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TWENTY CASES TREATED BY TUBERCULIN.

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IN carrying out the treatment by Koch's fluid, I must express my best thanks to my colleagues at the Throat Hospital, especially to Dr. Bond, for placing cases at my disposal, and for the interest they have shown in watching the results. I must also acknowledge my great obligation to Dr. William Rawes, demonstrator of physiology at the London Hospital Medical College, for making dilutions and arranging the dosage of the tuberculin, as well as for the great trouble he has taken in making repeated examinations of the *sputa* of the patients whilst the treatment has been going on. To Mr. Milson Rees, resident medical officer of the Throat Hospital, Golden Square, to Mr. Curling Bates, and to Dr. Arthur G. Root, of Albany, U.S.A., I am specially indebted for the great zeal and care which they have shown in taking notes, making sphygmographic tracings, and keeping hourly temperature charts, as well as for making frequent and minute examinations of the patients.

RETROSPECT.

1. The experiments were made on twenty cases, and of these, nine patients were suffering from pulmonary, or laryngo-pulmonary, phthisis, seven from lupus, and in four the experiments were carried out for purposes of diagnosis. The period of treatment extended over four months.

2. With the exception of two of the earliest cases, in which the treatment was made at the urgent request of the patients, who had carefully studied everything which had been written on the subject, the patients were carefully selected. Many others were rejected because the disease was too far advanced, and some because, though there was evidence of long-standing disease, the morbid process was quiescent at the time the patients presented themselves.

3. No other medical treatment than the injection of tuberculin was adopted, except that some of the phthisical patients wore inhalers containing carbolic acid at intervals for six hours daily.

4. No accident or immediately unfavourable result supervened, except that in one case (A) severe dyspnœa, apparently from spasm of the smaller bronchial tubes, and in another case (P) spasm of the glottis occurred. Of the sixteen cases treated (phthisis and lupus), eleven were benefited, four were unfavourably affected, and in one no benefit resulted.

5. In the phthisical and laryngo-phthisical cases, bacilli were found in every instance before the treatment was commenced. After one or more injections, the bacilli were found to be curved or irregularly bent, and in some cases apparently broken into smaller fragments.

6. The sphygmograph was used in most of the cases, and during the fever following the injections, except in one case, the tracings showed a pulse of exceedingly low tension, with a markedly dicrotic wave; in some instances, indeed, there was marked hyperdicrotism, such as is only seen in the severe and long-continued febrile diseases. In the exceptional case (F) referred to, the pulse became dicrotic in the intervals between the fever, whilst during the reaction it was firmer, and indeed almost normal.

7. In the phthisical cases, there were two in which the disease was confined to the lungs, and seven in which the lungs and larynx were both affected.

8. In the purely pulmonary cases, one was "much improved" and the other "improved."

9. In the laryngo-pulmonary cases, one patient was "much improved," one "improved," four "unfavourably affected," and one "not improved."

10. In the phthisical cases which were either "much improved" or "improved," the improvement was not greater than is occasionally seen, both in private practice and in hospitals, after a few weeks of other treatment, combined with rest and suitable food.

11. Of the four cases of laryngo-pulmonary phthisis unfavourably affected, two died. In one of these cases the death took place seven weeks, and in the other, six weeks, after the last injection. In both these cases death was believed to be accelerated by the injections. Attention must be called to the fact that, in both of these subjects, cavities existed in the lungs before the treatment by injection was commenced, and that it was only carried out at the earnest desire of the patients.

12. In the case which is returned as "not improved," the condition of the lungs was slightly ameliorated. The larynx was better at one part but worse at another. The general health had slightly declined.

13. The effect on the lungs from twenty-four to thirty-six hours after an injection was, in nearly every case, an increase of crepitation at the spot affected, and an extension of the area of crepitation. This was subsequently followed in the favourable cases by a drying up of the moist sounds and by a contraction within the original limits of the area of crepitation. In the unfavourable cases the area of crepitation did not contract after injection, and the softening resulted in the formation of cavities.

14. When any effect was produced on the larynx by injections, great redness of the mucous membrane usually occurred.

15. In three out of the seven cases, circumscribed acute œdema took place, but in no instance was any dyspnœa produced.

16. The natural tendency of the disease in laryngeal phthisis being slow, and the deposit being generally rather dense, the local appearance is usually somewhat anæmic; in the cases treated by tuberculin, the deposit or exudation was thinner, the vessels more injected, and the morbid process more acute.

17. In the seven lupus cases treated, every patient has been benefited, though no case can as yet be said to be completely cured.

18. The effect of the injections was more marked on the skin than on the mucous membrane, and also more active on the mucous membrane of the nose and lips than on that of the larynx.

19. The local reaction and general rise of temperature was much higher in lupus than it was in the pulmonary and laryngeal cases, but in the end the lupus cases tolerated much larger doses.

20. In one case, after .10 c.c. injected into the back had produced no effect, .002 c.c. injected into the turbinated body caused a decided local reaction and general rise of temperature.

21. In all the patients treated, in addition to other food, an abundant quantity of milk was allowed. Wine was given in several cases.

22. Before entering the hospital, one or two of the patients had been insufficiently fed, and one had continued to work when not in a fit condition of health.

23. The general result of injections as an aid to diagnosis was on the whole satisfactory, but it cannot be said that any great gain resulted from the use of the tuberculin—that is to say, the conclusions would have been just the same in every case, except one, even if no injections had been made. In the case referred to, although there was every reason to think that phthisis was present, no reaction took place, but as there was no expectoration, and therefore no possibility of determining the presence of bacilli, it cannot be said that the value of an injection for diagnostic purposes was invalidated.

24. Whilst the injection of Koch's fluid may not have deserved the enthusiastic reception it first met with, it does not merit its present obloquy. Professor Koch has made a most important discovery, and when the details as regards dosage have been thoroughly worked out, and conclusions have been arrived at as to the best kind of remedies, constitutional and local, to combine with it, tuberculin will prove a most valuable addition to the curative agencies in the hands of the physician.

FIRST REPORT OF CASES TREATED BY TUBERCULIN.

(A second and more detailed report will be published at the termination of twelve months after the last patient was injected.)

IN the cases reported below, neither the name, the sex, nor the exact age has been given, the decennium in which the age occurs being alone stated. It is thought that these reports may fall into the hands of some of the patients treated, and that they might have a depressing effect if they were able to identify their own cases.

(A) Thirty to forty years. PULMONARY PHTHISIS. Condition on admission : Fine crepitation at middle third of left lung. Six weeks under treatment. Bacilli present. Number of injections, 9 ; max. dose, '01 c.c. ; max. temp., 103'4 ; max. pulse, 105 ; max. resp., 40. General remarks : Injections always followed after twelve hours by increased moist sounds, lasting from thirty-six to forty-eight hours. On one occasion, three and a half hours after an injection, severe dyspnœa with a very frequent hacking cough came on ; very little air appeared to enter the chest, and the face, lips and nails became blue, but after a short time the spasm of the bronchial tubes gave way, and sibilant râles were heard all over the chest. These cleared up after a few hours. Condition on discharge : Moist sounds could not be heard ; cough and expectoration diminished. In the early part of treatment patient lost 7lbs., but regained it before leaving hospital, and a fortnight after discharge had gained 14lbs.

(B) Twenty to thirty years. PULMONARY PHTHISIS. Condition on admission : Slight consolidation at both apices, most marked on the right side. Five weeks under treatment ; bacilli abundant. No. of injections, 12 ; max. dose, '08 c.c. ; max. temp., 103'6 ; max. pulse, 122 ; max. resp., 26. General remarks : After each injection increase of moist sounds, which became dry on second or third day following. Condition on discharge : Less consolidation over left apex, but slight increase on right side ; the cough and expectoration less ; gained 1lb. whilst in hospital.

(C) Thirty to forty years. PULMONARY AND LARYNGEAL PHTHISIS. Condition on admission : At right apex dry sounds, at left apex softening ; epiglottis thickened and pale ; ventricular bands and inter-arytenoid fold thickened. Ten weeks under treatment ; bacilli in large quantities. No. of injections, 15 ; max. dose, '015 c.c. ; max. temp., 103 ; max. pulse, 100 ; max. resp., 18. General remarks : After the first injection the pale and slightly swollen right arytenoid cartilage assumed a pyriform shape, and became of a redder colour ; in fact, presented the appearance of laryngeal phthisis. The rest of the larynx subsequently became much inflamed, without, however, being distinctly œdematous. Condition on discharge : Epiglottis slightly swollen and very red ; ventricular bands and arytenoid red, swollen, and at parts superficially ulcerated. The softening has extended over the upper part of the left lung ; right lung in same condition as on admission ; increase of cough and expectoration.

(D) Twenty to thirty years. LARYNGEAL AND PULMONARY PHTHISIS.

Condition on admission : Harsh breathing at right apex, consolidation at left ; both arytenoids pale, both ventricular bands red, swollen, and covering the cords ; right ary-epiglottic fold slightly swollen, and left fold much swollen.

Eight weeks under treatment ; bacilli present. No. of injections, 17 ; max. dose, '015 c.c. ; max. temp., 104'4 ; max. pulse, 150 ; max. resp., 32. Condition on discharge : Cavity at right apex, softening at left ; moist sounds over the whole of the chest ; much swelling and redness of epiglottis ; both ary-epiglottic folds presenting pyriform swellings ; ulceration of left ventricular band. Pain in swallowing. Evening temperature between days of injections 100-101. While in hospital lost 2lbs.

(E) Forty to fifty years. LARYNGEAL AND PULMONARY PHTHISIS. Condition on admission : Moist sounds at both apices ; slight swelling of ary-epiglottic folds ; slight superficial ulceration of inter-arytenoid fold ; left ventricular band presents a flap-like thickening from its anterior half, which covers the anterior half of the left vocal cord ; the right ventricular band and right vocal cord normal. Four weeks under treatment ; bacilli numerous. No. of injections, 26 ; max. dose, '025 c.c. ; max. temp., 104'5 ; max. pulse, 104 ; max. resp., 20. General remarks : As a rule the constitutional reaction was very slight, the temperature seldom rising above 100 or 100'5. On the only occasion when the temperature rose high (104), more than twenty injections had already been made, and the strength of the dose was only '015 c.c. Shortly after the injecting process had commenced, œdematous swelling of a markedly inflammatory character took place in the right ary-epiglottic fold. This diminished slightly in the intervals between the injections, but increased again after each injection. The swelling, which was as large as a pigeon's egg, took place principally towards the lateral wall of the pharynx, and did not diminish the calibre of the laryngeal canal, but it caused slight odynphagia. Condition on discharge : Crepitation at both apices ; œdematous swelling of right ary-epiglottic fold ; ulcer on anterior half of left ventricular band (slough of projection previously in this situation). Patient lost 7lbs. whilst under treatment.

(F) Twenty to thirty years. LARYNGEAL AND PULMONARY PHTHISIS. Condition on admission : Cavity at left apex, consolidation at right ; epiglottis much swollen, arytenoids pale and swollen, ary-epiglottic folds pale and flabby, ventricular bands imperfectly seen. Four weeks under treatment ; bacilli present. No. of injections, 6 ; max. dose, '005 c.c. ; max. temp., 105'5° ; max. pulse, 120 ; max. resp., 28. General remarks : On one occasion after an injection the patient's temperature remained at 105 for seven hours. As the treatment was evidently doing no good, but apparently causing the lung to break down more quickly, the patient was discharged from the hospital on the 29th December, 1890, the last injection having been made on the 23rd December. Patient died at home 8th February, 1891. *Post-mortem* not allowed. Condition on discharge : Large cavity at left apex increased in size, softening at right apex ; epiglottis much more swollen.

(G) Thirty to forty years. LARYNGEAL AND PULMONARY PHTHISIS. Condition on admission : Cavity at right apex, consolidation at left ;

epiglottis red, swollen and roughened ; both arytenoids, especially the left, pale and swollen ; inter-arytenoid fold thickened and ulcerated ; ary-epiglottic fold and ventricular bands swollen and pale, completely covering cords. Two weeks under treatment ; bacilli in large quantities. No. of injections, 13 ; max. dose, '03 c.c. ; max. temp., 105'2 ; max. pulse, 160 ; max. resp., 32. General remarks : No benefit resulting from treatment, the patient was discharged from the hospital on 16th December, 1890, receiving the last injection on 12th December, 1890 ; died January 22nd, 1891. No *post-mortem* allowed. Condition on discharge : Increase of cavity at right apex ; left apex same as when admitted. Larynx much swollen in all parts ; ventricular bands and inter-arytenoid folds ulcerated.

(H) Forty to fifty years. LARYNGEAL AND PULMONARY PHTHISIS. Condition on admission : Dulness at left apex ; both ventricular bands and arytenoids swollen and red ; inter-arytenoid fold pale, swollen and projecting forward. Vocal cords covered by ventricular bands. In addition to physical signs, there is a history of specific disease. Considerable pain in left side of neck, shooting up to ear, on same side. Three weeks under treatment ; bacilli present. No. of injections, 4 ; max. dose, '06 c.c. ; max. temp., 101'8 ; max. pulse, 120 ; max. resp., 28. General remarks : Crepitation occurred at left apex, about twenty-four hours after the first injection. No change at apex after last two injections. Very slight local reaction followed injection. Condition on discharge : Area of dulness at right apex diminished ; no marked change in condition of larynx.

(I) Twenty to thirty years. LARYNGEAL AND PULMONARY PHTHISIS. Condition on admission : Deposit at both apices ; arytenoids enlarged, red, and roughened ; ary-epiglottic folds and ventricular bands swollen ; vocal cords slightly thickened and ulcerated. Five weeks under treatment, but still in hospital ; bacilli abundant. No. of injections, 18 ; max. injection, '09 c.c. ; max. temp., 101'2 ; max. pulse, 108 ; max. resp., 20. General remarks : Symptoms following injections only slight. Condition on discharge (still in hospital, but injections have ceased for a week or two) : No crepitation on left side, doubtful crepitation occasionally present on the right side. Ulcers on vocal cords healed, but they are still slightly thickened, and general appearance of the larynx nearly healthy ; the arytenoids being only slightly swollen, and of a healthy colour.

(J) Ten to twenty years. PRIMARY LUPUS OF THE LARYNX. Condition on admission : Epiglottis almost completely destroyed ; both arytenoids and epiglottic folds so swollen as to completely obstruct the larynx. The breathing had become so difficult, that six months previous to admission into the hospital, tracheotomy was resorted to. Sixteen weeks under treatment, but still in hospital. No. of injections, 27 ; max. dose, '10 c.c. ; max. temp. 105 ; max. pulse, 160 ; max. resp., 20. General remarks : In the earlier stages of treatment, local reaction followed each injection, the arytenoids becoming much swollen, the little space between them being obliterated. After thirty-six or forty-eight hours the inflammation subsided, and the arytenoids were less swollen than before the injection. The injections were followed once by sickness, and on two occasions by colicky pain. Subsequently 5 minims of Tinct. Opii. were administered before each injection, and no inconvenience was

experienced. Present condition, March 20th: The arytenoids and ary-epiglottic folds are still much swollen, but a good supply of air passes into the larynx, so that the patient, who was aphonic on admission, can now speak in a loud but rather hoarse voice. Before leaving the hospital no reaction followed after the injection of a decigramme. Patient since re-admitted. After several further injections, and reaching a maximum of '10 c.c., the orifice of the larynx was so well opened that the patient now breathes with a cork in the canula.

(K) Ten to twenty years. LUPUS OF THE LARYNX AND NOSE. Condition on admission: Primary lupus of the larynx, epiglottis swollen, rigid and granular, and has a red nodule at the free edge on each side. Both arytenoids are thickened, especially the right one; right ventricular band is swollen, and both vocal cords slightly thickened; the right one presented a nodule on its free edge, near the centre. A secondary lupus of the nose and lip, gums and hard palate, involving bridge, both alæ, both sides of the septum, the upper lip, anterior surface of the gums and front of the mouth, posterior surface of gums and hard palate. Sixteen weeks under treatment; still in hospital. No. of injections, 23; max. dose, '10 c.c.; max. temp., 104°0; max. pulse, 140; max. resp., 44. General remarks: After earlier injections the urine contained a slight trace of albumen. On two occasions slight colic followed injections. After earlier injections there was some discomfort in swallowing owing to swelling of the lips, palate and epiglottis. Present condition (March 20th): The patient's nose cured, with the exception of slight redness just below the bridge; lips slightly swollen, gums and palate cured. Epiglottis and larynx cured, with the exception of slight swelling on the centre of the right vocal cord, and very slight swellings on the edge of the epiglottis in the localities where there had previously been nodules. Patient retained in hospital until he is admitted into a convalescent institution. *Postscript*.—April 1. Relapse has taken place, affecting gums, palate, and nose.

(L) Forty to fifty years. LUPUS OF NOSE. Condition on admission: The right half of the framework of the nose is destroyed, the turbinated bone being exposed, and covered with vegetation. The malar extremity of the ulcer is much thickened, and presents a number of lupoid nodules. The anterior surface of the nose is ulcerated. There is also an isolated nodule close to the inner canthus of the right eye. The ulcer has extended from the nose downwards, and has nearly reached the red part of the lip on the right side. Eight weeks under treatment. No. of injections, 28; max. dose, '10 c.c.; max. temp., 104°4; max. pulse, 105; max. resp., 22. Present condition (March 20th): Thickening on malar edge of ulcer almost disappeared; deposit at inner canthus still visible, though much smaller; thickening over turbinated body diminished. This patient was discharged temporarily from the hospital on February 7th, scarcely any reaction following the injection of '10 c.c. of tuberculin. Re-admitted on the 13th, and '002 c.c. was injected into the substance of the turbinated body. This was followed by marked local reaction, and some slight general reaction. The second injection on the 17th was followed by a rise in temperature of 102°. The great effect of these injections of weak strength into the seat of the disease, after the injection

of 10 c.c. into the back had produced no rise of temperature or local change, is remarkable. Some observers thought that the ulceration had extended slightly across the bridge of the nose since the treatment had commenced, but this was strenuously denied by the patient himself. The patient lost 14lbs. in the early part of the treatment, but subsequently recovered all the loss, and gained 3lbs.

(M) Twenty to thirty years. LUPUS OF NOSE, UPPER LIP, AND RIGHT SIDE OF FACE. Condition on admission: Lupus erythem. of right cheek, lupus vulg. of lip and nose. Twelve weeks under treatment, but still in hospital. No. of injections, 24; max. dose, 10 c.c.; max. temp., 105.5; max. pulse, 172; max. resp., 44. General remarks: Patient stated that she had been cauterised and scraped upon various occasions, altogether thirty-two times; but she affirmed that she was better after the second injection than she had ever been before. In the earlier stage the injections were followed by an extensive roseolous rash, which after a few days became of a purple colour, and afterwards faded away. Present condition (March 20th): The patient is nearly cured, and very slight reaction now takes place after a dose.

(N) Forty to fifty years. LUPUS OVER THE WHOLE OF NOSE, UPPER LIP, AND PART OF BOTH CHEEKS. PULMONARY PHTHISIS. Condition on admission: Lupus vulg., but in parts almost erysipelatous; limited crepitation at the apices of both lungs. Fourteen weeks under treatment, but still in hospital. No. of injections, 19; max. dose, 0.45 c.c.; max. temp., 104.2; max. pulse, 106; max. resp., 22. General remarks: In addition to the disease already described, the examination of the pharynx shows extensive cicatricial contractions, the uvula being destroyed and the back of the palate adhering to the posterior wall of the pharynx. Present condition (March 20th): Condition of face very much improved.

(O) Forty to fifty years. LUPUS OF FOREHEAD, EYELIDS, NOSE, CHEEKS AND NECK. Condition on admission: Disease is active in all situations except on the neck, where it has undergone cicatrization. Six weeks under treatment, but still in hospital. No. of injections, 18; max. dose, 0.45 c.c.; max. temp., 102.6; max. pulse, 136; max. resp., 32. General remarks: Reaction always took place very rapidly after injection; the eyes became closed and large scabs formed over the inflamed parts, rash followed injection. Present condition (March 20th): General condition of face very much improved.

(P) Ten to twenty years. LUPUS OF NOSE, LIPS, HARD PALATE, FAUCES AND LARYNX. Condition on admission: Epiglottis slightly thickened, centre of free edge eaten away, but cicatrized; vocal cords slightly thickened, both arytenoids and ventricular bands slightly swollen and rough. No active disease going on in the larynx, but a little mucus hanging about the parts, and adhering in places—the appearance of the mucous membrane in fact resembling that seen in the naso-pharynx in cases of long-standing catarrh. Lupoid process involves mucous membrane and right ala of nose. Six weeks under treatment, but still in hospital. No. of injections, 15; max. dose, 0.3 c.c.; max. temp., 104; max. pulse, 136; max. resp., 32. General remarks: Injections followed by great swelling of the nose, completely obstructing both nasal passages. The

patient, on one occasion, had a severe attack of spasm of the glottis, almost necessitating tracheotomy. It is believed to have been caused, or at any rate aggravated, by the adhesion of dry mucus to the vocal cords. Present condition (March 20th) : Condition of nose much improved.

(Q) Twenty to thirty years. TUMOUR OF NECK. Injected for diagnostic purposes—in fact, to ascertain whether the disease was malignant or scrofulous. Two injections were made, max. dose, '01 c.c., but no effect either local or general was produced. The case was considered to be one of lympho-sarcoma. Fourteen days under treatment.

(R) Twenty to thirty years. SUPPOSED PULMONARY AND LARYNGEAL PHTHISIS. Injected for diagnostic purposes. Condition on admission : Crepitation at both apices ; nine days under treatment ; no bacilli found. Two injections. Max. dose, '005 c.c. ; max. temp., 99'8° ; max. pulse, 96 ; max. resp., 16. General remarks—Condition on discharge : No change as regards either the lungs or the larynx. Seen three months afterwards, no crepitation could be discovered in the lungs, but there was still slight thickening of the inter-arytenoid fold. It is very doubtful whether the disease in this case is tubercular or not. There is a strong family history of phthisis, father and mother and a brother and sister having died of phthisis, but the reaction from injections was less than it has been in any case of phthisis in this series.

(S) Twenty to thirty years. SUPPOSED PULMONARY AND LARYNGEAL PHTHISIS. Injected for diagnosis. Two weeks under treatment ; no bacilli found. Condition on admission : Slight crepitation at both apices ; congestion of the larynx, especially on the right side. Three injections : max. dose, '003 c.c. ; max. temp., 102'8 ; max. pulse, 138 ; max. resp., 28. General remarks : Moist sounds spread after injections, but the congestion of the larynx disappeared. The injection fully established the tubercular nature of the pulmonary affection.

(T) Twenty to thirty years. SUPPOSED PULMONARY PHTHISIS. Injected for diagnostic purposes. Two weeks under treatment ; no bacilli found. Condition on admission : Slight crepitation at apex of left lung ; marked dulness at right apex. Had lost 7lbs. during the last six months. Belonged to a family in which there was a strong phthisical tendency, four out of seven children (of whom patient was one) having died of consumption. Three injections : max. dose, '005 c.c. ; max. temp., 98'4 ; max. pulse, 68 ; max. resp., 15. General remarks : The absence of reaction tends to show that the disease is catarrhal and not tubercular.
