unusual fatality gives rise to the question whether the simpler and less heroic measures for the treatment of an abrasion are not freer from risk of this infection. Excision and closure of the wound would appear to produce a suitable nidus for the development of anaerobic organisms. If such an event can occur in a patient having the advantage of hospital treatment and observation, the relative rarity of such untoward results in street accidents is surprising. That it can occur should be borne in mind by all who treat casualties, so that a careful watch may be kept on the progress of such lesions, penetrating wounds, and even the site of subcutaneous injections, for these have been recorded as the origin of these cases. As infection by gas-forming anaerobic organisms is detected earliest by radiography it is advisable to have radiographs taken of the area of the wound if pain or fever develops or if there is any swelling or unusual discoloration. The radiographs should be scrutinized for the presence of gas bubbles. Absence of these should not be taken as conclusive evidence that such infection has not occurred, but the radiographic examination should be repeated after an hour or so if the signs and symptoms persist or show any evidence of progress. If gas bubbles are detected suitable measures should be instituted immediately.

Treatment

The radiographs will have revealed the presence of any metallic foreign body, and if the primary hygiene of the wound has not extended to its neighbourhood the foreign body should be accurately localized as a guide to the surgeon during the subsequent radical cleansing of the track. If the radiographs indicate that the infection is of the acute fulminating type of gas gangrene, which as yet does not appear to have extended beyond operable limits, the question of amputation of the part may arise, and this would seem to be the proper procedure. Kelly, Dowell, Russum, and Colien (1938), who have paid particular attention to the x-radiation treatment of the condition, and for this purpose have collected the evidence from 140 cases, are strongly opposed to amputation. They state: "We cannot over-emphasize our opposition to amputation because of gas gangrene, and feel that anyone amputating or advocating the amputation of an extremity solely because it is infected with gas-forming organisms is definitely out of touch with the proper and conservative treatment of the condition." Their technique is given as follows:

"The thicker the part the higher the voltage and the more filtration is indicated, but since it is only necessary to treat over a period of three days, or at the longest five days, making the number of treatments vary from six to ten, no complications should arise from the use of 100 r per port per treatment, regardless of how many ports it may take, if the correct voltage and filtration are used—at least 1 mm. of aluminium in all cases. The ordinary precautions against radiation burns should be taken."

They advise that treatment should be applied twice a day, and consider that the irradiation may have some antitoxic effect. They further state that "the use of serum is not absolutely essential to recovery and its use should be conservative, avoiding serum sickness, which only adds to the patient's difficulty"; for "up to this time no patient has died of gas gangrene who has received a treatment [irradiation] in the morning and a treatment in the evening for three days over all the involved tissue."

With such testimony one might feel justified in vigorously prosecuting all cases in this way, but more than an element of doubt is aroused in their statement: "One

should not become over-enthusiastic regarding the use of the x rays and neglect other measures. Surgery is commonly necessary in these cases and must be employed as indicated." How many of the cases treated by these measures were of the nature of those commonly seen in the great war and treated successfully by removal of the foreign bodies and adequate cleansing of the track one cannot estimate, but a more extensive investigation of the value of x-radiation in the cases which are of the acute fulminating type must be undertaken before it can be universally recommended. Until this evidence is forthcoming one would feel justified in recommending x-radiation treatment in all such cases in which the radiograph indicates that the infection has extended beyond reasonable bounds for amputation or in any other case in which surgery is contraindicated.

It is interesting to note that cattle suffer from a condition closely resembling the acute fulminating type of gas gangrene in man. The condition is known as blackleg, blackquarter, and quarter-evil, and by various other names. It appears to originate from an abrasion of the skin, its progress is very rapid, and the animal dies of toxæmia before the lesion has gone much beyond the bounds of the affected limb. Through the kindness of the late Sir John Robertson and Mr. E. Hothersall, chief meat inspector to the Birmingham Public Abattoir, I was privileged to see a number of these cases, and radiographs which I took in 1915 bear a striking resemblance to those cases of acute fulminating gas gangrene in man.

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EXPERIMENTS IN THE ACCELERATION OF WOUND HEALING

BY

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Those who, like myself, had the privilege during the last war of meeting Alexis Carrel at Compiègne have followed his subsequent work with the interest that arises from confidence in its integrity. It will be remembered that his studies in tissue culture and repair arose from and were associated with the technique of secondary closure of wounds when, after Carrel-Dakin treatment, the number of organisms in the wound discharge had been reduced to two or three per microscopical field. In 1916 Carrel and Hartmann published a paper on the cicatrization of wounds based on observations on animals; this confirmed findings, made in men in 1908, that the rate of repair was greater at the beginning than at the end of cicatrization and depended not at all on the age of the wound but on its size, being directly proportional to it.

Technique of Measurement of Wound Repair

The procedure of taking measurements is as follows. The surface of the wound is dried by filter-paper and a sheet of sterile cellophane is applied; the bare area is outlined by wax pencil on the cellophane, and this drawing is reproduced in ink on paper. From this the area is

estimated in square centimetres by means of a planimeter, and these measurements are repeated at intervals of four or five days. Carrel demonstrated that the value of the rate of cicatrization was geometric in character and could be expressed by a curve in which the time was carried in abscissae and the area in ordinates. This curve was expressed by du Noüy (1916) in a mathematical formula which is set out below; its clinical usefulness lies in the fact that it gives a yardstick wherewith to measure the progress of healing in a clean wound and the effect of different therapeutic measures on the rate of healing—for example, various antiseptics, chemicals, vitamin-containing ointments, tissue extracts, and even immobilization. The healing rate (see Graphs III and IV) is affected by the shape of the wound, the age of the patient, the existence of intercurrent disease, and, of course, by the presence of infection but not by the age of the wound.

Experiments with Embryonic Extract

In the course of his experiments in 1925 Carrel (Carrel and Baker, 1926) found that embryo-web porridge was effective in accelerating wound healing. This line of investigation was followed up by Dr. Albert Fisher, director of the Carlsberg Biological Institute of Copenhagen, who has succeeded in producing an embryonic extract which is sterile, stable, and easily applicable to the clean wound. Clinical experiments and observations with this substance have been carried out in several clinics in Copenhagen, especially in the Ortopaedisk Hospital by S. Kiaer (1927) and Nielsen, and a paper by the latter (Nielsen, 1939) must be acknowledged as the basis for this article. In this, after detailing the history of Carrel's observations and the du Noüy formula, Nielsen gives an account of controlled experiments on the healing of wounds in dogs carried out at the hospital and shows that the employment of the embryonic extract in dressing these wounds shortened the period of healing by an average of almost 32 per cent.

The embryonic material referred to has been named "epicutan." It is manufactured under Dr. Fisher's direction by Messrs. Lundbeck of Copenhagen, and was about to be marketed in this country before the outbreak of war. In May, 1939, Messrs. Lundbeck kindly provided me with enough epicutan to treat a considerable number of cases, details of four of which are here recorded. For Cases 1 and 2 the graph of healing under epicutan and the Carrel graph of normal epithelization are appended. These bear out the claim that epicutan reduces the time of healing by 30 per cent., and this is confirmed by clinical experience in my series of eighteen cases.

Case Reports

Case 1.—A French-polisher aged 19. First-degree burn of dorsum of hand; area of burn $2\frac{1}{2}$ by 2 inches. Treated after débridement by spirit dressing daily for four days; on fifth day epicutan and gauze dressing; repeated on tenth, fifteenth, and twentieth days. Area completely covered by epithelium on twenty-fifth day; the normal healing time for an area of this size given by the Carrel-du Noüy formula is thirty-five days (Table I and Graph I).

Case 2.—A collier aged 26. Glancing wound of left leg, with ablation of area of skin $4\frac{1}{2}$ by $2\frac{1}{2}$ inches. Eusol cleaning for five days, followed on the sixth day by epicutan-vaselin technique; repeated every four days. On the thirty-second day the area, with the exception of a spot the size of a sixpence in the centre, was completely covered by epithelium; by the Carrel-du Noüy estimation this area would have taken sixty-six days to heal (Table II and Graph II). My experience leads me to believe that it would have required skin-grafting.

TABLE I

Time (days)	5	10	15	20
Area (sq. cm.)	32	10.4	2.4	0.5

GRAPH I.—The graph of healing under epicutan (Case 1, experimental curve) and the Carrel graph of normal epithelization (calculated curve).

TABLE II

Time (days)	6	10	14	18	22	28	32	36	42
Area (sq. cm.)	68	45	24	11.4	5.6	4	3.14	2.26	0.5

GRAPH II.—The graph of healing under epicutan (Case 2, experimental curve) and the Carrel graph of normal epithelization (calculated curve).

Case 3.—A shipyard worker aged 36. Injury to third and fourth toes of right foot; both toe-nails loose, and removed. Dressed for three days with eusol; on fourth day nail-bed of third toe was treated with epicutan and sterile vaselin gauze, the fourth toe with vaselin gauze only, using this toe as a control; re-dressed on ninth, fourteenth, and nineteenth days. On the twenty-third day the nail of the third toe was completely regenerated, while regeneration of the fourth toe-nail had barely reached the middle of the nail-bed.

Case 4.—This case, that of an infant, deserves fuller description. The history was that at $1\frac{1}{2}$ months the patient suffered first and second degree burns of the head; he was admitted to hospital on December 20, 1937, and remained for two months; almost half the total area of scalp was denuded of epithelium. In February, 1938, the child developed measles and was discharged to an isolation hospital, and later attended the out-patient department at the former hospital. He was readmitted on several occasions, and in June, 1939, was admitted with the intention of grafting being performed. At

that time the bare area measured $3\frac{1}{8}$ by $2\frac{1}{8}$ inches; for eleven months it had remained stationary, and was dirty, offensive and covered with pus.

On July 29 the condition of the scalp was as shown in Fig. 1. Epicutan-vaselin technique was now begun, and a

FIG. 1.—Case 4. Condition of the wound on July 29, 1939, before treatment with epicutan.

FIG. 2.—Case 4. Condition of the wound on October 9, 1939.

removable plaster-of-Paris cap was fitted to prevent the child rubbing the head on the pillow. Dressing was renewed every five days; the condition improved steadily until on October 9 it was as shown in Fig. 2. With the exception of two areas the size of a shilling the whole wound was covered with epithelium. This is a remarkable case, as attempts to obtain epithelization had failed; the scald had existed for almost a year and a half and grafting seemed inevitable. Interruption to repair has now occurred, as the child has developed whooping-cough. Graphs of cases shown me in Copenhagen exhibited a noticeable delay in healing when an intercurrent disease supervened.

Mathematical Formula Used in Producing the Graphs

Du Noüy's formula from which the graphs have been obtained is $S_n = S_{n-1} \cdot [1 - i(t + \sqrt{nt})]$; where S_{n-1} equals the wound area at a known time; S_n equals the wound area t days later; t equals the intervening time; n equals the number of time periods; and i equals a variable factor, depending only on the size of the wound and the age of the patient.

Du Noüy in 1919 published a table based on several hundred wound measurements made on men, showing that the factor i can be found when the size of the wound and the age of the individual are known. By measuring the wound area S_{n-1} , and substituting in the above formula S_n , the size of the wound t days later can be calculated. Then, by using this value for S_n , and substituting in the formula as S_{n-1} , a second value for S_n can be found which will represent the wound area $2t$ days later. By repeating along these lines a series of values for the wound area at intervals of time can be calculated. These values are shown in the graph as a dotted curve. The line curves show the observed results.

Graphs III and IV give the curves showing the rate of healing in Case 1 and Case 2 respectively. The appropriate tables are shown as Table III and Table IV. It

TABLE III.—Case 1

Rate of healing (sq. cm. per day)	4.32	1.60	0.38
Time (days)	7.50	12.50	17.50

GRAPH III.—The daily healing rate in Case 1 (experimental curve) and the normal daily healing rate (calculated curve).

TABLE IV.—Case 2

Rate of healing (sq. cm. per day)	5.75	5.25	3.12	1.45	0.25	0.22	0.29
Time (days)	8	12	16	20	28	34	39

GRAPH IV.—The daily healing rate in Case 2 (experimental curve) and the normal daily healing rate (calculated curve).

will be noticed that after the first few applications of the embryonic extract the curve of the rate of healing of the observed cases falls below that of natural healing. This suggests that possibly the wound area has become resistant to epicutan and the response is slower, and it may be advisable in such circumstances to withhold the treatment for one of the time periods, and then to resume the treatment—that is, to stop the application of epicutan

at the point where the observed rate of healing intersects the calculated rate.

It will be observed that by this formula it is possible to predict how long a wound will take to heal, provided the area and shape of the wound and the age of the patient are known; and, by comparing the curve of actual measurement at similar t intervals, to ascertain whether the adoption of various techniques of treatment is actually effective in reducing the time of healing.

In the cases quoted, in addition to the use of the embryonic tissue extract, I have employed immobilization of the wound-bearing member, since this alone appears to have an influence in inhibiting a flare-up of infection which would interfere with repair; but immobilization alone does not appear directly to influence healing time.

Biological Considerations

Fisher's investigations show that the protein derivative of embryonic tissue is not of the nature of a hormone but exists intracellularly, and experimental and clinical observations indicate that it is present in all embryonic tissue but disappears rapidly with the close of embryonic life. It is permissible to surmise that at this biological epoch, when the passive aggregation of cells which we recognize as an embryo develops to a living entity and acquires individuality, it throws off its dependence upon undifferentiated cell activity and begins to elaborate the ontogenic hormones of its progenitors. Thus, for example, in the mammal the influence of the embryonic protein is replaced by that of the chondrotrophic growth hormone elaborated in the pars anterior of the pituitary body.

Epicutan is a protein derivative of embryonic tissue adsorbed to kaolin powder; the wound is powdered and covered with sterile gauze, and dressed every five days. The value of a preparation which by accelerating healing time will shorten convalescence by one month in three is obvious in the present national circumstances. A series of controlled experiments is being carried out at the Strangeways Research Laboratory, Cambridge.

Summary

The basic work of Carrel in tissue culture is recalled, and the technique employed in clinical experiments is detailed.

Case histories are given which demonstrate marked acceleration of wound healing under the influence of embryonic tissue extract.

The equations and graph curves referable to two of the quoted cases are set out; these confirm mathematically the clinical deductions drawn from these cases.

A note as to the form in which the tissue extract is available commercially is added.

I have already referred to the paper by Erfurth Nielsen, from which much of the technical detail, not to make too fine a point, is "cribbed." My indebtedness to Mr. J. M. Russell, lecturer in mathematics at the Technical College, Sunderland, for his kindness not only in providing the graphs but in instructing and explaining the attendant mathematics to me, I most gratefully acknowledge.

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The Swedish Health Office has issued a circular warning practitioners to exercise the greatest care in prescribing slimming cures, as their use in many cases has caused digestive and ocular disturbances.

THE KAHN TEST: A SIMPLIFIED TECHNIQUE

BY

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Many years' experience of this test carried out on upwards of a hundred thousand specimens has convinced me that (1) it can be performed more quickly and easily than as described by its author; (2) it is highly specific and sensitive as controlled by parallel Wassermann tests and clinical observation; and (3) it is not one which can be done by any medical man without previous training. Nevertheless the test is simpler than the Wassermann and requires fewer reagents and controls; the reading is less easy, but this and the technique of setting it up can be mastered in a comparatively short time by anyone of average intelligence. Moreover, it is a more suitable test than the Wassermann where small numbers of specimens have to be examined or where full pathological facilities are not available, and it is of great value as a check on the more complicated complement-fixation reaction. In addition it is particularly useful where a quick result is required: a report can be given within a few minutes after the specimen and necessary control sera have been inactivated.

Procedure

Tubes as described by Kahn himself are used, but ordinary Wassermann racks can replace the special three-tube racks. Instead of numerous finely graduated pipettes all that is required are two quill ones made by drawing out in the flame of a blow-lamp ordinary glass tubing with an external diameter of about 0.8 cm. One of these should be coarse—internal diameter roughly equal to that of the lead of an ordinary pencil—and the other fine. The coarse one should be fitted with a teat, a volume of about 0.15 c.cm. of fluid drawn up into it, and a mark made with a grease pencil at the upper level of the fluid; this is used for pipetting all sera. The fine one is passed through hole No. 54 in a Starrett wire gauge and cut off with a file at the point where it emerges. It will be found that twelve drops of diluted Kahn antigen delivered by holding this pipette vertically are roughly equal to one volume delivered from the coarse pipette. Sixty "drops" are weighed against five "volumes," and the mark on the coarse pipette is altered as necessary until the weights are exactly equal. In the test proper the three tubes used by Kahn are reduced to two—that is, the 1 to 12 and 1 to 6 of antigen and heated serum respectively.

Technique of Test.—Two tubes are used for each serum, including positive and negative controls, and two for antigen-saline controls. Into the back row one drop and into the front row two drops of suitably diluted and ripened antigen are delivered with the antigen pipette; one volume (0.15 c.cm.) of each serum to be tested is then added to each pair of tubes, the pipette being rinsed out two or three times in saline between any two consecutive sera and the same pipette being used throughout. The rack containing the tubes is now shaken for three minutes in the usual way (by hand if no mechanical shaker is available) and saline (roughly 1 c.cm.) added to each tube. Results are read with a hand lens with a magnification of about $\times 6$. For this purpose a slit-lamp as used for the sigma test is most convenient, but any shaded light with a dark background answers the purpose.