and the toxic effect of a single pregnancy produces a lesion from which the vein never recovers. In others the valves are less incompetent and the degree of recovery after the toxic effect has passed off is sufficient to allow the valves again to act competently. In some of these the valves may finally fail with the circulatory changes that occur at the menopause. Possibly other toxic or trophic conditions produce the same effect as pregnancy, but usually then the exciting cause is not intermittent and varicosis develops progressively. The endocrine disorders which are considered to be of importance in this connexion by Continental writers are regarded rather lightly in this country.

4. Any cause of obstruction to the venous return, such as pelvic tumour, thrombosis of the iliac or femoral vein. The effect of obstruction at openings in aponeurosis cannot be regarded as proved.

5. Any cause of abdominal straining—excessive efforts during defæcation or micturition, caused by constipation, urethral stricture, enlarged prostate.

6. The existence of a heart lesion resulting in venous back-pressure has the same effect as the upright position on full veins.

These exciting factors must all be considered in connexion with the treatment. In addition to blocking a superficial or perforating vein which is hopelessly impaired, it is necessary to keep up the muscular tone by massage and exercise, to avoid long standing, to remove where possible any intermittent or constant cause of back-pressure along the veins, and also to treat any toxic condition likely to impair other comparatively adequate perforating veins.

REFERENCES.

Briquet, P.: Thèse de Paris, 1824.
Verneuil, A. A.: Gaz. Hebd. de Méd., Paris, 1855, ii., 811; Gaz. Hebd. de Méd., Paris, 1861, viii., 428, 446, 477; Gaz. Mèd., 1855, 524.
l'Aulnoit, Houzé de: Thèse de Paris, 1854.
Le Dentu, A.: Thèse inaug. Paris, 1867.
Kosinski, C.: Jour. Anat., 1926, lx., 131.
Luschka, H. von: Anat. des Menschen, Tübingen, 1865–67, iii., 465.
Klotz, K.: Arch. f. Anat., 1887, p. 169.
Gaugier, L.: Proc. Roy. Soc. Med., 1928, xxi., 1837.
McPheeters, H. O.: Surg., Gyn., and Obst., 1927, xiv., 541; and 1929, xlix., 29.
Fabricius, H.: De venarum ostiolis, Padua, 1603.
Bardeleben, K.: Amtl. Ber. deutsch. Naturforscher u. Aerzte in München, 1877, l., 228. Sitzungsber. d. Jenäischen Gesellschaft, 1879–80, p. 42. Jenäische Zeit., 1880, vii., 467.

THE TREATMENT OF ERYSIPELAS WITH VACCINES.

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THE methods at present available for the treatment of erysipelas may be broadly classified as local applications, internal administration of drugs, and immunisation.

It would serve no useful purpose to enumerate the various medicaments employed as external applications or for internal administration. Most observers with an extensive experience of the disease will agree with Ker [1] "that all the systems of treatment advocated frequently fail to check the advance of the dermatitis, so frequently, indeed, as to justify us doubting whether they exert any favourable influence at all." Roger [2] is not impressed with the specific value of the various antiseptics applied externally, or drugs administered per os.

As pointed out by Meara [3] it is not easy to assess the value of any form of local treatment in a self-limited disease like facial erysipelas, the duration of which is so uncertain. It must be remembered that the natural tendency of the disease is towards cure, and we may reasonably assume that the patient gets better in spite of the remedies employed rather than because of them. A study of the literature from the therapeutic angle makes one wonder whether these points in the natural history of the disease are sufficiently appreciated.

Serum treatment has apparently been successful in the hands of some clinicians, whilst others have not been favourably impressed with the results obtained. Polyvalent antistreptococcal serum gave such disappointing results that its use in this hospital was discontinued several years ago. Recent research in the group of hæmolytic streptococci has led to the production of alleged specific antitoxic sera against scarlet fever, erysipelas, and puerperal infection. The specific scarlet fever antitoxic serum is of proven value. Conflicting reports about the efficacy of the respective antitoxic sera against erysipelas and puerperal infection are met with. These sera have been freely administered to patients in the City Hospital during the past three years. The results obtained will be published at an early date.

In that widely varying results have been reported by different observers, vaccine treatment is no exception to the other remedies employed in the treatment of infection with the *Streptococcus erysipelatis*. Whilst Sill,[4] Fischer,[5] Takaki,[6] Russell,[7] and Boidin and Tierny [8] have apparently obtained satisfactory results in isolated or small groups of cases; Erdman,[9] from his experience of vaccine therapy in 95 cases, concludes that this method of treatment is valueless. Vaccine treatment has also proved a failure in the hands of Boidin and Delafontaine.[10] Ker [11] wrote in 1920: "It is certainly desirable that more work on the therapeutic use of vaccines should be undertaken—a very long series of cases, adequately controlled, will be necessary to establish their efficacy in a disease so variable in its duration and severity."

In this paper I have collected observations on 570 cases of erysipelas, 470 of which were acute attacks, whilst 100 were of a subacute afebrile type.

Method of Investigation.

On admission to hospital, the cases were primarily classified into two groups. One group consisted of typical acute attacks characterised by marked constitutional symptoms. Subacute attacks, in which the systemic disturbance was negligible, formed the second group. To alternate patients in the acute group vaccines were administered, the others acting as controls. We thus have records of 235 acute cases treated with vaccines, and an equal number of patients suffering from acute attacks who received purely symptomatic treatment.

TABLE I.—*Original Site of Infection.*

Series.	Face, ears, or scalp.	Trunk	Genitals.	Arms.	Legs.	Total
Vaccine	207	10	4	0	14	235
Non-vaccine Acute ..	203	6	4	6	16	235
Non-vaccine Subacute	94	0	0	1	5	100
Totals	504	16	8	7	35	570

The original site of the inflammatory process in the various groups of cases is shown in Table I.

As might be expected facial cases preponderate, amounting to 88 per cent. of the vaccine-treated series and 86 per cent. of the control group.

Treatment.

The therapeutic measures employed for the relief of delirium, insomnia, and high temperature were the same in all cases. The following local applications were tried: (*a*) lint kept constantly moist with a cold saturated aqueous solution of magnesium sulphate to which 10 to 20 per cent. of glycerin had been added; (*b*) collosol iodine . and (*c*) a 5 per cent. aqueous solution of brilliant green (as recommended by Adams [12]). The latter two preparations were painted on and beyond the inflamed area morning and evening. The solution applied to the inflamed area in various groups of cases is shown in Table II.

TABLE II.—*Local Applications.*

—	Acute series.		Sub-acute series.	Total.
	Vaccine cases.	Non-vaccine cases.		
Magnesium sulphate ..	156	161	80	397
Collosol iodine ..	51	44	0	95
Brilliant green ..	28	30	20	78
Totals	235	235	100	570

It will be seen from Table II. that suitable control cases were obtained in the acute non-vaccine series for each group in the vaccine series. We thus hoped to assess, and eliminate if possible, any variation that might arise from the alteration of the local treatment.

VACCINES.

The vaccines administered may be broadly grouped into "stock" and "hospital." The former group included commercial preparations containing *S. erysipelatis*, or *S. pyogenes*, polyvalent streptococcal vaccine, and a combined streptococcal and staphylococcal vaccine. The "hospital" vaccine was prepared from strains of *S. erysipelatis* isolated from the inflammatory area in six acute cases of the disease. An autogenous vaccine was administered to five patients. The relatively brief duration of the disease in the vast majority of patients proves a stumbling-block to the extensive employment of autogenous preparations.

Whilst the vaccine was injected subcutaneously in all cases, the total dosage and the interval between injections varied considerably. One hundred and thirty-six patients received a course of six injections administered either daily, or at two-, three-, or four-day intervals. Fifty cases received either four or five injections of vaccine. To the remaining 49 individuals from one to a maximum of ten doses were administered. The actual number of cocci injected varied according to the severity of the infection and the age of the patient, ranging from a primary dose of 250,000 organisms in an infant 3 weeks old to a maximum primary injection of 50 million streptococci. The average course for an adult ranged from an initial dose of 5 million streptococci to a final injection of 200 million organisms. The usual interval between injections was three days. A course of daily injections ranging from 1 to 20 million cocci was administered to a small group of sharp cases. The dosage of mixed vaccine rose from an initial injection of 10 million streptococci combined with 500 million staphylococci to a maximum dose of 100 million streptococci plus 5000 million staphylococci.

Result of Vaccine Treatment.

In endeavouring to estimate the therapeutic value of the vaccine employed, attention was paid to (*a*) the duration of pyrexia, (*b*) the extent of spread of the inflammatory lesion, (*c*) the incidence of complications, (*d*) the occurrence of relapses and second attacks, and (*e*) the mortality-rate. The following criteria were adopted:—

Day of Crisis.—The day on which the morning or evening temperature was first normal and did not subsequently rise, except when due to an obvious complication, was considered as the day of crisis.

Day of Cessation of Activity.—Day on which the local inflammation had entirely subsided.

Wandering Type.—Implies invasion of neck or trunk from a primary focus on either face or limb, or of limb or face from an original focus on the trunk.

The age and sex of the patient, and the day of disease on which the patient was first admitted to hospital, are of importance, when the value of any method of treatment for erysipelas has to be assessed. Whilst the gravity of erysipelas at the extremes of life is common knowledge, the fact that the death-rate tends to be higher in males at all ages than in females is perhaps not so widely appreciated. The age and sex of vaccine-treated and control cases are noted in Table III.

TABLE III.—*Age and Sex of Acute Cases.*

Series.	Sex.	Under 1 yr.	Age-period in years.										Totals.
			1–4	5–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	80–89	
Vaccine	M	6	8	5	11	14	15	23	16	10	3	1	112 } 235
	F	6	4	3	18	17	15	24	18	14	4	0	123 }
Non-vaccine	M	7	6	1	6	4	13	22	18	13	4	0	94 } 235
	F	3	8	2	26	28	16	22	21	10	4	1	141 }
Totals ..		22	26	11	61	63	59	91	73	47	15	2	470

The number of patients under 5 years and above 60 years of age was 56 in both groups. Unfortunately, the sex incidence is not so strictly comparable. Males form 47·7 per cent. of the vaccine-treated group as against 40 per cent. of the control group.

Table IV. gives us information regarding the day of disease on admission to hospital in the two groups of cases.

TABLE IV.—*Day of Disease on Admission to Hospital.*

Series.	Day of disease.														Totals.
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Vaccine. ..	15	55	64	35	38	11	3	8	1	1	3	0	1	0	235
Non-vaccine..	13	61	57	50	24	11	8	6	0	0	2	2	0	1	235
Totals ..	28	116	121	85	62	22	11	14	1	1	5	2	1	1	470

The average duration of illness prior to admission to hospital in the 235 cases treated with vaccine was 2·67 days. In the 235 non-vaccine treated (control) cases it was 2·64 days.

The two groups are strictly comparable as far as age distribution and duration of disease prior to hospital treatment are concerned. The sex distribution unfortunately varies to a slight degree.

DURATION OF PYREXIA.

In facial erysipelas the temperature tends to fall more or less abruptly with the cessation of the inflammatory process. In the absence of complications, the period of pyrexia may be regarded as a fair estimate of the duration of the illness. Table V. shows the duration of pyrexia subsequent to admission to hospital in the two groups of cases.

TABLE V.—*Duration of Pyrexia Subsequent to Admission to Hospital.*

Series.	Days.														Totals.
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Vaccine.. ..	36	38	34	34	27	11	16	7	8	8	5	1	2	8	235
Non-vaccine..	18	33	40	34	38	20	9	11	4	7	1	2	4	14	235
Totals ..	54	71	74	68	65	31	25	18	12	15	6	3	6	22	470

The average duration of pyrexia subsequent to admission to the wards in 235 vaccine-treated cases was 4·97 days. When we add this figure to the average duration of illness before admission—namely, 2·67 days—we arrive at an average total duration of disease in the vaccine-treated series of 7·64 days. In the 235 control cases the average duration of pyrexia subsequent to admission to hospital was 5·41 days. When we add this to 2·64 days, the average duration of illness prior to admission to the wards, we find the average total duration of disease in the control group amounted to 8·05 days.

EXTENT OF SPREAD OF INFLAMMATORY PROCESS.

Should vaccine therapy be efficacious, one would expect that the tendency of the inflammation to "wander" would be much curtailed. The incidence of the wandering type of erysipelas in the two groups of cases is shown in Table VI.

TABLE VI.—*Incidence of "Wandering" Type.*

Cases.	Extent of spread.			Totals and per cent.
	Face to neck.	Face to trunk.	Trunk to limbs or vice versa	
In 235 vaccine	17	18	9	44(18·71)
In 235 non-vaccine ..	11	33	9	53(22·5)

Whilst the figures are in favour of the vaccine-treated group, it is to be noted that extensive spread of the inflammatory lesion occurred in 44 cases in spite of vaccine administration.

INCIDENCE OF COMPLICATIONS.

The various complications met with in the two groups are given in Table VII.

TABLE VII.—*Complications.*

—	Abscesses and cellulitis.	Broncho-pneumonia.	Nephritis.	Pyæmia.	Arthritis.	Totals.
Vaccine series (235) ..	10	2	2	1	0	15
Non-vaccine series (235)	10	4	2	1	1	18

It is disappointing to note that the development of abscesses and cellulitis was apparently unaffected by the administration of vaccine. The lower incidence of broncho-pneumonia in the vaccine-treated series is interesting, although, owing to the relative infrequency of this complication, not entirely convincing.

INCIDENCE OF RELAPSES AND RECURRENCES.

A recurrence may be defined as a repetition of the disease after an interval of months or years. As a purely arbitrary standard, we shall consider a reappearance of the disease within three months of the previous attack as a relapse. Where a period of more than three months has intervened, then a flare up of the erysipelatous process will be regarded as a recurrence. Sixteen cases in each group suffered from a relapse whilst still in hospital. In the vaccine-treated group another four patients were readmitted to hospital within three months of the previous attack and will thus be regarded as suffering from relapses. The percentage of relapses in the vaccine-treated series amounted to 8·5, as against 6·8 in the control series.

No fewer than ten patients who had received a course of vaccine during one attack of erysipelas were readmitted with, in most cases, an equally sharp second attack of the disease from four to 29 months later. Details of two of these cases, chosen at random, are appended:—

CASE 1.—Mrs. A., aged 35. Original attack December, 1921. Facial. Stock streptococcal vaccine. Five doses at three-day intervals ranging from 20 million to 400 million cocci. Second attack March, 1923. Facial. Stock streptococcal vaccine. Six daily doses, 5 to 15 million cocci. Relapse occurred fourteenth day in hospital.

CASE 2.—Mrs. B., aged 58. Original attack February, 1922. Facial. Six doses mixed streptococcal and staphylococcal stock vaccine administered every third day, ranging from 10 million streptococci plus 500 million staphylococci to 200 million streptococci plus 1000 million staphylococci. Second attack March, 1923. Facial. Temperature ten days.

MORTALITY.

In Table VIII. we have the deaths which occurred in the various age-groups.

TABLE VIII.—*Deaths.*

Series.	Result.	Under 1 year.	Age-period in years.									Totals.
			1–4	5–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	80–	
Vaccine	R	6	11	8	29	31	27	44	32	21	5	0	214
	D	6	1	0	0	0	3	3	2	3	2	1	21
Non-vaccine	R	6	12	3	30	32	28	40	34	19	6	1	211
	D	4	2	0	2	0	1	4	5	4	2	0	24

R = Recovered; D = Died.

The death-rate in the vaccine-treated series was 8·94 per cent. as compared with a rate of 10·21 per cent. in the control group. The slight variation in favour of the vaccine series need not, in my opinion, be regarded seriously. It is only fair to remember, however, that the preponderance of males in the vaccine-treated patients would have led one to expect a rather higher mortality in that group than in the control series.

LOCAL TREATMENT.

Without going into detail, it may be stated that a critical analysis of the various local applications led us to the conclusion that in no case did they limit the spread or materially diminish the activity of the inflammatory process. The patients certainly testified to the alleviation of subjective symptoms which followed the application of all three lotions. I still favour as a local application a cold saturated aqueous

solution of magnesium sulphate to which 10 to 20 per cent. of glycerin has been added.

Conclusions.

The study of 235 carefully controlled acute cases of erysipelas has led to the following conclusions. The administration of stock or autogenous streptococcal vaccines, or mixed staphylococcal and streptococcal vaccines, in erysipelas does not (*a*) shorten the duration of the attack, (*b*) prevent extensive spread of the inflammatory process, (*c*) lessen the incidence of common complications such as abscesses and cellulitis, (*d*) diminish the occurrence of relapses, (*e*) prevent recurrences, or (*f*) have any appreciable effect in diminishing the mortality from the disease.

REFERENCES.

1. Ker, C. B.: Infectious Diseases, 3rd ed., London, 1929, p. 480.
2. Roger, G. H: Nouveau Traité de Medécine, Paris, 1920, vol. i., p. 153.
3. Meara, F. S.: The Treatment of Acute Infectious Diseases, 2nd ed., revised, New York, 1921, p. 775.
4. Sill, E. M.: New York Med. Record, 1913, lxxxiii., 573.
5. Fischer, L.: Med. Record, 1916, lxxxix., 734.
6. Takaki, Y.: Sei-i-Kwai Med. Jour., 1913, xxxii., No. 1.
7. Russell, J. R.: Brit. Med. Jour., 1922, ii., 15.
8. Boidin, L., and Tierny, M.: Bull. et mém. Soc. méd. hôp. Paris, 1921, xiv., 165.
9. Erdman, S.: Jour. Amer. Med. Assoc., 1913, lxi., 23.
10. Boidin, L., and Delafontaine, P.: Bull. et mém. Soc. méd. hôp., Paris, 1921, xlv., 651.
11. Ker, C. B.: Infectious Diseases, 2nd ed., London, 1920, p. 487.
12. Adams, J. E.: Brit. Med. Jour., 1920, ii., 779.

SULFOSIN THERAPY.

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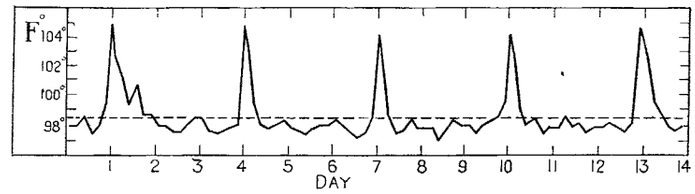
In a paper published at the end of last year Schroeder[1] advocated the use of a preparation of sulphur in oil, known as Sulfosin, in the treatment of general paralysis and certain other nervous and mental disorders. Since that date several other publications dealing with the same subject have appeared, among which may be mentioned those of Harris,[2] Shilvock,[3] and Patterson and Switzer.[4]

For a period of about eight months I have employed injections of sulfosin in the treatment of 14 cases of certified insanity, the majority being general paralysis of the insane. Unfortunately the type of general paralytic who finds his way into a mental hospital is more often than not in an advanced state of cerebral dissolution. His nervous tissue has already undergone a certain amount of irreparable damage and the most that can be achieved by any form of therapy is the arrest of the processes of destruction and the limitation of dementia. Exceptionally, patients are admitted at an early stage of the disease, and it is now generally conceded that very often these may be restored to complete normality by artificially induced malaria. Where, however, gross neuronic damage already exists, one can only appraise the therapeutic worth of any remedy by observing the treated cases over a number of years and noting whether or not the disease has been arrested. For this reason no attempt will be made here to comment on the curative value of sulfosin in the treatment of the complaint for which it was first advocated, but rather to indicate some points of interest about the therapy itself.

Pyrexia.

Regarded purely as a pyrexia-producing agent, sulfosin is, in my experience, far superior to any other substance which has been suggested for this purpose. If Schroeder's directions[1] are carefully followed, an intramuscular injection of this preparation will in the vast majority of instances produce a high temperature within the ensuing 24 hours, and this will almost invariably have completely subsided within 72 hours. By altering the dose the height of the temperature can be regulated with singular accuracy, and usually it is quite unnecessary to employ maximum doses in order to produce an intermittent pyrexia of 104° F.

CHART 1.

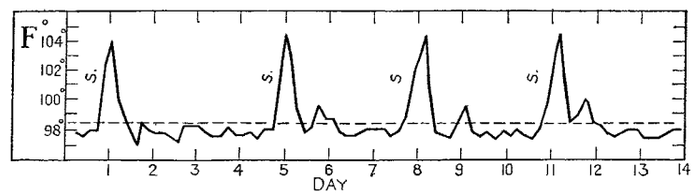


Pyrexia of induced quartan malaria.

A temperature chart closely resembling that of malaria can be obtained without any difficulty, as the accompanying records of actual cases clearly demonstrate.

Chart 1 is that of a case of a general paralytic undergoing treatment by induced quartan malaria and needs no special explanation. Chart 2 is taken from another case of general paralysis who was undergoing sulfosin treatment. In the malaria chart rises of temperature to between 104° and 105° F. are recorded regularly every 72 hours, whereas in the other chart similar pyrexial bouts are produced at any desired interval by an injection of 4·5 c.cm. of sulfosin at 11.30 A.M. on the previous day. As compared with the pyrexia associated with a malarial rigor, the temperature produced by sulfosin takes a little longer to subside, and there is usually a slight secondary rise on the second night following the injection. This secondary elevation is very characteristic of fever induced by sulfosin, but it should be noted that in the case illustrated the temperature had always entirely subsided within 48 hours.

CHART 2.



Pyrexia induced by sulfosin. Injection of 4·5 c.cm. sulfosin at S.

I usually confine myself to eight or ten injections in one course of treatment, but every case has to be judged on its merits as in malaria therapy. A few weeks are allowed to elapse before a second course of injections is given, and this may be followed later by a third course. No marked toleration appears to be established; similar rises of temperature can be obtained in the third course with very much the same doses as were employed at the commencement of the treatment.