to isolate staphylococci from wounds, and this may apply to swabs taken from noses and wounds at the time of operation. Compared with the extensive investigations of Williams and Miles (1949) our isolation rate of *Staph. aureus* from fresh lacerations was low. This was probably in part due to a difference in cultural methods, and in part due to the fact that our patients were attended to sooner after the accident and their lacerations were smaller. On the other hand, the much shorter time taken by the majority of wounds to heal is almost certainly because our patients were seen sooner after the operation, and were therefore eligible for earlier discharge. As did Williams and Miles (1949), we found that patients might become infected with staphylococci of the same type as those they carried in the nose. When allowance has been made for these reservations, it is still surprising that there was no apparent transfer of staphylococci from septic to clean patients. The explanation for this may perhaps lie in the careful surgical and nursing technique which was used.

In this series of patients with post-operative sepsis *Staph. aureus* accounted for less than a third of the infections at the first dressing. It is not possible to state a source for the majority of these organisms or for the other bacteria isolated from wounds. There can, however, be no doubt of the value to the patient and to the hospital of preventing post-operative infection. Return to work was quicker among the patients whose wounds healed without infection, and the length of their attendance in the casualty department was half that of the patients whose wounds became septic.

Summary

A series of 362 clean patients were operated upon in a casualty theatre used for clean and septic patients. At the first dressing, usually six to seven days later, 35 patients had wounds with pus. *Staph. aureus* was isolated from 11 of these wounds. All the strains were different in type, and none were of the same type as those infecting septic patients operated upon in the same theatre in the same period.

We are indebted to Mr. J. O. Robinson, surgeon in charge of the surgery, for permission to conduct this investigation, and to the sister in charge of the casualty theatre and her staff for their help. We would also like to thank the Medical Research Council for a grant supporting this work.

REFERENCES

- Clarkson, P. (1956). *Lancet*, 2, 31.
Nuffield Provincial Hospitals Trust (1960). *Casualty Services and Their Setting*. Oxford Univ. Press, London.
Williams, R. E. O., and Miles, A. A. (1949). *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, No. 266.

"The first general anaesthetics in Gloucester were tried out privately by local doctors, and not, surprisingly, by the Infirmary staff. It was at the house of a Mr. Clutterbuck in February, 1847, that a woman had a finger amputated under ether. Her comments on regaining consciousness were 'God be praised! it is off! Thank you, gentlemen.' It was also Mr. Clutterbuck who introduced the use of chloroform to Gloucester in December, 1847, preferring the latter to ether. Sir James Simpson had only announced his discovery of the anaesthetic properties of chloroform the previous month." (*The Story of Gloucester's Infirmary*, by Brian Frith.)

TRIAL OF PROCAINE IN THE AGED

BY

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In recent published work in Rumania it has been claimed that procaine injections in the elderly produce widespread beneficial effects. The evidence for this, together with an extensive bibliography, has been summarized (Aslan, 1960). Procaine is stated to have a general "eutrophic effect" due to a "vitamin-like" action. Favourable improvement is reported in a large number of disorders. Arteriosclerosis affecting the nervous system, Parkinson's disease, pseudobulbar palsy, and the sequelae of cerebrovascular accidents are said to improve. An increase in physical agility and dexterity occurs, and mental function is enhanced in respect of memory, concentration, and interest. Both degenerative and rheumatoid arthritis show benefit (Aslan and David, 1957). Accelerated union of fractures is stated to occur. Ectodermal effects noted were improvement of senile skin changes and keratoses, psoriasis, vitiligo, lichen planus, and alopecia. Repigmentation and regrowth of hair has been observed.

The treatment is said to have a rejuvenating effect, and much experimental laboratory, biochemical, and clinical work is cited in support of this contention (Aslan, 1957, 1960). Prophylactic administration is now advocated to prevent the onset of senile degenerative changes and to arrest the ageing process.

Medical opinion in this country has been sceptical that rejuvenation can be produced in this way, and the need for a controlled clinical trial has been stressed (*British Medical Journal*, 1959). Much of the confirmatory work supporting this treatment has been published in Eastern Europe. Trials in this country have been, in the main, limited to clinical experience in small series with conflicting results. This paper reports the result of an investigation planned to establish whether procaine injections are of benefit to elderly persons and produce any of the effects claimed for this therapy.

Method

The trial was carried out with two groups of elderly people. The first (group A) consisted of hospital in-patients who were bedfast, incontinent, and confused owing to the combined effects of cerebrovascular disease and old age. This is not an uncommon category of patient in hospitals for the chronic sick. They are all heavy nursing problems, and no form of treatment, or rehabilitation, is known to improve their general state. As definite objective effects were to be looked for in this group no control solutions were used.

The second category (group B) comprised elderly infirm residents in local authority welfare accommodation. It was explained to those who agreed to co-operate that the injections might produce an improvement in general health or be without effect. It was emphasized that the injections would be continued for many months but that they, the patients, could withdraw from the trial if they felt they were being upset or made worse by them. This was a carefully controlled "double-blind"

trial. Each patient was given a trial number. A statistician prepared a randomized list allocating 40 patients into two treatment groups (procaine and isotonic saline). This was kept by the pharmacist, who freshly prepared and labelled the ampoules with the trial numbers. The key to the solutions was not divulged until all the data had been collected. It was anticipated that observer bias by both patient and physician might be high in this group.

Dosage.—Care was taken to see that this corresponded to that recommended by Aslan (1960). Single-dose ampoules containing 5 ml. of 2% procaine solution at a specified pH (3.3–4) were prepared. Identical ampoules of isotonic saline were prepared for the control injections. A test dose of 0.5 ml. was given subcutaneously in case of sensitivity. Thereafter 5 ml. was given by the intramuscular route three times weekly for a four-weeks course. This was followed by a rest period of 10 days. Each patient had nine four-weeks courses of injections over a one-year period of observation. The first course was started in May, 1960, and the ninth course ended in April, 1961.

Criteria of Assessment

Each patient in both groups was assessed four times during the trial. A careful clinical examination was made before treatment, and progress was measured after three, six, and nine courses of injections.

In group A objective criteria were used in respect of the mental state, mobility, and incontinence. Each patient was graded and given a score as follows:

Mental State

0. Severe or constant confusion.
1. Moderate confusion—lucid intervals.
2. Mild confusion—usually during the evening only.
3. Normal for age—takes interest in affairs.
4. Fully orientated—reads newspapers, etc.

Mobility

0. Bedfast—requires feeding.
1. Bedfast, but feed themselves.
2. Sits out of bed (more than four hours daily).
3. Walks with help or sticks.
4. Walks alone.

Incontinence (Urine and Faeces)

0. Double, with dirty habits.
1. Constant incontinence, with clean habits.
2. Occasional double incontinence (more than once weekly). Will ask for bottle or bedpan.
3. Urinary incontinence only.
4. No incontinence.

A clinical photograph (colour transparency) was taken before and after treatment to record changes in the facies and hair colour. Care was taken to standardize the method of photography.

If procaine was to be of proved benefit to this type of patient it was felt that evidence of increased interest in their surroundings and self-respect would be noted. An increase in the score for the above-described criteria after the injections would reveal clear evidence of this.

The patients in group B were assessed in a different way. These patients were residents in a home for infirm aged persons and were mentally alert. In each case a full clinical history and examination was made. A record of memory for contemporary events was taken. The patient's weight was recorded as well as subjective comments in respect of appetite, activity, and general sense of well-being. Two tests of agility were timed if the patient was well enough to co-operate. (a) Walking test: time taken to rise from an armchair, walk 10 yards, turn, and return to the seated position.

(b) Stair-climbing: time to rise from an armchair, climb and descend a standard flight of stairs, and return. The conditions of these tests were kept the same for each subsequent examination. The patients were graded (a) worse, (b) stationary, or (c) improved by both their subjective sensations and the observer's objective findings. After final collection of all the results the code used for the procaine and control solutions was released.

Results in Group A Trial

This group consisted of 24 patients (12 of each sex). Their ages ranged from 61 to 94 years. They all showed degenerative changes due to old age or obvious evidence of cerebrovascular disease (eight patients). All the patients were doubly incontinent, and 21 had dirty personal habits. Attempts in retraining them had failed. Mental confusion was present, in varying degree, in all of the patients; 14 were severely demented. All were bedfast nursing cases except when put into chairs by the staff for short periods. The final result after one year's treatment is shown in Table I.

TABLE I

	Men	Women
Died	4	6
Worse	2	3*
Stationary	5	3*
Slight improvement	—	—
Marked	1	—
	12	12

* One patient ceased injections after six courses as she became unsettled and upset by them.

The ages of those who died and of the survivors showed no special difference. The one patient to improve was a hemiplegic man whose course was in keeping with the known vagaries of cerebrovascular disease. With this one exception the injections were without effect on the mental state, incontinence, habits, and degree of mobility. A comparison of the clinical photographs showed no change in the facial appearance or in colour or growth of the hair. It was concluded that procaine injections had not produced any demonstrable beneficial effect in this group.

Results in Group B Trial

This group consisted of 20 men and 20 women. The ages of the men were 73–89 years and of the women 65–90 years; 32 (80%) of the subjects were over 80. They were cared for in a home for elderly people, the majority being "ground floor" types of case. They showed many of the physical infirmities of old age yet their mental function was very good for their years.

The final assessment after one year's treatment is given in Table II. It is seen that nearly half of both groups had deteriorated or died, and that the clinician's and patient's personal assessment of deterioration were

TABLE II

		Control			Procaine		
		F	M	Total	F	M	Total
Patient's subjective assessment	Worse or died	3	6	9	5	5	10
	Stationary ..	4	4	8	1	3	4
	Improved ..	2	1	3	5	1	6
Clinician's objective assessment	Worse or died	3	6	9	5	5	10
	Stationary ..	4	3	7	4	4	8
	Improved ..	2	2	4	2	—	2
Deaths		—	2	2	3	3	6

the same. Six patients receiving procaine died in comparison with two deaths in the control group. More patients stated that they felt subjectively better in the procaine group. With the clinical criteria used this was not confirmed, as four of the control group showed improvement in comparison with two of the procaine group. None of these differences is significant statistically.

The subjective response of the patients after each three-course period is given in Table III. The number who subjectively improved in the procaine group remained constant throughout the trial, whereas the control group decreased. The numbers who became worse or died is very similar in both control and procaine groups.

TABLE III

No. of courses of injections ..	Control			Procaine		
	3	6	9	3	6	9
No. improved	9	6	3	6	6	6
„ stationary	7	8	8	9	7	4
„ worse or died	4	6	9	5	7	10

In addition to the eight deaths, two control and three procaine patients refused to continue the injections. The change in weight of the 27 patients who completed the trial is given in Table IV. An increase or loss up to 2 lb. (0.9 kg.) is regarded as stationary. More patients in the control group both put on and lost weight than in the procaine group, but this is again of no statistical significance. There is no evidence of procaine causing a gain in weight.

TABLE IV

	Control			Procaine		
	F	M	Total	F	M	Total
Increase	5	3	8	3	—	3
Stationary	2	1	3	4	3	7
Loss	2	3	5	—	1	1

It is concluded that there was no evidence of benefit in the procaine compared with the control group.

Discussion

This trial fails to confirm the claims of Aslan (1960). In the first group, consisting largely of examples of arteriosclerotic dementia, no benefit was recorded in 23 out of 24 patients given the treatment. In the second controlled series isotonic saline and procaine had little different end-result. There was no statistical or clinical evidence to favour procaine as a "rejuvenator."

Improvement after procaine injections is reported to occur after the first course of injections (Móra, 1960) or within a few months (Guidi and Scardigli, 1958). Parhon and Aslan (1957) state that within one or two months of treatment benefit may be noted. The trial carried out here lasted 12 months, and it would be thought reasonable to expect improvement over this period of time. In no case in the trial was it thought of any advantage to continue the injections after this time.

Many of the cases in group B classified as "improved" showed only minor degrees of change at the end of 12 months. Bearing in mind the advanced age of many of the patients it was felt that a minor degree of improvement was noteworthy. There was no example of marked improvement anywhere in this series in either group or any sign of rejuvenation.

In a group of aged individuals such as this it is important to look for evidence of prevention of physical and mental decline in the procaine-treated group. It might be argued that the maintenance of a stationary state represents a response to the drug in an aged infirm individual. The figures again do not show any significant difference in the two groups.

No side-effects due to procaine were observed, although several of the patients found the repeated injections irksome. A total of five patients refused to have further procaine injections because of this, or because they felt they were being made worse by them. After completion of the trial no patient asked for the injections to be continued.

The value of procaine in the elderly being accepted, several proprietary products include it in various mixtures of vitamins, rutin, and even cyanocobalamin (vitamin B₁₂) for parenteral or oral administration. We feel it is improper and hazardous to give cyanocobalamin to an elderly patient without proper haematological investigation and diagnosis. The addition of procaine to these preparations would not seem to have any therapeutic value.

Aslan (1957) cites several very aged persons who improved with procaine (including a man aged 107). In the case histories no mention is made of the subjects' social or environmental background. It is commonplace in geriatric practice to see the isolated or neglected patient improve greatly with hospital admission or day hospital attendances. This may be a possible factor, together with the psychological effect of an intensive course of injections, in providing an explanation of the rejuvenating action attributed to procaine. This category of patient also becomes extremely susceptible to suggestion in response to interest in their progress and improvement. Thus there may be other explanations of the benefit recorded in published series. This present trial did not record any significant benefit from injections of procaine.

Summary

A clinical trial of procaine injections in 44 elderly patients over the period of one year is reported.

With one exception, no demonstrable effect was noted in a series of 24 bedfast and incontinent demented patients.

A controlled trial with 40 elderly infirm residents in an old people's home showed no statistical difference between the effects of procaine and of saline injections.

It is concluded that procaine injections are of no value in these two groups of patient.

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REFERENCES

- Aslan, A. (1957). *Therapiewoche*, **8**, 10.
- (1960). *Geront. clin. (Basel)*, **2**, 148.
- and David, C. (1957). *Therapiewoche*, **8**, 1.
- Brit. med. J.*, 1959, **2**, 1163.
- Guidi, G., and Scardigli, G. (1958). *G. Geront.*, **6**, 325.
- Móra, S. (1960). *Z. Altersforsch.*, **14**, 17.
- Parhon, C. I., and Aslan, A. (1957). *Rev. Sci. méd. (Buc.)*, **2**, 5.