In spite of all these adverse criticisms, some workers used tuberculin steadily, and McCall Anderson was one of these, being the only one or nearly the only one in this country to do so. In 1898 he said⁵¹ that after a wide experience, he saw no reason to depart from the opinion he expressed in 1890, that the discovery of tuberculin "marked the commencement of a new era both in diagnosis and therapeutics".

In spite of all opposition and discouragement, Koch,/

Koch, not being satisfied with the Old Tuberculin, worked away to produce a tuberculin which should immunize against the bacilli as well as against their toxins. In April 1897, he introduced that type of tuberculin known as T.R. This preparation gave a stimulus to tuberculin treatment for a time, and again there was a set back; some said that there was great benefit after using it, while others said there was little or no improvement. Heron⁵² was a great believer in T.R., and thought it of more use than any other drug in the curative treatment of very early stages of tuberculosis affecting the skin or lungs. It was used in a quiet way and then came into prominence again when Wright introduced his opsonic index for controlling the results. Since then tuberculin has been more freely used; especially has its use increased during the last few years, until to-day it is quite a usual method of treatment. The dose of T.R. which Koch recommended was 500 mgr., but it is not usual to give this dose to start with now. 2000 mgr. is the initial dose generally given, and that and 1000 mgr. may be given over prolonged periods at intervals of fourteen days. I think that where lupus is steadily treated with T.R., there is no doubt that great improvement may be brought about. If there is no improvement, it is, according to Sir A. E. Wright⁵³, because the skin is too poorly supplied with blood so that the anti-bacterial matters are not able to act upon the tubercle bacilli.

Besides the characteristic reaction which has already/

already been described as following an injection of Old Tuberculin, various other effects have been noted. Koch mentioned an icteric tinge and an eruption like measles occurring. Burney Yeo⁵⁴ described a rash like that of scarlet fever, which was followed by desquamation, another was raised and patchy. The occurrence of diarrhoea was frequently observed in children. Philip sam an exanthem something betweem a roseola syphilitica and measles, but in other cases more papular. A few of his cases were uncommonly pale, loss of consciousness was not uncommon, while in a few cases epistaxis occurred. A papular itchy eruption has been described, while Cornil ⁵⁶ had two cases in which haematuria occurred. Neumann⁵⁷ drew attention to the appearance of a bullous eruption, while Heron⁵⁸ mentioned a case in which a purpuric eruption occurred. Herpes labialis, inflammation of the cornea and conjunctiva, and albuminuria have also been described. With regard to the albuminuria, in some cases it seems to be of the febrile type, occurring at the height of the reaction, but I have noticed that it also occurs where there is no temperature, and in these cases it is possibly toxic. One patient after going home, had what seemed a menstrual discharge, though the menopause had occurred some years earlier. It is possible that there may have been some tubercle of the genital tract, but there were no symptoms, and before the matter could be cleared up, the patient ceased to attend. Unusual symptoms following the injection have been described, such as jaundice, pain/the region of/

of the heart, spleen and bowels. In some cases no reaction has occurred after the injection, though there has been no doubt as to the nature of the case. In these cases, it is possible that the patient was too weak and not able to react. It is not uncommon to get a local reaction but no general reaction. More unusual is it to get no local reaction though the temperature rises.

With regard to the specificity of tuberculin, there was a great difference of opinion. Koch stated that its action was on tuberculous tissue alone. Most observers support this view but there is quite a number who oppose it. Professor Crocq said that there was no evidence to show that it was other than a pyrotogenous agent which produces local reaction by specially acting on the locus minoris resistentiae. Hutchinson stated that the lupus nodule was often left uninfluenced while the inflammatory swelling was affected. Further, he held that if this view were supported, we would be obliged to suspect that the remedy was one for certain conditions of the inflammatory process and not for tuberculosis. It is quite possible, however, that the lupus nodule may not be affected, e.g. when it is shut off from the circulation by scar tissue. The tuberculin cannot then penetrate to the disease. McCall Anderson⁶⁰ suggests that in such cases the nodule be penetrated with a stick of caustic, and then the inoculation will cause a certain amount of reaction. Bristowe⁶¹ thought that/

that any poisonous influence evoking high temperatire would tend to cause aggravation of inflammation in parts already the seat of inflammatory mischief. Against this view, it may be pointed out that injections of salvarsan evoked high temperature but did not have any effect in causing an increase of inflammation in parts already inflamed. Wheaton thought that Old Tuberculin acted as a septic poison, while Klein⁶³ held that it did not act on tuberculous tissue, but that it caused an increase in the power of exciting inflammation and suppuration possessed by strepto- and staphylo-cocci. It has been said that other diseases besides tubercle react to an injection of tuberculin. Among these so mentioned are leprosy, chilblains, lupus erythematosus and eczema. It has also been pointed out that, while this may be the case, yet the reaction is of a different character, one observer stating that whereas tuberculin improved tuberculous lesions, it tended to make nontuberculous ones worse.

The chemical nature of tuberculin has been the source of difference of opinion also. Koch stated that it was a glycerine extract of purecultivations of tubercle bacilli. He thought that the active principle was a derivative of albuminous bodies, but that it did not belong to the group of so-called toxalbumins. Hunter⁶⁵ states that tuberculin owes its activity to at least three or probably more different substances. Its active ingredients are of the nature of albumoses, alkaloidal substances and extractives, and the action of/ of these is in certain instances antagonistic. Its remedial and inflammatory reactions are connected with the presence of certain of its albumoses, while its fever producing properties are chiefly associated with substances of a non-albuminous nature. The fever produced by tuberculin is unessential to its remedial action, nor is the inflammation necessary though it sometimes helps. Hunter⁶⁶ succeeded in obtaining a substance which would have the healing effect of tuberculin without inflammation.

How does tuberculin act? There are various theories as to the nature and mechanism of the tuberculin reaction, but there does not seem to be any general acceptance, though the majority of such theories assume the specificity of the tuberculin reaction and of tuberculin itself. Koch stated at the outset that tuberculin did not kill the tubercle bacilli but that it acted on the tuberculous tissue, and caused it to break down. He believed that the bacilli in the body produced a substance which caused the tissues round them to become necrotic. When this stage was reached, the conditions became unfavourable to the nutrition of the bacilli, so that they could not develop further and finally died off. Koch thought that if this necrosis-producing substance were artificially added to the body, the necrosis would extend further and the conditions of nutrition of the bacilli would be made more unfavourable than is usually the case. The more completely/

completely necrosed tissue would then slough, and where this is possible - would take with it the enclosed bacilli, carrying them outward, and the bacilli left would be disturbed in their growth to such an extent that they would die off much sooner than under ordinary conditions. This view of Koch's is not now held.

Ehrlich⁶⁷ believed that the reaction was localised to the middle of the three cell layers which encircle the tuberculous focus. The production of antibodies took place in this layer, which had been damaged by the bacillary toxins, but not so badly as to prevent it reacting. This production of antibodies was the essential part of the mechanism of the reaction.

Wassermann⁶⁸ thought that the reaction was after the nature of complement-fixation. The antibodies, produced in the neighbourhood of the tuberculous focus, extract the whole of the injected tuberculin out of the blood and concentrate it in the tuberculous focus. With the union of the antigen (tuberculin) and the antibody, a fixation of complement occurs, and with this a new production in the tuberculous focus of those elements such as leucocytes and ferments which have the property of digesting albumen and so producing softening of the affected tissue. This he believes to be the nature of the focal reaction, and it is generally accompanied by fever, the result of the absorption of softened tuberculous tissue.

Wolff/

Wolff Eisner's⁶⁹ theory is a modification of Wassermann's. He believes that tuberculin itself is of low toxicity but that it is split up into highly toxic bodies by an antibody already in the tuberculous body. The split up tuberculin or lysinized tuberculin is what causes both the general and focal reactions. Bandelier and Roepke believe that the curative action of tuberculin depends mainly on the production of a tox-immunity and the local hyperaemia. They hold that phagocytosis in Metschnikoff's sense has an important role to play in the mechanism of immunity in tuberculosis during specific treatment. According to them⁷¹, the local action of tuberculin must be conceived as follows: first of all, general infiltration of the diseased tissue with blood and its corpuscles, followed by the carrying away of the inflammatory elements by the blood and lymph circulation when the hyperaemia abates; repetition of these processes, leading to a gradual complete absorption; finally, where the tuberculous change in the tissue has reached a stage where absorption is no longer possible, softening and breaking down.

Hunter⁷² believes that the action of the remedial substance is mainly on the cells, and the chief results of their increased activity is to cause absorption of the tuberculous tissue, the changes pointing to an increased activity of the leucocytes.

Tuberculin has been used in many different ways. Koch gave it hypodermically, but it has also been given in other ways; these are the intravenous, intrapulmonary, by/

by inhalation, per os, per rectum and per cutem. Koch himself recommended the intravenous method, and Jacob the intrapulmonary. Kapralik and Schroetter 73 drew attention to the employment of tuberculin inhalation for producing immunity, but the dosage in this way is very uncertain, and the total amount of the drug used is great, while only a very small part of it is effect-Freymuth⁷⁴ used tuberculin per os ively utilised. in the form of keratinised pills, but the absorption from the alimentary canal is relatively inert. Tuberculin has also been given per rectum in the form of suppositories and enemata. Spengler⁷⁵ employed an application per cutem in the case of very weakly phthisical patients with fever and hypersusceptibility to tuberculin, mostly infact children. Unna⁷⁶ has had favourable results in lupus by means of a soap made up of lard incompletely saponified by caustic potash and containing 5-20% tuberculin. The most usual way, however, is the hypodermic. This is the most convenient and by this method one can regulate the dose with more precision.

A great many different kinds of tuberculin hawe been introduced and of these I will mention the most important. Most of them are prepared on the assumption that tuberculin is an active immunizing agent. By this is meant that after an injection, the organism must carry through a reaction due to the introduction of the products of the tubercle bacilli, and this reaction leads to the appearance of protective bodies. The/

The body, therefore, to be able to produce antibodies must have a certain store of strength. The want of this strength may be the explanation of these instances where an injection did not produce a rise of temperature.

First of all, there are the preparations of Koch. He had an unconcentrated preparation at first and this is known as T.O.A. Then came the O.T. and later the T.R. Another preparation is the Bacillary Emulsion and it is thought by some observers to be the most efficacious of all his preparations. These are all prepared from human bacilli, but there are corresponding bovine preparations. These are known as P.T.O., and P.T.

Krause⁷⁷ believed that every tuberculous subject houses his own specific disease producer, and that treatment must be conducted with tuberculin produced by the patient's own bacilli. This method, however, is impracticable on a large scale.

Denys⁷⁸ filtered tubercle cultures through porcelain and avoided boiling the filtrate, assuming that useful toxins were thereby destroyed. This tuberculin is nothing else than Koch's original non-concentrated Old Tuberculin, and it does not seem to have any superiority over the concentrated solution.

Landmann⁷⁹ has a preparation known as Tuberculol. It contains the toxins of the culture fluid, as well as those of the bacterial bodies. He lays great stress on prolonging the treatment.

Klebs/

Klebs⁸⁰ has several preparations. He thought that there was something harmful as well as curative in tuberculin, and this he split off by alcohol and bismuth. To the resulting preparation he gave the name of Tuberculocidin. As this was not yet pure, he prepared a purer substance by precipitating the filtrate of a tubercle culture with sodium-bismuth-iodide in acetic acid and absolute alcohol, and this he called Antiphthisin. He has other preparations also, such as selenin for mixed infection cases. He recommends that all cases should first be treated with tuberculocidin-selenin, and then tuberculo-sozin, a substance obtained from dead tubercle bacilli by extraction with glycerine. Opinions vary as to the value of these preparations.

Béraneck's⁸¹ Tuberculin is composed of extracellular toxins of a broth culture of special formula, and of intracellular toxins extracted from the protoplasm of the bodies of the bacilli with 1% orthophosphoric acid. This tuberculin has been greatly praised by Sahli and, in this country, is probably the most widely used after Koch's preparations.

Spengler⁸² believes that the toxins of bovine tuberculosis are less toxic to tuberculous man, far less than the tuberculins of human tubercle bacilli, but that as immunizing and curative agents they are far superior. He holds that there is an antagonism between the bovine and human bacilli, and believes that the bovine bacillus originated from man. He therefore treats/

treats tuberculosis by injecting a vaccine of the bacillus which is not the cause of the trouble, and only later on, after a preliminary immunizing course with this vaccine, is the toxin proper admissible and then generally advantageous. He has several preparations of Tuberculin and Tubercular Vaccines.

Behring⁸⁵ has several preparations. Tuberculase is a vaccine prepared by treating tubercle bacilli with chloral hydrate, but this he uses exclusively now for combating tuberculosis in cattle. For treating man, he uses a preparation called Tulase, which is made by treating the tubercle bacilli with chlorate of potash. From this it has to be converted into a uniform milky emulsion, Tulase Lactin, in which the bacillary somatin remains uniformly suspended.

Rosenbach⁸⁴ prepares a Tuberculin by inoculating cultures of tubercle bacilli six to eight weeks old with particles of trichophyton fungus. These are allowed to grow for ten or twelve days and then undergo a further preparation. Good results are said to be obtained with this preparation.

Friedmann⁶⁰ reports the immunizing action of tortoise bacilli in guinea pigs but the latest reports seem to be unfavourable to its action in man.

Various other tuberculins on the lines of Koch have been made, but they do not seem to have come into prominence or anything like common use.

Various attempts were made to produce an active immunization/

immunization by means of substances prepared on the lines of Pasteur and Jenner. The cultures of the tubercle bacilli were attenuated in various ways and then injected, but the results do not seem to have been very satisfactory.

Turning now to the substances used to produce passive immunity, we find that v. Behring⁸⁶ has a preparation called Anti-tulase. This contains the antibodies evoked by the injection of Tulase, and can be obtained in considerable quantities from the blood of highly immunized animals.

Better known is the antituberculous serum of Maragliano⁸⁷. To produce this serum, he injected the filtrate of young and virulent tubercle cultures combined with a watery extract of virulent dead bacilli. The serum of the animals so treated is what he uses. The results obtained by different observers vary .

Marmorek⁸⁸ has an antituberculous serum. This he makes by growing tubercle bacilli on a special medium. The evidence with regard to his preparation is conflicting.

The dose which Koch recommended was .Ol c.c. of old Tuberculin. The reaction was allowed to come completely to an end and then another injection of .Ol c.c. was given. This was continued till the reaction became weaker and weaker and then ceased. He assumed that the gradual disappearance of the reaction was a sign of healing. This is now known not to be the case and it is/ is assumed that tuberculin tolerance is immunization against a bacterial toxin. The dose which Koch recommended was the one generally given to begin with, but less was given in the case of children or weak persons. Early in December 1890, the opinion was expressed that the usual dose of .01 c.c. was too great for even ordinary lupus cases, and that the initial dose should be .001 c.c. This dose was even recommended by Koch. 89McCall Anderson some years later appealed for a wider use of tuberculin, and recommended that the initial dose be $\frac{1}{2}$ - 1 c.c. of a 1 in 1000 solution, that is .0005 c.c. - .001 c.c.

In the early days, the interval between the injections seems to have varied. In some cases, the injection was given after two days, in others a week seems to have elapsed, though this was not so common. The usual procedure was that an injection was given every second or third day, but in some cases they were given on successive days.

It was noticed by various observers that improvement took place even when there was no reaction after the injection, and from this has sprung the reactionless treatment, which is perhaps the one most used at the present day. According to Sahli⁹⁰, Lichtheim was the first to advocate reactionless treatment. As early as 1891, Lichtheim said "On account of these observations, I consider it expedient to avoid as completely as possible all signs of reaction in the phthisical". This was quite contradictory to the prevailing views, and Lichtheim/ Lichtheim modified it later, saying that quicker progress was made, if actual febrile reactions were produced from time to time. Wright shows that the negative phase of immunity may last over the febrile period, so that the enrichment of the blood by opsonic antibodies takes place exclusively in the afebrile period. It may be, as Sahli holds, that the value of the fever depends not on the increased temperature but on the circulatory changes which occur. He believes, however, in the afebrile treatment. Another argument in favour of the reactionless treatment is that it is free from unpleasantness for the patient. There is also no need for him to lie up, but he can always follow his employment.

Watson Cheyne⁹¹ believed in the intensive method. By this is meant the gradual increase of the dose till the maximum which best suits the patient is reached, and then this is continued as long as possible. The intensive reactionless treatment is very satisfactory and is probably the best way of administering tuberculin. The injections in such a course of treatment are given twice a week and in the case of the stronger solutions once a week. If a reaction occurs at any time, the dose must not be increased. It is indeed better to diminish it, and advance cautiously, if necessary giving the same dose on several occasions to avoid reaction.

Reaction is this sense does not mean high temperature. According to Sahli⁹², if the temperature rises/

rises half a degree F., it must be taken as a reaction, even though it does not rise above normal. Sahli mentions other things which must be counted as a reaction as well as rise of temperature. These are an increased pulse rate, or the occurrence of dyspnoea, also any general indisposition shown by loss of appetite, depression, headache, or sleeplessness. Any progressive loss of weight shows the necessity for a reduction of the dose or a suspension of treatment. In addition to the general phenomena, there are the focal reactions. All these must be taken as signs of a toxic tuberculous action. There is often an increased leucocyte count during the reaction, even though there is nothing else noted as a reaction. It is said to be a finer test of toxic tuberculin action than any other clinical phenomena.

In the Royal Infirmary, Dr. Walker for some years past has been using T.R. in doses of $\frac{1}{2000}$ or $\frac{1}{1000}$ mgr. every three or four weeks. More recently he has been using 0.T. This is given every month in gradually increasing doses. The initial dose is .0005 c.c. 0.T. and the largest which has been reached in this way is .015 c.c. 0.T. Generally there was a reaction with a temperature of 100°F. or so. Most of the cases treated in this way improved, some very considerably. In other cases, in spite of the thinning and disappearance of the trouble in some parts, yet fresh spots appeared at the margins.

In the Summer of 1913, Dr. Walker started giving tuberculin on the intensive system. The patients were/

were started on a small dose of T.R., and this dose was doubled every three days till, in some cases, $\frac{1}{3}$ mgr. was reached. The Old Tuberculin was then substituted and the dose of this was more gradually increased. If this is done with care, no reaction follows. If there is a reaction, the dose is not increased, and in some cases is diminished till the reaction is at an end. At first the patients so treated were in the ward, but latterly Dr. Walker has given it to out-patients. Care must be taken when the O.T. is reached, as no reaction must be allowed to take place. It is advisable to weigh the patients at least once a fortnight, and if there be a progressive loss of weight, the treatment must not be pushed, but the dose advanced more gradually.

Dr. Walker has been in the habit of using Old Tuberculin for some years past in another way. As the result of observation of v. Pirquet's reaction in numerous cases carried out by Dr. Low, Dr. Walker thought it would be interesting to observe the result of the direct application of Old Tuberculin to lupus tissue. A thorough investigation was made, and the results were published by Dr. Verge⁹³ who was House Physician at that time. The following account is largely verbatim from Dr. Verge's paper. An ointment is made up of Old Tuberculin in vaseline in the strength of 5%. The lupus tissue is thoroughly cleaned up, all crusts and exudation being removed. The ointment is then well rubbed in for one to two minutes and then a piece of lint/ lint well smeared with the ointment is applied. This is bandaged on, or, if the part cannot be conveniently bandaged, strapping is applied to keep the lint in position and so prevent the ointment getting to undesirable places. On removal of the application twenty-four hours later, varying degrees of hyperaemia and swelling are seen in the actual lupus tissue, with a moderate amount of hyperaemia with reddish papules extending one or two inches into the surrounding healthy skin.

After cleansing the surface, similar applications are made for the next three or four days, the number being regulated by the pain experienced, in some cases considerable, and by the natural objection of the patient to the peculiar odour which arises in all cases. In forty-eight hours the swelling and hyperaemia are very well marked. As one proceeds with the treatment, the part becomes more and more inflamed and swollen, small vesicles appear over the situation of the lupus nodules, and these on rupturing leave small ulcers behind, showing that the nodules have been eroded.



Lupus Vulgaris before application of Old Tuberculin Ointment.







ation of Old Tuberculin Ointment.



Ointment.

The appearance of the lesion now closely resembles that produced by the application of a salicylic acid plaster. This is the desired effect and the treatment is now suspended, and the inflammation allowed to subside under some soothing application. The coloured plates show the appearance of the various stages.

The most outstanding features are the diminution in extent of the actual disease and the reduction of the infiltration and thickening. This is especially marked in lupus of the face where infiltration and thickening are so often to be seen. None the less noticeable is the improvement in colour and the softer and more pliable nature of the lesion.

Perhaps the best results can be obtained where the lupus tissue surrounds joint areas. Here where formerly, owing to the contraction of the scar tissue, the joints were rendered almost useless, or much restricted in action, in some cases there was practically complete restoration of movement, in others much improvement.

In none of the cases treated was there any general systemic reaction. The temperature and pulse remained normal. No headache was complained of in the face cases under treatment, but many of these patients objected to the odour. The pain, which is considerable, prevented more than one or two applications in some cases. In others six or seven could be endured, and in the latter series more beneficial results were obtained.

In/

In the early investigations reported by Dr. Verge, the attitude of the patients treated in this way gave great satisfaction. Although objecting somewhat strongly to the pain, odour, and inconvenience of having an unsightly application on their faces, the majority returned for a second and third course of treatment when they saw the results obtained.

To prevent the tuberculin ointment from coming into contact with the healthy skin, it is advisable to cover this with zinc paste on a cloth with a hole in it shaped to the lupus and then to apply the tuberculin ointment on cloth above that.

This method of treatment deserves to be more widely known than it seems to be. Senger⁹⁴ used an ointment of Old Tuberculin 3-5% in Vasenol in conjunction with X-rays but this is the only mention I have come across of any local application of tuberculin.

Since the early investigations were carried out, Dr. Walker has used tuberculin ointment regularly both in diagnosis and treatment. The diagnostic use has already been referred to, but it might be better to state here that its action is specific for tuberculous tissue. It has been applied to psoriasis, lichen, syphilis, and other skin lesions but in no disease except tuberculosis does a reaction occur. With regard to the therapeutic use, after the ulcerative stage has been reached, instead of applying a soothing remedy, Dr. Walker now applies either carbolic acid or uranium nitrate powder. A dental burr dipped in carbolic acid/ acid may be bored into the holes left by the nodules, thus rendering the destruction more complete. In the same way, uranium nitrate is spread fairly thickly over the surface and a piece of wool placed over it. This also seems to render the destruction of the lupus more complete.

I will now mention the cases which have been treated with Tuberculin. The notes of the injections and the results of these are taken from the cards on which the treatment of each patient is recorded. I give a history of the disease in each case, and the treatment which was employed previous to the administration of Tuberculin.

Lilian D. act. 22.

This patient has had the lupus for about five and a half years, but there was some nasal trouble before that. The lupus started as a dull red spot on the lower part of the nose and spread rather rapidly. Two spots also appeared on the right cheek. About a year after the skin trouble began, she came to the Royal Infirmary and had the inside of the nose attended to. This was followed by good results as far as the skin condition was concerned. The cheek was scraped at this time. She had salicylic creosote plaster for the nose at first and then the brown ointment. The spots on the right cheek were frozen with CO2 snow four weeks after the operation on the nose. The result was excellent and these spots have not troubled her/

her since. The photograph shows the two whitish areas, but they are not so apparent to the naked eye. The nose was frozen at intervals, the brown ointment being used between times. The inside of the nose, too, was attended to on various occasions. In March 1911, T.R. injections of 2000 mgr. were given and were continued at intervals till July 1911 when she was getting 1000 ngr. During the rest of 1911, freezing was the treatment adopted. In the early part of 1912 the nose was again frozen and the T.R. injections were begun again and continued till November 1912. In addition to this treatment, she had X-rays in April and May, receiving in all six exposures of 15 minutes each. She went deaf in the month of March and no satisfactory explanation was forthcoming as to the cause of it. In February 1913, she was admitted for 0.T. injections.


May 29, 1913.







January 18, 1915.

February 17. .001 c.c. 0.T. T = 100.8 and kept up longer than usual. Headache but no rash.

March 20. Small injection which gave hardly any reaction.

May 29.

.001 c.c. O.T. T = 100. On this occasion, the 61d Tuberculin cintment was applied to the tip of the nose while she was in the ward.

q1.







the/

the six months previous to the taking of the last one, she had had only one injection and no other treatment. The result was that there was a slight relapse, but the first two photographs show the improvement that can take place under steady treatment.

Esther L. Aet. 15.

Family history. Patient's mother had a running neck when a girl. The patient herself had a gland excised and her left malar bone scraped at the Sick Children's Hospital eight years ago. When she was a child, she had her hands scraped for what was presumably a tubercular condition.

The lupus started on the right side of the neck six years ago, and on the left side in front of the ear three years ago. It spread gradually but it was only during the year previous to her coming to the Royal Infirmary that the disease spread down the left side of the neck.

She was first seen towards the end of January 1913, when she was given the brown ointment. About six weeks later she was put on the injection list.



June 7th, 1913.

On April 9, 1913 she received the first injection of .0005 c.c. 0.T. This caused no local reaction nor had she any temperature. There was a slight erythematous rash.

June 7. .0005 c.c. O.T. No rise of temperature but a slight rash. O.T.ointment gave a typical reaction.

July 28. .001 c.c. O.T. T = 103.2, 12 hours later. There was a marked local reaction and an erythematous rash with some punctate spots. She felt rather sick. At this time all the patients had rather sharp reactions.



April 1913.

July 1913.

- September 11. .001 c.c. O.T. T = 101.4. Faint erythematous rash and good local reaction. On this occasion there was some albuminuria which lasted for three days after the injection.
- October 21. .001 c.c. 0.T. T = 103.3. Very sudden reaction and a good deal of general disturbance, also some albuminuria. There were some symptoms suggesting laryngeal reaction.



September 1913.



October 1913.

January 26, 1914. .0005 c.c. O.T. T = 99. Had a large tuberculous abscess under the chin. This was opened and packed with uranium nitrate gauze. Some of the pus was handed to Dr. A. P. Mitchell for investigation and he reported that it was sterile.

March 20. Lupus much better but glands all round neck. Passed on the the surgeons.

It is quite possible that these glands were the cause of the steady increase in the temperature after the same dose of tuberculin. Nothing was noticed till the abscess made its appearance. It is possible that a course of T.R. after this would have been suitable for It would have tended to prevent the the patient. glands suppurating, while the lupus would still have had benefit.

Mrs. 0'D. aet. 37.

This patient has had the disease about sixteen years. It started on the bridge of the nose, and was treated with plaster and an ointment and was finally scraped. About a year after the scraping it was almost healed. It then broke out again and grew slowly till it was about the size of a shilling. It was about this time that she first came to the Infirmary; this was in 1904. She had X-rays frequently and when she went out of town the nose was painted twice a week with chloride of antimony. She then came back to the Royal Infirmary and had X-rays till March 1907. She then ceased to attend till June 1910 and during these three years, she had practically no treatment. During 1910, she had X-rays and potassium iodide and perchloride of mercury. In 1911 patches appeared on the right cheek and the forehead. These were frozen with CO2 snow at intervals during 1911 with apparently indifferent results. 0.T. ointment was also tried, and at another time she had the brown ointment and a plaster. Nothing seemed to be done between 1911 and April 1913.



June 12th, 1913.

January 9th, 1915.

On April 13, 1913 she had an injection of .001 c.c. 0.T. Temperature rose from 97.2-98, and there was no local reaction.

June 11.

.002 c.c. 0.T. T = 100.2. Good local reaction.





July 31.

.0025 c.c. 0.T. Temperature rose very rapidly to 103 and remained up for some time. It then fell to 99 and rose eight hours later to 100.8. It fell to 98 and in/



March/





This patient shows a distinct improvement. There is no disease at the tip of the nose, though the last photograph almost suggests it. The picture was taken just after she came in, when the weather was responsible for the colour.

George A. Aet.22.

No family history is obtained from this patient. The lupus started in 1908 in front of the left ear, and the first appearance suggested a boil. Shortly after this, a nodule appeared at the bend of the left elbow. In two years time it had spread about two inches down the face. It spread more slowly on the arm, which was treated with an ointment which healed it up entirely. About this time, i.e. two years after the disease started and when the arm was healed, he attended the the Victoria Hospital, Glasgow, and had X-rays for about eighteen months, sometimes with considerable intervals between the exposures. After being healed for/

for about six months, the lesion on the arm broke out again as the result of a fall which bruised it considerably. It spread fairly rapidly during the next eighteen months. He ceased attending the Victoria Hospital about the beginning of 1912. During 1912 he treated it with lint dipped in boiling water and covered with gutta percha tissue. He occasionally dipped the lint in buttermilk, but this did not benefit him except that it seemed to cool and soothe it. He used a preparation called Gipsy Ointment on the face for three days, but it ulcerated the part so badly that he stopped it. He had also tried some blood mixture without success.

He came to the Royal Infirmary, Edinburgh, first in January 1913, and at that time there was a patch $4" \ge 2\frac{1}{2}"$ on the left cheek and one 6" $\ge 4"$ on the left arm. He was given the brown ointment and his name was put down on the 0.T. list.



May 6th, 1913.

He was admitted on February 1, 1913. The O.T. ointment was applied to the upper part of the arm with the normal reaction. On February 5, he received an injection of .001/0.T. T = 101.6 The local reaction was most marked in the region to which the O.T. ointment had/

had been applied, but gradually this spread to all the edges of the arm patch and later to the face. The restriction of the joint was greatly improved and there was marked change in the whole condition.



February 1913.

May 3.

.0015 c.c. 0.T. T = 101. 0.T. ointment applied to central external edge of arm patch. There was a good local reaction and the ointment was kept on for five days. The arm was immensely better when he went out.





July 1.

1. .0015 c.c. O.T. T = 100.4. Face carbolised. The arm moves much more freely and he can almost straighten it now. Went round golf course in 77.





July 1913.

August 9.

.002 c.c. 0.T. Temperature rose quickly to 102.6 but no rigor . Marked punctate rash and he was rather sick. He developed albuminuria the second day after the injection and he still had a trace when he went out. His face was treated with carbolic acid before his departure. On this occasion he complained of his throat being a little sore after the injection.





As it was not very convenient for him to come to Edinburgh for his treatment, he was advised to go to one of the Glasgow hospitals to have it carried out there. This case shows what a marked change can be brought/ brought about. He was only about six months under treatment and there was a marked improvement in that time. This was most noticed in the case of the arm which he could move much more freely than when he came first to Edinburgh for treatment.

Mary C. Act. 20.

This patient gave rather an unsatisfactory history. She had a patch on the nose, and extensive lesion on the right thigh, and one on the right arm. About these two latter she could give no information, though from the size of the thigh lesion, it had been there several years. The lesion on the nose started in 1910 and gradually spread. She had tried various ointments without success and came to the Royal Infirmary in April 1911. At this time, she had a tuberculous condition of the eye, in addition to the lupus. She was sent to the Ear, Nose and Throat Department to have the nasal mucous membrane scraped.



May 1st, 1913.







Resp.

In spite of the improvement, the patient did not return when written for and has not appeared at the Skin Department since.

Isa R. Aet. 17.

This patient said the disease started on the nose in 1911, but it is likely that there was some intranasal trouble previous to that. This had been scraped, and it was while attending for nasal treatment that she was sent to the Skin Department. From March to June 1911, she had X-rays and three injections of 2000 mgr. T.R. She was rather neglected, but in spite of this, the lupus seemed to improve, especially after the intranasal scraping.



June 17th, 1913.

On April 12, 1913, she received her first injection of O.T. when she got .001 c.c. O.T. T = 100.8. Local reaction fair, but the general reaction was fairly well marked.

June 17. .001 c.c. 0.T. T = 101.8. Local reaction.



April, 1913.

June 1913.

August 11. .001 c.c. 0.T. Temperature rose quickly with a rigor to 103.6. Marked local reaction and a faint rash. She was a little sick. After the injection bile and albumin appeared in the urine. Temperature took forty-eight hours to fall.





This girl was a farm hand and when the next injection was due, she was helping with the crops. Though she was written for once or twice after that, she did not attend for treatment.

Annie B. Aet.23.

No history of tuberculosis was obtained. At the age of 12, this patient developed lupus on some part of the nose. After being treated for a year, during part of which time she had pyrogallic acid applied, she came to the Royal Infirmary in February 1905. It was only on the tip of the nose and the upper lip at that time. She was treated with X-rays till 1907 with intervals between the exposures and at these times she used the brown ointment. Occasionally some of the nodules were spiked with carbolic. She was not seen again till the end of 1908, and at that time it was on the nose and lip only, the tip of the nose being destroyed and an X-ray scar visible. During 1909 and 1910, she used the brown ointment and had some T.R. injections. During 1911 she had X-rays regularly and also during the first half of 1912. She then had some T.R. injections at home, but as she was not doing very well, she was put down for O.T. injections.



May 21st, 1913.



January 15th, 1915.

November 30, 1912. .001 c.c. O.T. T = 99.6. Marked local reaction.

January 26, 1913. She was admitted with influenza and her temperature went up to 103 but fell again immediately.

January 29. .001 c.c. O.T. No reaction.





March 6. Hypertrophic at edges. Scraped on March 7. Injection on March 10, .006 c.c. 0.T. Copious discharge of pus from the scraped surfaces. No sickness and little temperature. On the 12th inst. the temperature rose to 102, but this was possibly due to the onset of menstruation. Some of the scrapings were sent to Dr. S. Griffiths, who later reported a pure culture of human bacillus.

April/



This patient was not doing so well as was hoped. She is a weaver and is indoors all day. As the bacillus in this case was of the human type Dr. Walker put her again on 0.T. in the hope that more substantial improvement may take place.

Mrs. B. Aet. 52.

<u>Family history</u>: her youngest son had glands on the left side of the neck which were lanced three or four times.

This patient has had the disease eight years, when it started as a spot at the junction of the left nostril and cheek. This gradually spread and it was about the size of a pigeon's egg when she came to the Royal Infirmary about ten months after the disease began. Under potassium iodide the lesion almost entirely disappeared. Soon after, some spots appeared on the left cheek and also on the nose. Some perchloride of mercury was added to the iodide with benefit. This treatment was continued for some months till August 1908, when the lesions on the nose began to look more like lupus. The antisyphilitic treatment was then stopped, and she applied the brown ointment. Von Pirquet's test was done but was negative, and in a few days the resemblance to lupus went. After three month's treatment for lupus, the patient disappeared and did not return for four years. During the early part of this time she had medicine from her family doctor, later the/

the application of silver nitrate with some benefit till just before she returned to the Infirmary, when the disease began to spread down the right nostril. She returned in June, 1911, and at this time the whole appearance of the disease suggested lupus. She was treated with the brown ointment and potassium iodide for fully nine months, and during this time she had a fifteen minutes exposure to X-rays which made the nose was red and tender. She/now started on the injections of 0.T., and the disease at first seemed to get worse, spreading over the left cheek and becoming lumpy. After the fifth injection, it seemed to improve, the lumps going down. Just before the first injection, a Wassermann reaction was done, but was negative.



May 3rd, 1913.

October 29, 1912. .001 c.c. O.T. T = 99.8. Marked local reaction and rash.

December 4. .002 c.c. 0.T. T = 100. Marked local reaction.



July/





At this point the patient ceased to attend, because her doctor thought she had had enough tuberculin. There was no doubt about the improvement, especially towards the end of her attendance.

The occurrence of the vaginal discharge after the injection is a little difficult to explain. It may be that there was some latent genito-urinary tuberculous infection. The patient had no symptoms, however, and before the matter was cleared up, she ceased to attend.

Nellie S. Aet. 23.

There is no history of tuberculosis in the patient's family, but she herself had glands on the right side of the neck when about two years old.

The lupus started when the patient was 3-4 years old, about an inch in front of the left ear. It was about the size of a sixpence when first treated. It was poulticed with meal, and had various other types of treatment. It had been excised, and in the Western Infirmary, Glasgow, she had some X-ray treatment. When she/

she came to the Royal Infirmary first, it was about the same size as the lesion shown in the first photograph. This was in April 1907 and from then to July she had X-rays twice a week, under which treatment the condition improved. In July she was given the brown ointment and the improvement continued, especially in the centre. In December 1907, she had another exposure to X-rays and after that she was put on salicylic creosote plaster which acted well. In March and April 1908 she had more rays and it was spiked with carbolic at intervals during that year. In May 1909, T.R. ointment was used and a fortnight later, 0.T. ointment was applied, and after using this there was a Moro reaction all round the diseased area. During the rest of 1909, the brown ointment was used with intervals of salicylic creosote plaster. At the beginning of 1910, the disease looked well, but in May there were a few nodules at the edges, and/



April 28th, 1913.

January 21st, 1915.

and the patient then had a few injections of T.R. That Autumn CO₂ snow was employed with evident benefit. In 1911, she had the brown ointment and salicylic creosote plaster. In 1912, she had the Finsen Reyn light but did not seem to improve much, so she was started on 0.T. injections.

Huly 29, 1912. .001 c.c. O.T. T = 101.8. Not much local reaction.

October 11. .001 c.c. O.T. T = 99.8. Quite marked local reaction. Lupus much better.

November 29. .001 c.c. 0.T. T = 98.6. Little local reaction.



July 1912.

November 1912.

January 22, 1913. .002 c.c. O.T. No temperature reaction, and a very slight local reaction. There was some suspicion about the O.T.

March 5. .002 O.T. T = 99.2. Very little reaction of any kind.



October 27. .005 c.c. O.T. T = 98.6. Lupus distinctly better.





March 1914.

- May 5. Lupus looks much better. Mercury vapour lamp applied for fifteen minutes to cheek. May 6. .015 c.c. P.T.O. No reaction.
- June 6. Face where lamp was applied last time is distinctly thinner than the rest. Lamp ten minutes to two areas. .015 c.c. P.T.O. No headache, sickness nor temperature.
- August 4. Face very much better. Two areas again lamped for ten minutes. .02 c.c. P.T.O. No reaction.
- October 26. Lupus much thinner. Two areas lamped for ten minutes. .02 c.c. P.T.O. Some headache but no temperature.
- December 7. .03 c.c. P.T.O. No reaction. Two areas lamped for ten minutes.
- January 21, 1915. .04 c.c. P.T.O. No reaction at all. Face much better. Two areas lamped for ten minutes.

Though about the same in extent, the lupus is much thinner and more superficial than when the first photograph was taken.

Mrs. H. Aet. 53.

There was no history of tuberculosis in this patient's family.

The disease started when the patient was about 14 years old on the right cheek and slowly spread. When she was about 18, a patch appeared on the left cheek. She was treated by Dr. Joseph Bell about this time. Her spine troubled her and she was in the Longmore Hospital for nearly eight years, and while there the lupus was scraped. Shortly after she left the Longmore Hospital, a patch appeared on the right side of the nose, and about eighteen years ago she came under the care of Dr. Byrom Bramwell. She was in his ward for eight months on one occasion, and the following year was again admitted for two months. On both occasions, she got thyroid treatment, and all three patches of lupus healed up. After leaving hospital she took thyroid and cod liver oil occasionally.

In 1909, a spot appeared on the left cheek and spread gradually. In June 1910, she came to the Royal Infirmary and got X-rays, which seemed to cause the disease to spread. About a year after the cheek broke down, a small patch appeared on the tip of the nose. This also got X-rays, but with little benefit. After the rays were stopped, the disease spread rapidly in spite of ointments.




March 24th, 1914.





March 15th, 1915.

On March 24, 1914 she received .0005 c.c. 0.T. There was no reaction at all.

May 9. .002 c.c. P.T.O. Slight headache. Some local reaction but no temperature.

June 9. Face and nose rather better. Lamp ten minutes to lowest area on face. .005 c.c. P.T.O. Delayed temperature reaction to 99.4.

107.



January 12, 1915. Nose very crusted. Start intensive method as she can't get up for three days. The nose rapidly improved and in a month she expressed satisfaction at the progress made.

January 12, 1915. .002 c.c. P.T.O.

15/

11

109.

January	15,	1915.	.002	c.c.	P.T.O.
11	18	11	.002	c.c.	P.T.O.
11	21	ff	.003	c.c.	P.T.O.
**	24	11	.003	c.c.	P.T.O.
"	27	11	.003	c.c.	P.T.O.
11	30	"	.004	c.c.	P.T.O.

Bella M. Aet. 40.

This patient first came to the Skin Department in March 1903. Before that time she had laryngeal lupus and when she came first there was a patch on the inner surface of the upper lip and the adjacent gum. She was treated with X-rays during the rest of 1903 and at intervals in 1904. In 1905 she had X-rays till the end of August, and then the Finsen light till the end of the year. X-rays constituted the treatment in 1906. About this time the lip was nearly well, but a patch appeared on the left ala of the nose. This was treated during 1907 with X-rays, brown ointment and carbolic, but in spite of this treatment it spread rapidly over all the nose. About a year later it attacked the left cheek, and she had X-rays and a few T.R. injections. In the Autumn of 1908 she ceased to attend and did not return till October 1912. During this time she attended a layman who was said to cure lupus among other things; but in spite of his treatment, the disease spread and attacked the right Getting tired of his want of success, she cheek. returned to the Royal Infirmary in October 1912. She was given the brown ointment, and used it for two months, when O.T. ointment was applied. In 1913, she came only/

only three times to the Skin Department, the last being April, when it was looking a little better. In February 1914, her next appearance, she was sent to Dr. Logan Turner for his opinion about the laryngeal condition, before giving her the 0.T. injections. Dr. Turner reported that the whole of the pharyngeal and laryngeal condition was cicatrised, so she was admitted on February 16, and received .0005 c.c. 0.T. No temperature resulted.



February 16, 1914.



January 12, 1915.

March 27.	.001 c.c. 0 local react	.T. No ion.	temperature but marked
May 12.	.002 c.c. P	.T.O.	Good local reaction.
June 12.	.004 c.c. P	.T.O.	Local reaction good.
Actober 9	.004 c.c. P	.T.O.	T = 99.
November 23.	.006 c.c.	P.T.0.	T = 98.6. Improving.
January 12,	1915008	c.c. P	.T.O. No reaction.

111.

Thomas B. Aet.14.

The disease started five years ago on the right side of the nose. He had no treatment for a year and then came to the Royal Infirmary in May 1910. He was given the brown ointment and sent to have the inside of his nose attended to. He had X-rays and CO2 snow in 1910, but the disease spread. Little seems to have been done till the beginning of 1913.

January 21, 1913. .00075 c.c. 0.T. No reaction at all. March 11. .00075 O.T. T = 100.8. A little local reaction.

May 17.

.001 c.c. 0.T. T = 99.6. Some headache and a slight local reaction.



March 1913.





July 4. .002 c.c. O.T. T = 101. Local reaction.

uria.

August 13. .002 c.c. 0.T. T = 102.6. There was the usual local reaction and some albumin-







December 11. .005 c.c. P.T.O. No reaction at all. January 21, 1915. .006 c.c. P.T.O. No temperature, no local reaction.

George A. Aet. 11.

The family history is that one brother had glands in the neck when at school.

This patient was just over a year old when the lupus started on the face. There had been an abscess on a finger of the right hand, and in the hope of checking the disease, the finger was amputated. Shortly after that the left thigh broke out and about the same time the leg also showed signs of the disease. An abscess occurred on the left side of the neck, and the lupus spread all over that part when the abscess was opened. One also occurred below the left eye and this too was opened. The left foot also was the site of an abscess.

He came to the Royal Infirmary first in March 1912, and/

and during that year he had T.R. injections. Early in 1913 he got the brown ointment to use, and the injections were continued.



November 13th, 1913. January 19th, 1915.







November 13th, 1913. January 19th, 1915.





The photographs of this case show the improvement which has taken place, especially on the face. There is more healthy skin showing and the disease itself is very much thinner.

Andrew McG. Aet. 13.

Family history. A brother had glands in his neck and the patient had a gland removed in the Sick Children's Hospital in 1908.

The disease started in the Spring of 1911 in the right cheek, where it remained for two or three months and then went completely away. In September of that year his upper lip was burned, and the lupus appeared where the burn had been. It spread to the right cheek, then to the nose, and then to the left cheek.



August 7th, 1913.



October 26th, 1914.

He came to the Royal Infirmary in July 1912, and at that time the disease was fairly extensive. It was on the nose, upper lip, right cheek, gums, and on each side of the neck below the ear. He did not come/ come to the Skin Department again till December 9, 1912, when he was admitted and given :0005 c.c. 0.T. which produced a rather prolonged but not severe reaction, the temperature being 99.6. After this it was April 10, 1913 before he appeared again when he was sent by



December 1912.

his doctor to Dr. Dawson Turner for radium treatment, but being unsuitable for that treatment he was sent to the Skin Department. He received an exposure to X-rays on that date and had doses at intervals of a fortnight till May 22. A month elapsed before he had another on June 19, but this treatment did not seem to do any good, though there was slightly less inflammation.

July 7. .001 c.c. O.T. T = 102.2. There was a distinct improvement after this. On July 24, he had another dose of X-rays.

August 16. .001 c.c. 0.T. T = 103.4.





January/





This patient shows what a vast improvement can be brought about by even a short course of Tuberculin. He was getting ointments and X-rays and was getting worse in spite of them, but there was a distinct change even after the first injection. This improvement has steadily continued. The photographs show the different appearance after less than twelve injections.

James N. Aet. 30.

At the beginning of 1909, the disease started at the edge of the left nostril. It spread rapidly at first over the nose and upper lip, and from there has spread out. Two years before the face troubled him, there was something similar on the palate, but this healed up under iodide of potassium. He came up to the Royal Infirmary in May 1909, and got T.R. injections every fortnight till December 8. At this time the/ the nose, upper lip, gums and palate were affected. A Wassermann reaction was negative. He was treated in the Ear and Throat Department, the mouth being scraped and the gum being cut away.

On December 23, 1909, he was admitted. A von Pirquet reaction was strongly positive. He was treated with salicylic creosote plaster for a month and hardly complained. He improved and towards the end of January 1910, he received potassium iodide, grs.xv, three times a day and the improvement seemed to be more rapid, especially on the palate, which was being treated locally with lactic acid. In April 1910, the appearance was more specific, and the disease tended to spread, though in other respects it seemed to improve. He was again admitted in June, and the appearance of the lesion led to a doubt as to the diagnosis. A piece was excised, and the architecture resembled that of tuberculosis, and a bacillus like the tubercle bacillus was found. The O.T. ointment test was posit-The treatment during the rest of the year conive. sisted of freezing with COp snow with evident benefit, brown ointment, lactic acid for the palate, T.R. injections, and the uviol lamp pressed to the cheek.

In the early part of 1911, he was treated with CO2 snow and T.R., but did not do well. In May 1911 he was admitted and received an injection of 606. This resulted in the breaking down of the nodules, and two months later the appearance was distinctly better. In August/ August, he received a second dose of 606 and again improved, but later in the year he relapsed. In January 1912, he was admitted and had a third dose but did not react much. In March all the lesions were worse, and he was put on perchloride of mercury and improved.



June 29th, 1913.

On August 5, 1912 he received .001 c.c. 0.T. T = 101.8 on the 6th and 103.2 on the 7th. Scarlatiniform rash all over the body, but this faded in three or four days. Was sick the same night as he received the injection. Very marked local reaction; all the lesions on the face swelled and suppurated, and the eyes were closed. The face healed up under zinc paste and he went out improved, especially on the central part of the face. This improvement continued for some weeks, though the palate broke down after the injection.





May 3. .002 c.c. 0.T. T = 100.6. Some reaction locally.







May 9. The surface is smoother and much less nodular. He was advised to get into the sunlight as much as possible and to use the brown **oint**ment.

August 29. Has been getting T. R. injections more or less regularly for the last two months. Now up to 425 mgr.

Since August the face has been lamped three times with distinct/

distinct benefit. He is still receiving injections at home and seems to be doing well.

Mary G. Aet. 31.

This patient was sent up from England for admission without being previously seen. There was not very much lupus when she came up. The disease had lasted for fifteen years and the condition when she arrived is shown in the photograph. She had had X-rays in Halifax Infirmary five days a week for eighteen months, and there were well marked X-ray scars. There was a good deal of induration in the breast. She was at once put on tuberculin in increasing doses.



July 4th, 1914.

11 7 11 # 11 11 " 15/

July 4, 1913. 2000 mgr. T.R. 1000 mgr. T.R. 500 mgr. T.R.

126.

July	15,	1913.	$\frac{1}{250}$ mgr. T.R.
11	18	11	125 mgr. T.R.
"	22	Ħ	<u>l</u> mgr. T.R.
"	25	n	1 30 mgr. T.R.
**	28	"	15 mgr. T.R.
Augus	st l	"	.0005 c.c. 0.T. T = 100.4.
"	8	. "	.001 c.c. 0.T. $T = 99.8$. A marked local reaction followed which resulted in a superficial ulcer, which took a

127.

The patient then returned to her home, the condition being much improved and the induration greatly lessened.

long time to heal under salve muslin.

Mrs. G. Aet. 42.

This patient was first seen in March 1913 when the disease had only been present two months. It started as a pimple on the skin in front of the right nostril. This was treated for two months with an ointment, and then she came to the Royal Infirmary. When she first attended, the lesion was a little like a rodent ulcer and she got mercury and carbolic plaster. There was little change for some time, except that some nodules were visible above the sloughy centre. In June the lesion looked definitely like lupus, and O.T. ointment was applied and gave a typical reaction. Pure carbopic and uranium nitrate were applied at intervals till the end of the year. About Christmas 1913, the disease began to spread towards the point of the nose, and since then it has gradually extended and has also spread back along the nostril.

At/

At the beginning of 1914, she was advised to get tuberculin injections from her doctor. This was done with some benefit and she continued these till she was put on the intensive method in July 1914. In contrast to the last case, this patient was treated as an outpatient and it is interesting to note that she did not complain of any discomfort during the whole time she was under treatment.



July 6th, 1914.

2000 mgr. T.R. July 6. 1000 mgr. T.R. 9. 500 mgr. T.R. 12. 15. 250 mgr. T.R. 18. 125 mgr. T.R. 21. 50 mgr. T.R. 24. 20 mgr. T.R. 10 mgr. T.R. 27. 30/

128.

July 30. $\frac{1}{5}$ mgr. T.R. August 2. $\frac{1}{2}$ mgr. T.R. 5. .0005 c.c. P.T.O. 11. .001 c.c. P.T.O.

14. .001 c.c. P.T.O.

Unfortunately the outbreak of the war led to some trouble about getting tuberculin, and the treatment was not carried out as far as was wished. On September 15, she was again seen, and there was no doubt that the disease was better. The ulcer had healed and the lesion was smoother. The patient herself was quite satisfied with the progress she had made. As she had been away for three months, she was anxious to return home, and was advised to use pyrogallic acid in an ointment, the strength 3i - 3i. This she continued till the end of the year and there was no sign of a relapse at that time.

Mrs. Donella G. Act. 55.

In 1909 the disease began inside the nose and spread to the skin outside. She was attending the Nose Department of the Infirmary from which she was sent to the Skin Department. During 1910, she had the lupus spiked with carbolic and had 0.T. ointment applied at intervals, between which she used the brown ointment.

In 1911 she had X-rays from January to March. She then disappeared and did not return till June 1914. By this time the disease was worse, as a spot had appeared on each cheek and on the upper lip towards the end of 1911/

129.

These spots had all spread. She was at once 1911. put on the intensive method as an out-patient. 5000 mgr. T.R. June 4. 2000 mgr. T.R. 7. $\frac{1}{1000}$ mgr. T.R. 10. $\frac{1}{500}$ mgr. T.R. 13. 250 mgr. T.R. 16. 100 mgr. T.R. 19. 50 mgr. T.R. 22. 20 mgr. T.R. 25. $\frac{1}{10}$ mgr. T.R. 28. ± mgr. T.R. July 1. 1 mgr. T.R. 4. 7. .0005 c.c. P.T.O. 10. .001 c.c. P.T.O. 13. .001 c.c. P.T.O. 16. .002 c.c. P.T.O. 19. .003 c.c. P.T.O. 22. .003 c.c. P.T.O. 25. .004 c.c. P.T.O. 28. .004 c.c. P.T.O. 31. .005 c.c. P.T.O. 3. .005 c.c. P.T.O. August .006 c.c. P.T.O. 6. 9. .006 c.c. P.T.O. 12. .007 c.c. P.T.O.

15. .007 c.c. P.T.O.

Here the supply of tuberculin ceased on account of the war/

war and the patient went home. Except for an occasional headache there was no sign of a reaction, the patient taking her food well throughout the course of the treatment. When she went away she expressed her gratitude at the improvement which had taken place. One point of interest in this case is the age of the patient before the disease started, she being close on 50 before the trouble began.

Martha L. Aet. 16.

The disease started ten years ago as a lump on the left side of the neck; this was cut in the Royal Infirmary. Some four years after the commencement, a spot appeared on the left side of the nose and this spread to the upper lip, and also on to the cheek and over the nose. She was badly neglected at home, and this hastened the spread of the disease. About this time she attended the Falkirk Infirmary where she had X-rays.

She came to the Royal Infirmary, Edinburgh, in March 1911. She had, in addition to the lupus, a corneal ulger and had not opened her eye for seven months. She was admitted and under X-rays, brown ointment, and T.R. injections there was a marvellous improvement and she went out on June 6. She had T.R. injections at intervals till the end of the year. She did not attend again till January 18, 1913, when it was found that she had again been neglected and had lost ground. At this time she had a large abscess in front of the right ear and/



June 25th, 1913.





R. I

February 21st, 1914.



August 1st, 1914.

and this was opened. On January 21 she was admitted and received an injection of .00075 c.c. O.T. which resulted in a temperature of 99. The O.T. was suspected and on January 28 .001 c.c. was given, T = 102.4. The abscess discharged through a small opening and on February 5, O.T. ointment was injected into the cavity. There was some local reaction. She was sent to the Convalescent Home, and when she returned, the abscess was much better.







January 1913.

February 28.

- .001 c.c. O.T. T = 102.6. Good local and general reaction, and she was much improved when she went out.
- April 16. .001 c.c. O.T. T = 99.8. The general condition is distinctly improved.



February 1913.



reaction.

June 24. .002 c.c. 0.T. T = 101.8. Local

.002 c.c. 0.T. T= 103.2 and remained August 8. there for nine hours. Marked local reaction.



June 1913.



September 24. .002 c.c. O.T. T = 99.2. Very little local reaction. Some albuminuria before injection and more distinct after it.

November/



addition the mercury vapour lamp at intervals. During the time she was in the ward, no temperature resulted from/

135.

from the injections except where stated. 10,000 mgr. T.R. March 29. 5000 mgr. T.R. April 1. 4. 2500 mgr. T.R. 1000 mgr. T.R. 7. 500 mgr. T.R. 10. 250 mgr. T.R. 13. 100 mgr. T.R. 16. .0005 c.c. P.T.O. T = 99.6 48 19. hours later. T = 99.2 24 hours .001 c.c. P.T.O. 22. later. 27. .002 c.c. P.T.O. .004 c.c. P.T.O. T = 102.4 24 30. hours later. .002 c.c. P.T.O. May 4. .003 c.c. P.T.O. 7. .004 c.c. P.T.O. 10. .004 c.c. P.T.O. 13. .004 c.c. P.T.O. 16. .005 c.c. P.T.O. 19. .006 c.c. P.T.O. 22. .007 c.c. P.T.O. 25. .008 c.c. P.T.O. 28. .008 c.c. P.T.O. 31. .01 c.c. P.T.O. 3. June .015 c.c. P.T.O. 10. .02 c.c. P.T.O. 13. .02 c.c. P.T.O. 16. .025 c.c. P.T.O. 19. .03 c.c. P.T.O. 22.

25./

June	25.	.03	c.c.	P.T.0.
	28.	.03	c.c.	P.T.0.
July	2.	.04	c.c.	P.T.0.
	5.	.05	c.c.	P.T.0.
	10.	•06	c.c.	P.T.0.
	13.	•06	c.c.	P.T.O.
	16.	.07	с.с.	P.T.0.
	19.	.07	c.c.	P.T.0.
	22.	•08	c.c.	P.T.0.
	25.	.08	c.c.	P.T.0.

She left the Infirmary early in August and was advised to continue using the brown ointment. The improvement in her condition was very striking as will be seen from the photographs. The improvement was even more marked than is apparent, as the sensitive plates picked out the red more than the naked eye, and in addition the face was a little red as the result of the lamping. Though the improvement was great on both sides, yet the left side was better than the right side. So much was this the case that the patient's parents wanted the right side also lamped. At the end of September the improvement still held and the left side was freer from nodules than the right. She has been having injections once a week at Falkirk and she comes to Edinburgh once a month to report. When last seen, in January, there was no sign of relapse.

Mrs/

When this patient was 13 years of age, the lupus began. She was pricked with scissors inside the left nostril, and it was soon after this that the lupus appeared out**si**de the left nostril. This is one of the very/



May 26th, 1913.



November 2nd, 1914.



March 5th, 1915.

very few cases where any definite cause was suggested. The disease gradually spread, eating away the left nostril. She had the lesion scraped soon after it commenced, and after it had lasted about a year she had X-rays to the nose. This treatment was all that she had for a year. She then had some ointment and a paint and under this treatment healing took place, and the lesion remained healed for about two years. It then broke out again and spread, attacking the right nostril as well. She was then for some time without treatment. In 1910 a patch appeared on the right cheek, and this was the state when she came to the Royal Infirmary. The inside of the nose was affected and this was treated as well as the skin. During 1912 she had a 25% uranium paste which improved it considerably. In August this was stopped and the brown ointment was used, but towards the end of the year a patch appeared on the right side of the chin . She was then put down for 0.T. injections.

December 9, 1912. .001 c.c. 0.T. T = 98.6. Very little local reaction or general discomfort.

February 8, 1913. .002 c.c. O.T. T = 100.4. Both local and general reactions were distinct. Good rash.





one or two spots on the upper lip.

July 24. .004 c.c. 0.T. T = 100.8. Slight local reaction.

September 8. .004 c.c. 0.T. T = 100.6. Good local reaction.



She did not attend the Infirmary between the beginning of January and the end of October 1914 owing to family circumstances. During that time there was little or no treatment carried out with the result that the disease became worse. As it was thought that she was a suitable case for the intensive method, she was written/ written for, and at the beginning of November she started that method.

Novembe	er 2.	1 1000 mgr. T.R.
	5.	<u>1</u> 500 mgr. T.R.
	8.	1 250 mgr. T.R.
	11.	1 100 mgr. T.R.
4	14.	$\frac{1}{60}$ mgr. T.R.
	17.	$\frac{1}{20}$ mgr. T.R.
	20.	$\frac{1}{10}$ mgr. T.R.
	23.	$\frac{1}{5}$ mgr. T.R.
	26.	.0005 c.c. P.T.O.
	29.	.001 c.c. P.T.O.
December	2.	.002 c.c. P.T.O.
	5.	.002 c.c. P.T.O.
	8.	.003 c.c. P.T.O.
	11.	.003 c.c. P.T.O.
	14.	.003 c.c. P.T.O.
	17.	.004 c.c. P.T.O.
	20.	.004 c.c. P.T.OL
	23.	.004 c.c. P.T.O.
	26.	.005 c.c. P.T.O.
	29.	.005 c.c. P.T.O.
January 2,	1915.	.005 c.c. P.T.O.
	5.	.006 c.c. P.T.O.
	8.	.006 c.c. P.T.O.
	11.	.006 c.c. P.T.O.
	14.	.007 c.c. P.T.O.
	17.	.007 c.c. P.T.O.
	1	

20/
January	20.	.008	c.c.	P.T.0.
	23.	.008	c.c.	P.T.0.
	26.	.008	c.c.	P.T.O.
	29.	.009	c.c.	P.T.O.

Dorothy B. Aet. 14.

The disease started when the patient was 7 years old/



April 22nd, 1913.



January 20th, 1914.



October 15th, 1914.



February 16th, 1915.

old as a small papule on the right cheek. It was scraped and had X-rays, but it spread in spite of this. When she came to the Royal Infirmary first, in March 1911, it was treated with CO₂ snow, and it was frozen and X-rayed at intervals during that year. Early in 1912 she had strumous ulceration of the eyes, while the lupus was very catarrhal. She was admitted and had starch poultices applied, and then uranium paste which subdued the catarrh rapidly. She improved greatly during the three months she was in the ward. She had some T.R. injections in 1912, but no treatment got a proper chance on account of the crusting which was allowed to exist. Towards the end of 1912, the disease spread extensively, and she was put on the 0.T. injection list.

November 22, 1912. .00075 c.c. O.T. T = 101. Very marked lichen scrofulosorum rash.

January 15, 1913. .00075 c.c. O.T. No rise of temperature and no local reaction. There was, however, some suspicion about the tuberculin.

March 8. .00075 c.c. O.T. T = 103. On the whole, some improvement.



November, 1912.

March, 1913.



January 20, 1914. Not so well again, badly neglected at home and crusts allowed to form. .004 c.c. 0.T. T = 103.8.

March 20. Better than last time she was in. .004 c.c. 0.T. T = 100. Good deal of breaking down as the result of the injection.



January 1914.

May 1.

. .004 c.c. P.T.O. T = 99.4. Local reaction. Lamp for ten minutes to two areas of cheek. The lupus is spreading under the eyebrow, but taken as a whole is much thinner.



May 1914.

July 23.

August/

Improving but still neglected. Three areas of cheek lamped for ten minutes. .005 c.c. P.T.O. T = 98.8.

146.

March 1914.

August 19.	Two	areas of right cheek lamped ten minutes.
September 3	No roun lamp ten	t so impetiginous as usual, except d the neck where it is spreading. The ed areas are decidedly thinner. Lamp minutes to two areas on right cheek.
September 2	34. S minu	till crusted on neck. Lamp ten tes to two areas on right cheek.
After this	visit	she was put on the intensive method.
October	15.	1000 mgr. T.R.
	18.	500 mgr. T.R.
	21.	250 mgr. T.R.
	24.	125 mgr. T.R.
	27.	50 mgr. T.R. She said she was slightly sick after this injection.
	30.	50 mgr. T.R.
November	2.	30 mgr. T.R.
	5.	$\frac{1}{20}$ mgr. T.R.
	8.	10 mgr. T.R.
	11.	5 mgr. T.R.
	14.	늘 mgr. T.R.
	17.	.0005 c.c. P.T.O.
	20.	.001 c.c. P.T.O.
	23.	.001 c.c. P.T.O.
	26.	.002 c.c. P.T.O.
	29.	.002 c.c. P.T.O.
December	2.	.003 c.c. P.T.O.
	5.	.003 c.c. P.T.O.
	8.	.003 c.c. P.T.O.
	11.	.004 c.c. P.T.O.
	14/	

147.

December	14.	.004	c.c.	P.T.O.
	17.	.004	c.c.	P.T.O.
	20.	.005	c.c.	P.T.O.
	23.	.005	c.c.	P.T.O.
	29.	.005	c.c.	P.T.O.
anuary 2,	1915.	.005	5 c.c.	. P.T.O.
	5.	.006	c.c.	P.T.O.
	8.	.006	c.c.	P.T.O.
	11.	.006	c.c.	P.T.O.
	14.	.007	c.c.	P.T.O.
	17.	.007	c.c.	P.T.O.
	20.	.008	c.c.	P.T.O.
	23.	.008	c.c.	P.T.0.
	26.	.008	c.c.	P.T.0.
	29.	.009	c.c.	P.T.O.

J

Here again the photographs show the excellent results which can be obtained in spite of adverse conditions. The disease is very much thinner and though it spread earlier in the treatment, that now seems to have been checked.

Isa T. Aet. 17.

One of the patient's brothers had glands in the neck. The patient was only 8 years old when the disease started on the cheek. It was about the size of a sixpence when she first got treatment, this consisting of the patch being scraped. It was twice scraped at intervals of six months, and about six months after the second scraping she came to the Royal Infirmary. At first/ first she was treated with salicylic creosote plaster and in April 1908 she had X-rays. She had the rays every three weeks for a year. She then went to the Skin Dispensary where she got the Finsen light and an ointment/



May 6th, 1913.



October 19th, 1914.

February 16th, 1915.

cintment. She attended there for two and a half years and all that time there was no improvement. She was then sent to the Electrical Department where she got X-rays for another year. In September 1911 she returned to the Skin Department and was treated with salicylic creosote plaster and oleate of mercury ointment till the end of the year. She used uranium oxide ointment with intervals nearly all 1912, but still the disease spread, though thinner, till it was nearly as large as the patch shown in the first photograph. She was then, at the end of 1912, put on the 0.T. injection list.

November 30, 1912. O.T. ointment was applied locally for four days with a very good reaction, after which the part was carbolised. On December 11 she received .001 c.c. O.T. T = 100.8.



December 1912.

February 12, 1913. 0.T. ointment was applied to the front portion of the patch. Two days later she received .001 c.c. 0.T. T = 102. The bit to which the 0.T. ointment was applied, was distinctly more inflamed. On February 17, the ointment was stopped, but gradually the local reaction spread to the whole patch, affecting the nodules in the characteristic way. There was no question of accidental spread, as the posterior part was covered with zinc paste.



February 1913.

- May 6.
 - 6. .001 c.c. 0.T. and 0.T. cintment to cheek. She had recently had an injection of tuberculin at home, probably T.R., and no reaction followed. There was no reaction after this 0.T. injection either.
- July 10. .001 c.c. 0.T. T = 103.6. Rash within an hour and a marked local reaction. 0.T. ointment was applied to the patch also.



July 1913.

August 23. .0005 c.c. 0.T. No reaction.

October 6. .001 c.c. O.T. T = 101.2. There was a good deal of sickness after this injection and also some urticaria on the face.

November 15. .001 c.c. O.T. T = 99. Tuberculin ointment and then uranium nitrate locally.

151.



July 3.

Face better where it was lamped, patient wants other areas lamped also. Two areas lamped for ten minutes. .004 c.c. 0.T. T = 100.2. Rather sick and bad headache.





In October she was put on the intensive method. 500 mgr. T.R. October 19 250 mgr. T.R. 22 100 mgr. T.R. 25 60 mgr. T.R. 28 31 30 mgr. T.R. 10 mgr. T.R. 3. November 5 mgr. T.R. 6. 9. 1 mgr. T.R. .0005 c.c. O.T. 12. .001 c.c. 0.T. 15. .001 c.c. 0.T. 18. 21. .002 c.c. O.T. .002 c.c. 0.T. 24. .003 c.c. 0.T. 27. .003 c.c. 0.T. 30.

December 5. .004 c.c. O.T. T = 99. This reaction is due to the increased dose after a longer interval than usual between the injections.

December	8.	.004	c.c.	0.T.	
	11.	.004	c.c.	0.T.	
	14.	.005	c.c.	0.T.	
4	17.	.005	c.c.	0.T.	
	20.	.005	c.c.	0.T.	
	23.	.006	c.c.	0.T.	
	26.	.006	c.c.	0.T.	
January 2,	1915.	.006	c.c.	0.T.	
	5.	.007	c.c.	0.T.	
	8.	.007	c.c.	0.T.	
	11.	.008	c.c.	0.T.	
	14.	.008	c.c.	0.T.	
	17.	.008	c.c.	Ó.T.	
	20.	.009	c.c.	0.T.	
	23.	.009	c.c.	0.T.	
	26.	.009	c.c.	0.T.	
	29.	.009	c.c.	0.T.	

This is perhaps the most stubborn case of all. The lupus is tough and for a while the injections did not seem to affect it. Latterly, however, there has been a distinct though slow improvement. The patch is now much thinner and the patient is now satisfied that an improvement is taking place.

James C. Aet. 17.

This boy had an operation on the legs in the Sick Children's Hospital, and had glands removed in the Infirmary. He has also had some trouble with his right hand and arm.

Early/

Early in 1908 he fell over a bannister and a lump appeared under the right eye. This was treated at the Sick Children's Hospital and got quite well again. Some months after, it broke out again and spread over the nose. He came to the Royal Infirmary in December 1908 and at that time both sides of the nose, the palate, upper jaw, and gums were affected. He had X-rays from this time till July 1909 and a few T.R. injections. He disappeared and did not return for treatment till the beginning of 1912, but he had been in the Longmore Hospital for one year and seven months of this time. In 1912 he had frequent doses of X-rays and used the brown ointment as well. He came up at intervals in the early part of 1913, and it was usual to find the face very much crusted. He did not attend between May 1913 and June 1914 and during all that time he had been in town, and as he was not working there was nothing to prevent his attendance. During part of this time he used a preparation known as Tar When he came to the Skin Department in June, Cream. it was observed that there had been a spread of the disease at the edges. He was advised to use the brown ointment, but could not afford to get it. At the beginning of July he was started on the intensive tuberculin treatment.



August 9th, 1914.

Jul	y 9.	1 2000 mgr. T.R.
	12.	1000 mgr. T.R.
	16.	500 mgr. T.R.
	19.	250 mgr. T.R.
	22.	100 mgr. T.R.
	25.	50 mgr. T.R.
	28.	20 mgr. T.R.
	31.	10 mgr. T.R.
August	з.	$\frac{1}{5}$ mgr. T.R.
	9.	1/2 mgr. T.R.
	12.	.0005 c.c. P.T.O.
	17.	.0005 c.c. P.T.O.
	20.	.0005 c.c. P.T.O.
At this	point	treatment was stopped by the war, but
when the	suppl	y of Tuberculin was assured, he was
written	to, an	d the treatment was continued.

October/

October 30.	.0005 c.c. P.T.O.
November 2.	.001 c.c. P.T.O.
5.	.001 c.c. P.T.O.
8.	.002 c.c. P.T.O.
11.	.002 c.c. P.T.O.
14.	.003 c.c. P.T.O.

He did not attend till November 23, when he reported that he had had some swelling of the face, but no sickness or headache. He had had a similar attack about this time on each of the two previous years. He had had an attack while in the Longmore Hospital and thought he heard it was erysipelas. His face improved after it. It is quite possible that he had an attack of erysipelas on this occasion.

November	23.	.003	c.c.	P.T.0.
	26.	.003	c.c.	P.T.0.
	29.	.004	c.c.	P.T.O.
December	2.	.004	c.c.	P.T.0.
	5.	.004	c.c.	P.T.0.
	8.	.005	c.c.	P.T.0.
	11.	.005	c.c.	P.T.0.
	14.	.006	c.c.	P.T.0.
	20.	.006	c.c.	P.T.0.
	23.	.007	c.c.	P.T.0.
	26.	.007	c.c.	P.T.0.
	29.	.008	c.c.	P.T.0.
January 2,	1915.	.00	08 c.	c. P.T.O.
	5.	.008	c.c.	P.T.0.
	8./			

January	8.	.009	c.c.	P.T.O.
	11.	.009	c.c.	P.T.0.
	14.	.01	c.c.	P.T.O.
	17.	.01	c.c.	P.T.O.
:	20.	.02	c.c.	P.T.O.
;	23.	.02	c.c.	P.T.O.
;	26.	.02	c.c.	P.T.O.
:	29.	.03	c.c.	P.T.O.

From the study of these cases and their accompanying photographs I think it will at once be admitted that tuberculin is of great value in the treatment of lupus. It may be objected that these results are valueless as there have been no cases used as controls. Against this, I may point out that these cases were previously being treated by other methods, and were not showing much improvement in some cases, and in others were actually getting worse in spite of the treatment. When they were put on tuberculin, they began to improve, some with extraordinary rapidity. If this improvement had only happened in one or two cases, it might have been put down as a coincidence, but I think there are too many cases quoted to leave any ground for such an opinion. These cases are not in any way chosen, but represent/

represent practically all of the cases treated in this way during the last few years. Some attend at intervals to get T. R. injections, but the cases I have quoted are all that have been treated either with Old Tuberculin alone or on the intensive system. I do not hold out Tuberculin as guaranteed to cure every case of lupus, but I do believe that all cases ought to have the benefit of a course of such treatment. Even though the Tuberculin does not benefit them, yet it seems to influence the disease in such a way as to render it more amenable to other treatment. This alone is a distinct advantage. There does not seem to be any specific cure for lupus, and one often finds it desirable to combine two remedies, when each seems to supplement the other. For example, the combination of Tuberculin and the mercury vapour lamp seems to produce a more marked improvement than either remedy Patience and perseverence are required both alone. by the sufferer and by the doctor, and in every case the time is long. This is a lesson which Finsen taught us, and which is quite as necessary to-day as it was then. To be of any avail, the treatment must be thorough whatever method is adopted and we would do well to follow Brocq's advice that lupus should never be left to itself for a single instant, until a complete cure has been obtained.

In conclusion, I would like to express my thanks to Dr. Norman Walker for so freely placing at my disposal his notes of the cases treated in his Wards.

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