

FILE NAME: Welding (WELD)

DATE: 1936 Apr 1

DOC#: WELD001

DOCUMENT DESCRIPTION: Journal Article - X-Ray Appearances of the Lungs of Electric Arc Welders

within an hour or two; but this degree of acidity was not invariably maintained throughout the day. As we are both of about average weight (10 st. 2 lb. and 10 st. 9 lb.) we concluded that somewhat larger doses should generally be given for the treatment of patients.

Four patients were treated with ammonium mandelate, and in all four a sterile urine was effected in a week or less, though all had a chronic infection. Case 26, a man of 13 st., required doses of 51 grains four times daily (1½ oz. of the elixir). Case 27, a child of 6 (weight 3 st. 7 lb.) with acute nephritis as well as *B. coli* infection, was given 17 grains four times daily. Case 28 had 34-grain doses. In Case 29 the urine was alkaline to litmus before treatment, and 51-grain doses supplemented by 30 grains of ammonium chloride were necessary to produce a satisfactory acidity and cure the infection.

In the light of this short experience, together with what is already known of mandelic acid treatment, we feel justified in saying that ammonium mandelate, suitably prepared, is a convenient means of administering mandelic acid, and that in the majority of cases the use of ammonium chloride can thereby be obviated. The suitable dose of ammonium mandelate is probably the same as that of the sodium salt—namely, about 50 grains four times in the day, the equivalent of about 3 grammes of mandelic acid.

TREATMENT OF PYELONEPHRITIS IN GENERAL

The disease "pyelitis" affecting, as it does, the parenchyma of the kidney as well as the renal pelvis, ureter, and bladder, is better known as pyelonephritis. The term cystitis may be restricted to the occasional infection of the bladder only, by catheter or otherwise, before an ascending spread has taken place.

Acute pyelonephritis is often associated with high temperature, rigors, and general symptoms of which severe headache is one of the most frequent. For such severe cases, alkalis if given in sufficient doses are so efficient in bringing down the temperature and controlling the distressing symptoms that we have not used mandelic acid therapy, fearing to cause a temporary exacerbation of symptoms or to induce vomiting. It should be noted that it is often necessary to give as much as 30 grains of potassium citrate and 30 grains of sodium bicarbonate every two hours in order to produce the effect. We have recently seen two patients in whom the pyrexia remained despite an alkaline urine, until the dosage was pushed to this extent.

When the acute stage has been controlled, a few cases rapidly clear up spontaneously, especially in women after delivery. In many more, however, pus cells and bacilli remain in the urine, and a chronic pyelonephritis develops. Often there are acute exacerbations and for years the patient suffers from poor health and has intermittent attacks of frequency, dysuria, pyrexia, or urticaria. A few eventually develop renal failure.

As nearly all these chronic infections are now avoidable, we would like to stress the importance of not discharging any case of pyelonephritis, especially when acute, until it is known that the urine is sterile. If, after an acute attack has settled down, bacilli are still present, mandelic acid therapy should be employed at once, before waiting for chronic changes to develop.

For those who show a marked tendency to recurrence we are trying the effect of giving two consecutive days of mandelic acid treatment in each month. Between these brief courses, fluid intake should be

liberal, and both constipation and the over-use of aperients should be avoided as far as possible.

SUMMARY

Of 29 cases of urinary infection treated with mandelic acid 24 showed sterile urine within 2-21 days. Of the successful cases 2 had also a concurrent nephritis in an active stage, which was not adversely affected by the treatment. Of the 5 failures at least 3 were unsuitable cases in which cure was not to be anticipated.

Ammonium mandelate was found to be as effective as the sodium salt, and when it was used it was usually unnecessary to give the unpleasant ammonium chloride.

The proper use of these remedies will prevent chronic pyelonephritis.

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X RAY APPEARANCES OF THE LUNGS OF ELECTRIC ARC WELDERS

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(WITH ILLUSTRATIONS ON PLATE)

ATTENTION has been directed recently to the acute pulmonary conditions which may occur in welders as a result of their occupation. Adler-Herzmark¹ in 1929 described the illness and death of an electric arc welder from pulmonary oedema which he attributed to nitrous fumes. In 1934 Bridge^{2a} recorded a number of cases of acute poisoning by nitrous fumes occurring in oxy-acetylene welders who were working in a confined space in a ship. Williman's recent case³ of acute fatal pneumonia in an electric arc welder was that of a man who had been welding galvanised iron in a confined space; and Titus, Warren, and Drinker⁴ have shown after a series of animal experiments that the pulmonary oedema associated with welding (not necessarily of galvanised metal) in confined spaces is caused by the gases (nitrogen peroxide and ozone) generated at the electric arc and not by the fine particles of iron oxide found in the fume. The symptoms associated with the welding of galvanised metal appear to be comparable with those of metal fume fever and were described by Bridge^{2b} in 1921, by Koelsch in 1923,⁵ and also by Drinker⁶ and his co-workers in 1927. Similar symptoms in welders working on galvanised metal have been noted by Dickson⁷ and by Anderson.⁸ Metal fume fever is a transient malady and is characterised mainly by malaise, pyrexia, and shivering attacks.

Some of the occupational risks in welding—e.g., metal fume fever and poisoning by nitrous fumes—are common to both electric arc and oxy-acetylene welding, but each method has its proper risks. Wirschafter and Schwartz⁹ state that the oxy-acetylene welder is exposed, under various working conditions, to poisoning by the products of incomplete combustion of the oxy-acetylene flame, especially

carbon monoxide and acetylene, and also by impurities in commercial acetylene. Westhofen,¹⁰ who made a statistical study of the health of 146 electric arc welders, shows that a large number of them suffer from colds and inflammatory conditions of the upper respiratory tracts, a fact which he believes can be explained by the irritating properties of the metal fume and by the sudden changes of temperature to which welders are exposed.

Chronic pulmonary lesions directly associated with the occupation have not been recorded up to the present time as occurring in electric arc welders. This fact is not surprising because the process is a comparatively new one and it is only during the last ten years that it has been widely adopted. It may be noted also that covered electrodes have only been used for about ten years. We present in this paper the results of a clinical and radiological examination of the chests of 16 electric arc welders. They are apparently healthy men and are actively engaged at their occupation. Nearly all of them are young men who were apprenticed to electric welding at 14 years of age and who have worked at no other trade. The X ray films of 6 of them show a generalised fine mottling over both lung fields; the remaining films show less marked changes, but none could be considered to be a picture of a completely normal chest. The conditions which have to be considered in the differential diagnosis include miliary tuberculosis, asbestosis, silicosis, and other pulmonary conditions caused by dust or fumes. The X ray film in the first case, in view of the family history, was for some time thought to be an example of miliary tuberculosis. In the present early stage of the investigation we are not prepared to be dogmatic about the interpretation of the radiographic and clinical findings, especially because no opportunity for histological examination of the lungs has arisen. In this paper we merely wish to record the results of our examinations as far as they have gone and to discuss in a general way the possible factors in the aetiology.

THE FIRST TWO CASES

CASE 1.—Aged 44. This man was seen by one of us (A. T. D.) at the Rotherham Tuberculosis Dispensary on June 28th, 1933, because his sputum had been stained slightly with blood for a few days. He felt well except for slight debility which had followed an attack of influenza six months previously.

Family History.—His father and grandfather, both of whom had been tin miners in Cornwall, had died from silicosis.

Occupational History.—He left school at 14 years of age and for 1 year stoked boilers in a clay mine (above ground). For 18 years (until 1925) he worked as a blacksmith, but during this time he had done occasional electric welding jobs. He has been an electric arc welder for 11 years.

X Ray and Other Examinations.—On June 28th, 1933, an X ray film showed fine mottling * evenly distributed over both lung fields. The sputum was examined on July 4th, 1935, for tubercle bacilli and for asbestos bodies, with negative results. The glass shield used by the man to protect his eyes during electric welding was examined on Sept. 29th, 1933, at the Government laboratory. The report stated that "the fume deposited on the glass consists essentially of magnetic iron oxide (Fe_3O_4). Slight evidence of the presence of silica was obtained but this was probably derived from the glass slide, the surface of which was damaged by red-hot particles thrown off from the electrodes." Further X ray films were taken of his chest on Dec. 26th, 1933, and also on Sept. 3rd, 1934

* We have used the word "nodule" as a convenient term to describe the individual shadows without reference to their size. "Stippling" is used to indicate the very fine "nodulation" seen in several cases, whereas "mottling" is used to describe a coarser type of "nodulation."

(Fig. I. on Plate). The appearances differed in no essential point from those of the original film. It was thought however that the punctate shadows seen in the later film were slightly larger, especially in the fifth right costal space close to the hilum.

The patient has not lost any time from work and when seen recently was found to be in fairly good health. Since 1933 he has been wearing a mask over his nose and mouth during actual work at electric welding. Physical examination revealed few abnormal signs with the exception that the breath sounds were harsh over the apices and bases of the lungs, and that a few post-tussic crepitations could be heard at both bases. The movement of the chest was equal on both sides but the degree of expansion was somewhat limited.

CASE 2.—Aged 35. This man was asked to attend for X ray examination because of the nature of his work. His occupational history shows that after leaving school he worked in an office for 6 years; for another 3 years he was engaged in a steel works as a cold steel roller, and for the 11 years he has been working continuously as an electric arc welder. For the last year he has been working as storekeeper because he thought the fume from welding was affecting his health. There is no family history of tuberculosis. He has a slight cough and occasional morning sputum, but otherwise is in good health. He was first radiographed in September, 1934, the film (Fig. II. on Plate) showing features similar to those of Case 1. The lung fields generally show a fine mottling, the individual shadows being irregular in size and having soft outlines. The mottling is distributed fairly uniformly, although the upper two-thirds of each lung field are rather more affected than the lower thirds. Both lungs are equally affected. A recent radiogram of the chest (Jan. 6th, 1936), taken a year after he had given up electric welding, shows that the mottling noted in the first film is still present but less marked. In some of the larger nodules a minute central core is visible. Clinical examination of the chest shows that the expansion is equal on both sides but is rather less than normal. The percussion note is not impaired, and the breath sounds are harsh with prolongation of expiration over both lower zones, especially in the mid-axillary lines. Post-tussic crepitations are heard at both bases. Examination of the sputum (March 12th, 1936) shows that it contains large numbers of macrophages or dust cells which are packed with fine granules of iron oxide. No asbestos bodies are seen.

On account of the findings in the first 2 cases, 14 more welders were asked to attend for examination. Brief notes of the history and of the results of the X ray examinations of the chest are given. In a few cases the results of clinical examination of the chest have been added.

FOUR "POSITIVE" CASES

Four showed X ray appearances comparable with those seen in the first 2 cases, and are therefore classed as *positive*.

CASE 3.—Aged 25. Electric arc welder for 9 years. No other occupation. No family history of tuberculosis. Has a slight cough with copious black sputum, especially after welding inside tanks. Movement diminished over the left upper part of the chest. No impairment of percussion note. Breath sounds harsh over left upper region and also at both bases posteriorly. Crepitations were heard at both bases in the axillary lines but more clearly on the left side. **Radiography** (Jan. 6th, 1936). Skeleton, heart, and diaphragm normal. Shadow of lung roots not enlarged. Prominent (? calcified) opacity in the upper pole of left root. Fine bronchial ramifications slightly accentuated generally. Fine stippling throughout both lung fields, the nodules being irregular in size and shape. The stippling is slightly more marked in the upper half of the right lung.

CASE 4.—Aged 23. Electric welder for 7 years. Health good and no family history of tuberculosis. Slight cough with morning sputum. **Radiography** (Jan. 8th, 1936). Skeleton, heart, and diaphragm normal. The shadow of the right hilum is definitely enlarged. The

bronchial markings are not increased. Over both lung fields there is generalised stippling. The nodules are irregular in size and shape and consist of single and aggregated units. Their outlines are soft but some of the larger ones have a hard central core.

CASE 5.—Aged 26. Electric arc welder for 9 years. Had an attack of acute bronchitis 5½ years ago, since when has had a persistent cough with black sputum. *Radiography* (Jan. 8th, 1936). Skeleton, heart, and diaphragm normal. Bronchial markings prominent. Right lung clear. Over the upper half of the left lung fine stippling is seen. Both hilar regions normal.

CASE 6.—Aged 28. Electric arc welder for 12 years. Health good. No symptoms apart from slight cough and sputum. Examination of the chest shows that the expansion is good and equal. Percussion note good. Breath sounds well transmitted with a slight prolongation of the respiratory murmur. No adventitious sounds. Heart sounds normal. *Radiography* (Jan. 15th, 1936). Skeleton, heart, and diaphragm normal. Right interlobar septum visible. Generalised fine stippling throughout both lung fields, the shadows being irregular in size and having soft margins.

THREE "SUSPICIOUS" CASES

Three more cases showed X ray changes which were not so definite as those presented by the first 6 cases. We have classified them as *suspicious*.

CASE 7.—Aged 26. Electric arc welder for 9 years. No other occupation. No family history of tuberculosis. Has had a cough with morning sputum on and off for 10 years. The cough is worse after he has done a welding job in an enclosed space, and the sputum then becomes black. Finds that he gets very tired, especially on night shifts. *Radiography* (Jan. 6th, 1936). Skeleton, heart, and diaphragm normal. The bronchial shadows are accentuated generally in both lung fields. There is fine stippling distributed over the left upper zone, especially in the area immediately surrounding the upper pole of the left root.

CASE 8.—Aged 25. Electric arc welding for 11 years. No family history of tuberculosis. Has only a slight cough which is worse after working in an enclosed space, and brings up a certain amount of black sputum mainly in the mornings. Examination of the chest revealed no abnormal physical signs. *Radiography* (Jan. 6th, 1936). Skeleton and heart normal. Right dome of diaphragm slightly blurred. Slight enlargement of the hila, especially on the left side. There is only a slight increase in the bronchial trunk shadows, but the fine bronchial ramifications, especially in the mid-zones, present a honeycombed appearance. A few faint soft and fairly coarse nodules are present in both lung fields. These are mainly situated peripherally and give a coarse mottled effect. The mottling in this case is not nearly so well marked, nor the nodules so fine as in the definitely positive cases.

CASE 9.—Aged 22. Electric arc welder for 8 years. Health good, and only has a cough after doing welding inside a tank. *Radiography* (Jan. 8th, 1936). Skeleton, heart, and diaphragm normal. Bronchial shadowing is prominent in the right upper lobe, and some calcified nodules are present in the right hilum and upper perihilar area. Fine bronchial ramifications are increased generally, and both lung fields have a slightly stippled appearance, the nodules being poorly defined and well spaced. Actual nodulation is however present.

"RADIOGRAPHICALLY NEGATIVE" CASES

The remaining 7 cases have been classified as negative from a radiological point of view. It will be seen however that a number of the films showed increased bronchial striation or fine honeycombing as opposed to definite mottling, and could not strictly be called normal X ray films of the chest.

CASE 10.—Aged 41. Oxy-acetylene welder for 3 years during his apprenticeship, and electric arc welder for 17 years. No family history of tuberculosis. Had a slight attack of influenza 2 years ago which kept him

away from work for a week. Has a slight cough with morning sputum. *Radiography* (July 13th, 1934). Heart rather bulbous and slightly enlarged to the right. The right dome of the diaphragm is elevated, and the right costophrenic angle obliterated. The shadow of the left hilum is enlarged. The bronchial trunks in both lungs are markedly accentuated. Close examination reveals a suggestion of fine stippling in the upper lung fields, but this feature is not definite.

CASE 11.—Aged 23. Electric arc welder for 9 years. Health good and no family history of tuberculosis. Has no symptoms. *Radiography* (Jan. 8th, 1936). Skeleton, heart, and diaphragm normal. Right interlobar septum very faintly seen. Fine bronchial ramifications show a slight honeycombing but no definite nodulation. An appearance of nodulation is present, especially in the third and fourth right intercostal spaces as a result of the crossings of the fine bronchial ramifications.

CASE 12.—Aged 25. Has been an electric arc welder for 10 years. He attended the dispensary because his wife was suffering from open pulmonary tuberculosis. Has no cough or sputum. *Radiography* (March 18th, 1935). Skeleton, heart (small), and diaphragm normal. Bronchial shadows not definitely increased in the lower zones. A slight degree of stippling is present in the second right intercostal space and also in the second and third left intercostal spaces.

CASE 13.—Aged 23. Electric arc welder for 8½ years. No other occupation. No family history of tuberculosis. Has no cough as a rule, but brings up black sputum after doing electric welding inside tanks or boilers. *Radiography* (Dec. 23rd, 1935). Skeleton, heart, and diaphragm normal. Bronchial markings generally intensified. No definite stippling present. In certain areas—e.g., the fifth right and fifth left intercostal spaces—the lung parenchyma shows a fine "honeycombing."

CASE 14.—Aged 31. Electric arc welder for 3½ years. Health good. No symptoms. No family history of pulmonary tuberculosis. Examination of the chest shows no abnormal signs. *Radiography* (Jan. 15th, 1936). Skeleton normal. Left auricular region of the heart shadow appears to be enlarged. Increased bronchial striation but no parenchymatous mottling.

CASE 15.—Aged 27. Electric arc welder for 11 years. Health good. Slight cough and sputum. Examination of the chest reveals no abnormal physical signs. *Radiography* (Jan. 15th, 1936). Skeleton, heart, and diaphragm normal. Slight increase of bronchial markings but no parenchymatous stippling.

CASE 16.—Aged 32. Electric arc welder for 9 years. Health good. Slight cough and sputum. Clinical examination showed no abnormal physical signs. *Radiography* (Jan. 15th, 1936). Skeleton, heart, and diaphragm normal. Definite increase of bronchial striation with very slight fine honeycombing but no definite stippling of the lung parenchyma.

DISCUSSION

The diagnosis of the underlying pulmonary lesions which have given rise to these striking X ray changes is a matter which is both interesting, and in the absence of histological examination of the lung tissue, highly speculative. Little doubt exists, however, that the lung changes have been brought about in these men by the dust or fume which they have inhaled while working as welders. During welding operations dense white or greyish-white fume rises up continuously from the spot which is being welded. The welder is obliged to bend closely over his work because he holds in front of his face a coloured glass screen which protects his eyes from the strong light but impedes his vision. If no protective measures are adopted, the welder cannot fail to inhale large quantities of fume during the time he is actually working.

The electrodes or welding rods which contain a core of metal and an outer covering are consumed

gradually by the heat generated (about 1500° C.) during the welding operation. The metal in the core of the rod becomes molten and, assisted by the flux contained in the covering, spreads over the surface of the metal which is being welded. The fume is therefore made up of the volatilised constituents of the coverings of the rods together with fine particles of oxidised metal, usually in the form of iron oxides. In addition the fumes probably contain gases such as nitrogen peroxide and ozone which are formed by the action of an electric spark on the air. The composition of the coverings of the electrodes or welding rods becomes, in the circumstances, a matter of some importance. Many substances, all of which we do not propose to enumerate, are used. The basis of the majority of the coverings is sodium silicate which acts as a flux. Again, the coverings of a certain type of electrode contain asbestos. The rods are sometimes dipped in a mixture containing powdered asbestos and sodium silicate, or asbestos yarn is wound round the rod and fixed by sodium silicate. In some cases the asbestos completely covers the rods, and in others it is merely a cord which is wound spirally about the rod.

The composition of the fumes arising from electric welding electrodes has not yet been fully investigated. Mr. L. C. McNair, H.M. Engineering Inspector of Factories, has however had partial analysis made of the fumes evolved from an asbestos-covered electrode and some asbestos fibres were found. When the particulate matter of the fumes was collected in an Owen's dust-counter, it was seen that a large proportion consisted of iron oxide particles, with an occasional asbestos fibre.

The X ray appearances in the well-marked cases differ from the usual picture of asbestosis. In none of the positive cases and in only one of the suspicious cases was there any blurring of the diaphragmatic shadow, and in no case was the heart outline blurred. The line of the interlobar septum (a feature present in a number of films of cases of asbestosis) is seen in only one positive case. The opacities in the films are not accentuated at the bases of the lungs, but on the contrary the upper lung fields appear to be the earliest, and in established cases, most markedly affected. Before asbestosis can be eliminated from the differential diagnosis it must be remembered that the asbestos fibres are being subjected to intense heat and are not in the same physical state as the fibres which are inhaled by workers in an asbestos factory. It is possible that an atypical picture of asbestosis might be produced by the inhalation of altered asbestos. Merewether¹¹ says that—

"the radiographic appearances of the developed or advanced stages of asbestosis are distinctive, although they are not specific. While, as is the case with silicosis, certain radiographic appearances may be looked upon as typical of the disease, frequently modifications of and departure from the typical picture occur."†

The X ray appearances in our cases most closely resemble those of a fine silicosis, but the clinical features show two important differences. In the first place, the electric welders whom we examined are all in good health and are fit to work. The only symptoms observed were slight cough and morning expectoration, and in the first case a small hæmoptysis occurred. This man has not been away from work even for a day since he was first seen in June, 1933,

† We have submitted our films to Dr. Merewether and he is of the opinion that "while some of the films give a general impression of asbestosis, further examination reveals so many points of difference in detail from the currently accepted radiographic appearance of asbestosis, as to negative such a diagnosis."

DESCRIPTIONS OF ILLUSTRATIONS ON COLOURED PLATE

DR. MANSON-BAHR

- A.—ACUTE BACILLARY DYSENTERY. Shiga's bacillus isolated. General œdema of mucosa, spasm, sub-mucous hæmorrhages. Early healing stage.
- B.—CHRONIC BACILLARY DYSENTERY. Flexner-Y infection. Agglutination test positive to Flexner 1:180. Great improvement on intestinal lavage.
- C.—AMEBIC ULCERATION of lower rectum giving rise to symptoms suggestive of carcinoma.
- D.—AMEBIC DYSENTERY. Chronic stage, showing "pitting" of mucous membrane.
- E.—ACUTE AMEBIC DYSENTERY. Active ulceration of mucosa with blood and mucus exudate.
- F.—INTESTINAL BILHARZIASIS. Early stage. Patches of granulation tissue containing eggs of *Bilharzia mansoni*.
- G.—MUCOUS COLITIS. Showing the pale colour of the mucosa and the masses of adherent mucus.
- H.—ACUTE ULCERATIVE COLITIS. First stage. Usually called hæmorrhagic colitis.
- I.—ACUTE ULCERATIVE COLITIS. Showing plum-coloured, easily traumatised, mucosa in the second stage.
- J.—ACUTE ULCERATIVE COLITIS. Early stage, showing granular mucosa, with purulent exudate covering the surface. Note the lack of normal folding of the mucosa.
- K.—ULCERATIVE COLITIS. Superficial ulceration in the third, or ulcerative stage.
- L.—TUBERCULOUS ULCERATION OF RECTUM. Case in which tubercle bacilli were found in material obtained through the sigmoidoscope. The patient was suffering from chronic diarrhoea with blood and mucus in the stools.

and his health at the present time is good. None of the men suffers from dyspnoea. Secondly none of them has concomitant pulmonary tuberculosis.

Miliary tuberculosis can be ruled out of the differential diagnosis for clinical reasons, and to some extent on the radiological appearances. None of the cases shows the dyspnoea, cyanosis, and tachycardia of acute or subacute miliary tuberculosis. Chronic or healed miliary tuberculosis is rare and it is difficult to imagine that a condition of such rarity would be found in 6 out of one group of 16 men. In the X ray films of the welders' chests (see Plate) the fine opacities are irregular in size and shape, whereas in miliary tuberculosis of the lung the shadows are more uniform.

A further possible explanation of the X ray appearances in this series of cases is that the inhalation of small quantities of nitrous fumes together with the superadded effect of fine iron oxide dust might set up small areas of chronic inflammatory change, congestion, or fibrosis in the lungs. Again, the iron oxide particles might be opaque to the X rays and produce the picture without the associated presence of fibrosis and congestion.

SUMMARY

1. The chests of 16 electric arc welders who have been engaged at the trade for periods varying from 6–16 years have been examined radiologically.

2. In 6 cases the X ray films showed fine nodulation over both lung fields; in 3 cases stippling was present over a more limited area; the remaining cases showed varying degrees of accentuation of the bronchial shadows, but no stippling. In no case was a completely normal radiogram obtained.

3. Clinical examination of the chests revealed few abnormal signs.

4. The alterations in the pulmonary or bronchial tissues underlying these X ray changes have been

DESCRIPTIONS OF ILLUSTRATIONS ON PLATE

DRS. DOIG AND McLAUGHLIN

FIG. I.—Radiogram showing the fine mottling discovered in Case 1 (September, 1934). The portion outlined in white is reproduced (as an inset) on a larger scale.

FIG. II.—Radiogram from Case 2 (September, 1934).

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FIG. II.—High magnification of endometrium showing metaplasia into cornified squamous epithelium. The islets of squamous epithelium in the submucosa are derived from deep prolongations of tubular endometrial glands. Note the marked fibrosis of the endometrium which simulates scar tissue.

FIG. IV.—Histological picture of a part of the tumour shown in Fig. III. Large cavernous sinuses surrounded by anterior lobe tissue.

FIG. V.—Small adenoma in the anterior lobe of an oestrin-treated rat; probably first stage of tumour formation. The cells in the area of the adenoma are much larger than those of the surrounding pituitary tissue.

FIG. VI.—Small adenoma of the intermediate lobe of the pituitary of an oestrin-treated rat. Note the irregular structure of the posterior lobe with light dots corresponding to vacuolised cells.

FIG. VIII.—Scirrhus fibro-adenoma of the mammary gland in an oestrin-treated rat.

set up by the inhalation of fume which arises during electric arc welding.

5. The probable composition of the fume has been discussed.

6. We wish to emphasise that these X ray appearances have been found in men who are apparently in good health.

7. Up to the present time we have come to no conclusion as to the exact diagnosis of the condition.

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SOME EFFECTS OF PROLONGED ADMINISTRATION OF OESTRIN IN RATS

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(WITH ILLUSTRATIONS ON PLATE)

THE discovery that the continued administration of oestrone, subcutaneously, led to squamous metaplasia of the uterine epithelium of castrate female rats¹ has been confirmed and extended by further experiments reported elsewhere² in which treatment was continued for periods up to 132 days. It

is the purpose of this communication to record the results of experiments of even longer duration. Cramer and Horning³ have reported the appearance of hamorrhagic chromophobe adenomata of the anterior pituitary in 3 male mice of a series of 12 receiving external applications of oestrone dissolved in chloroform for prolonged periods, up to 44 weeks; many of their animals showed cachexia, atrophy of the spleen and thymus, and degenerative changes in the adrenal cortex—effects which they ascribe in part to hypopituitarism. Simple enlargement of the pituitary was observed in 8 of their series of 12. It is known that the administration of large doses of oestrin to female rats may lead to hypertrophy of the anterior lobe within a few days,⁴ and that this is accompanied by enlargement, probably secondary, of the adrenal cortex; but these changes were much less marked in males or in castrates.

Six castrate female rats, initially 3-4 months old, received daily subcutaneous injections of 30 γ of oestrone, dissolved in corn oil, for 331 days; vaginal oestrus was maintained, with very rare lapses, throughout this period. The animals were sacrificed after a further 30 days, during which all (save one) were either left untreated or were injected with solutions of crystalline progesterone (corpus luteum hormone), and in either case had returned more or less rapidly to an anœstrus state. The progesterone-treated animals did not differ materially from those in which all treatment had been discontinued.

At post-mortem examination the horns of the uteri were found to be nearly solid, pearly white, and hard; histological study revealed an extreme hypertrophic fibrosis, pushing the mucosa and muscular coats aside and enlarging the volume of the organ (Fig. I.). Squamous metaplasia of the epithelium was present in five cases (Fig. II. on Plate). These alterations in the uteri were also observed in biopsy specimens taken between the 300th and 330th day of treatment; occlusion of the cervix with secondary pyometrium was not encountered in this series.

The pituitaries were enlarged in all cases, and large cavernous adenomata of the anterior lobe were present in three; one showed a small adenoma of the intermediate lobe, and vacuolisation of the posterior lobe was noted several times. In one case

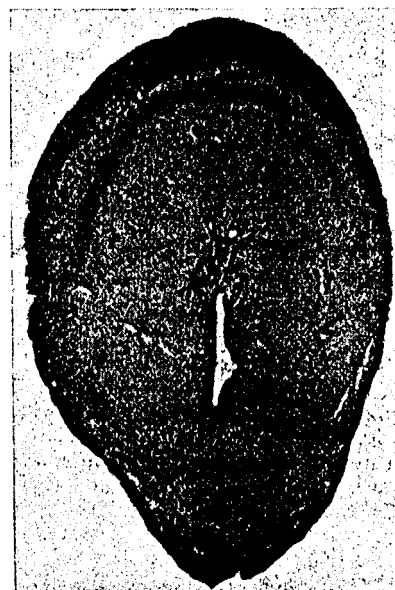


FIG. I.—Transverse section across the uterus of oestrin-treated rat. Note the enormous development of fibrous tissue in the submucosa which leads to partial obliteration of the uterine cavity. The epithelium shows no metaplasia in this case.