Thus in Derbyshire, as in Devonshire and West Shropshire, there is a remarkable body of evidence showing that patients with early phthisis die more often and recover more rarely when residing in exposure to strong prevalent rain-bearing winds than when residing in shelter from them, and this to a degree which cannot be considered negligible.

It is obviously important that phthisis sanatoriums should be located in shelter from these winds, and even more important that phthisis patients, on leaving their sanatoriums, should be advised to reside for some years in such shelter.

ON IRRADIATED ERGOSTEROL AS A DRESSING FOR WOUNDS:

WITH SUGGESTIONS AS TO ITS MODE OF ACTION.

BY

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AN inquiry undertaken four years ago into the effect exercised by irradiated and non-irradiated cholesterol and some other unsaturated fatty substances on the cellular constituents of the blood (recorded in a communication to the Physiological Section of the British Association last September) had previously demonstrated the fact that blood incubated in a closed cell on a film of cholesterol crystals deposited from ether on a slide showed increased leucocytic activity and also agglutination, followed by haemolysis of the red cells, and that these changes were much more marked in the irradiated than in the non-irradiated film. It was this fact which led to the use of cholesterol, dissolved to saturation point (about 3½ per cent.) in liquid paraffin, as a dressing for ulcers and granulating wounds.

In 1925 a very extensive wound of the upper limb, in which, as the result of a machine strap accident, the entire skin surrounding the elbow had been stripped from the limb, and in which two unsuccessful attempts at autogenous skin grafting had been previously made, was dressed daily for some weeks with this cholesterol paraffin mixture, and later, when the sloughs had separated and granulations began to appear, the surface of the wound was irradiated through the cholesterol paraffin coating every other day with the ultra-violet rays from a mercury vapour lamp. After nearly six months of this treatment the wound eventually healed without cicatricial contraction, and the lad recovered with a functionally useful arm.

Following the discovery by Rosenheim and Webster in England, and Windauss and Hess in Germany, that irradiated ergosterol contained a much higher content of antirachitic or vitamin D substance than irradiated cholesterol, irradiated ergosterol, dissolved in the same way in liquid paraffin, was used in the place of the cholesterol as a dressing for varicose ulcers and for infected and granulating wounds. Good results were obtained both in the reduction of infection and in the promotion of healing.

Latterly "radiostol" in oil, diluted with liquid paraffin and soaked in gauze, has been found to be a convenient form of dressing. In two cases in which healing had been delayed by *B. pyocyaneus* infection it was noticed that the infective process was arrested in the part of the wound in contact with the irradiated ergosterol dressing, although it was still present in the area dressed by liquid paraffin, used as a control.

These observations showed that irradiated ergosterol so applied to wounds not only reduces infection and promotes healthy granulations; it also stimulates the ingrowth of epithelial cells from the margin, and so favours the healing process.

Experiments have also been carried out to test the bactericidal effect of irradiated as compared with non-irradiated ergosterol. Films of ergosterol were spread on the under surface of glass slips, some of which were irradiated and the remainder used as controls. The irradiated and the non-irradiated films were then inoculated with a suspension of *Staphylococcus aureus* in normal saline and placed film downwards on agar or blood serum

jelly, and incubated in Petri dishes. The colonies were found to be more numerous and larger on the non-irradiated than on the irradiated films.

These experiments require, however, to be repeated with other types of organisms, both aerobic and anaerobic.

Mode of Action.

The first suggestion I wish to make is that the beneficial effect of irradiated ergosterol, when used in solution in liquid paraffin as a dressing for wounds, may be due to a further continued irradiation effect on the wound tissues after the primary irradiation of the sterol by the ultra-violet rays from the mercury vapour lamp has ceased. The question of the physical and chemical action of the irradiated substance still remains.

In the *BRITISH MEDICAL JOURNAL* of October 8th, 1927 (p. 637), I described a colour test for distinguishing irradiated from non-irradiated ergosterol, which depends on the oxidation of potassium iodide by liberated oxygen, and the formation of a pink or a blue coloured iodide of starch when a solution of boiled starch dissolved in potassium iodide solution is applied to such an irradiated film. This and similar colour tests with ammonium ferrous sulphate and potassium thiocyanate solutions, and the haemolytic effect of the irradiated sterol on a suspension of washed red cells previously described, and the fact that ergosterol can be activated by ozonized air, all suggest that the taking up of oxygen during irradiation and the subsequent liberation of the oxygen may be the mechanism by which the irradiated sterol acts upon the blood and tissue cells and epithelial cells in the wound.

According, however, to Rosenheim and Webster (*Lancet*, September 17th, 1927) the conversion of ergosterol and the formation of vitamin D is brought about equally well in an atmosphere of nitrogen, the supposition perhaps being that the change consists in a molecular rearrangement only.

Experiments carried out by myself, in which thinly spread ergosterol films were irradiated through water covering the film, and also with films spread on the under surface of quartz slips, placed film downwards on mercury, and then irradiated through the quartz (atmospheric oxygen being thus excluded), showed that no activated substance had been formed capable of liberating iodine when tested by the starch potassium iodide and other colour tests.

These and other observations suggest the conclusion, either that ergosterol when treated by ultra-violet radiation takes up oxygen which can be subsequently liberated and is itself vitamin D, or that two substances are formed from the sterol during radiation—one a vitamin, which does not take up and subsequently liberate oxygen, and the other a substance of a peroxide character, which does take up oxygen and gives the starch potassium iodide colour reaction, and which haemolyses the red cells. If two substances are formed then the further question arises which of these substances exercises the stimulating and healing effect on wounds.

The fact that the activated substance which forms during irradiation is a fat-soluble material is of considerable importance; for, unlike a water-soluble material, a fat-soluble substance can transmit oxygen through the lipid coatings of the cell and its nucleus, and if it is also an oxygen carrier, soluble in fats, it may exert its influence on red cells, leucocytes, and tissue cells in the way described.

In support of this view it is interesting to find that when large and well-formed crystals of ergosterol, deposited slowly from solution in tetrachlorethane (Westron) on a slide, are viewed with polarized light after irradiation only the very small crystals become completely isotropic or non-polarizing. The larger crystals still contain a luminous core surrounded by a non-luminous non-polarizing layer of resinous material, which appears to protect the central core from further change.

If we assume that only one fat-soluble oxygen-absorbing and oxygen-discharging substance is formed during irradiation, then such an assumption seems also to imply that it is in virtue of this fat-soluble character, in conjunction with its capacity for liberating oxygen, that vitamin D exerts

its physiological effect on both general and local metabolism.

The further fact that irradiated ergosterol ("radiostol") after long exposure to atmospheric oxygen (especially in a warm temperature) is found to lose its antirachitic value, and also its capacity for liberating oxygen, and no longer oxidizes potassium iodide, as shown by the starch test, is also important. It may perhaps be explained on the assumption that the oxygen additive compound undergoes rearrangement, in consequence of which the oxygen is no longer easily liberated, the final product being the inactive resinous material.

My object in putting forward these suggestions is, first, to point out the value of certain irradiated sterols when used as a dressing for wounds, and secondly, to indicate certain directions in which, as it seems to me, further research would be very useful in throwing light on the mode of action of vitamin D.

Put shortly, the present position is this: we know from the brilliant work of a number of observers that irradiation will convert ergosterol and other unsaturated sterols into a substance having antirachitic qualities—that is, vitamin D. We have now shown that irradiation will also produce from the ergosterol a fat-soluble substance containing oxygen, some portion of which can be readily liberated. We also know that ozonization (and possibly other methods) will convert ergosterol into an oxidizing substance, but we do not yet know whether ozonization will produce an antirachitic substance. Neither do we yet know whether the vitamin D and the oxidizing substance are one and the same thing.

AUTOGENOUS RESIDUAL VACCINES:

THE THERAPEUTIC RESULTS OBTAINED IN A SERIES
OF 360 CASES.

BY

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THE method of preparation of these vaccines was described in this JOURNAL six years ago. On that occasion the results obtained by the treatment of cases of chronic bronchitis in the out-patient department of Salford Royal Hospital were presented and compared with cases treated by a similar stock vaccine prepared according to the older and usual method. The conclusion was drawn that the residual vaccine was superior.¹

The original technique for the preparation of residual vaccines has been slightly modified. One washing, combined with the use of hydrogen peroxide as introduced by Dean,² is found to be sufficient. This paper contains the results obtained when autogenous vaccines are used, and the whole of the cases now described were treated with that type of vaccine.

Detailed comment is best made under the separate group headings, but it is necessary to draw particular attention to the means employed for assessing the benefit or otherwise of the treatment. Almost without exception the result has been assessed by some other medical practitioner, usually the patient's private doctor. A minority of the records were upon hospital case sheets, and where I have been compelled to pass an opinion upon them myself I have classed as successful only those cases which showed a marked improvement obviously related to the administration of the vaccine; cases which showed a slight improvement or no change are failures, and those cases which, from inadequacy of notes or some other reason, showed an obvious benefit not attributable with certainty to the vaccine therapy, are classed as "Not traceable." Cases which slowly improved after vaccine therapy had ceased a month or so previously are deemed to be failures. The remainder of the untraced cases are so owing to disappearance of the patient or to my failure to establish contact with the patient's doctor.

It will be seen that the standard of assessment is of a simple order—succeeded or failed. Obviously such a classifi-

cation must be considered in relation to the disease. Thus the successful treatment of furunculosis means a complete and lasting cure. On the other hand, an advanced case of rheumatoid arthritis cannot be expected to yield so completely to vaccine therapy that all bony deformity disappears; in this case one looks for freedom from pain, disappearance of the swelling of the soft tissues, increased mobility of the affected joints, cessation of periodical acute attacks, and the patient's restoration to a more active life. An early case may be expected to clear up completely. Every case, however, is susceptible to analysis by means of a simple question—Was the vaccine therapy really worth while considering the results and the nature of the case?

I wish to offer my thanks to all the medical practitioners whose time I have taken up and whose memories I have racked in my efforts to assemble these records.

The results now published comprise all the autogenous residual vaccines made between January 1st, 1924, and December 31st, 1926.

Total vaccines prepared ...	...	...	...	...	448
Results not traceable ...	...	...	...	...	53
Still under observation ...	...	...	...	...	35
Results now recorded ...	...	...	...	...	360

The cases still under observation will be mainly, but not necessarily, the most recent. A vaccine for chronic nasal catarrh requires some time before its result is apparent so far as prophylaxis is concerned, whereas the result to be obtained in a case of rheumatoid arthritis may, and frequently does, declare itself after two doses.

It will be convenient to consider the results in seven groups.

GROUP A.

Disease.	Total Cases.	Success.	Failure.	Percentage of Success.
Furunculosis	45	40	5	88.9
Pyogenic abscess	4	4	0	—
Sycosis	3	2	1	—
Total of group	52	46	6	88.5

The failures in furunculosis include a diabetic who refused to limit his diet in any way, and a patient in whom a large carbuncle had already spread to the cord and produced myelitis when I first saw him. The three cases of sycosis barbae show two-thirds of successful results, which is probably unduly flattering.

GROUP B.

Disease.	Total Cases.	Success.	Failure.	Percentage of Success.
Rheumatism and rheumatoid affections	63	50	13	79.3
Gonococcal arthritis	3	3	0	—
Total of group	66	53	13	80.3

In the gonococcal cases the organism was isolated in pure culture from the affected joint. The rheumatic group require explanation and comment. Before a vaccine is prepared a preliminary bacteriological examination is always undertaken. Cultures are made from the throat and faeces as a routine. When pyorrhoea or some other suppurative lesion is present the appropriate cultures are made. The predominating organism I have found to be a streptococcus—*haemolyticus*, *salivarius*, or *faecalis*—or the enterococcus. I have never seen anything to suggest that these streptococci concerned in the rheumatoid group are in any way different from the standard types of these varieties; it is, of course, quite possible that in a susceptible case certain strains do produce toxins which have rather more affinity than usual for the joints and heart valves.

The majority of the vaccines in this group were made from the faeces, and an arbitrary standard of suitability