at random, the only discrimination being that those considered unlikely to develop symptoms were excluded. At the onset of nausea or vomiting, tablets A, B, or C, 2 t.d.s., a.c., were prescribed. If after 48 hours there was no relief, in the best interests of the patient prochlorperazine, 10 mg., t.d.s., a.c., was substituted for the unknown tablets. The effect of the tablets on anorexia and lassitude was also noted.

Results

Observations were made of 57 patients who were expected to suffer side-effects from therapeutic irradiation; 12 did not develop symptoms. The results of treating the remaining 45 during the first 48 hours are shown in Table I.

From these figures: $\chi^2 = 12.4$. D.F. = 4. $P < 0.02$. A probability of this order is significant.

The 20 patients showing only partial or no improvement were changed to prochlorperazine after 48 hours. In 11 cases the symptoms were completely relieved. There was some improvement in five cases, but in the remaining four there was no improvement. Two of these had, of course, already had prochlorperazine. These resistant cases were finally improved by giving a combination of prochlorperazine and chlorpromazine, but in two cases having a marked psychical element phenobarbitone had also to be given.

TABLE I.—Effect of Prochlorperazine, Pyridoxine, and Inert Tablets on Nausea and Vomiting in 45 Patients Receiving Therapeutic Irradiation

Drug	No. of Cases	Complete Alleviation	Partial Improvement	No Improvement
A (inert)	15	5	4	6
B (prochlorperazine)	16	14	2	Nil
C (pyridoxine)	14	6	5	3

TABLE II.—Analysis of Effect of Prochlorperazine, Pyridoxine, and Inert Tablets on Alleviating Side-effects of Irradiation, Including Anorexia and Lassitude

Drug:	B Prochlorperazine	C Pyridoxine	A Inert Tablets
Total No. of cases treated	34	14	15
Cases improved	25 (73.5%)	5 (36%)	6 (40%)
Complete relief of all symptoms	5 (15%)	4 (29%)	2 (13%)
Lassitude present	18 (53%)	2 (14%)	2 (13%)
Mild anorexia present	14 (41%)	2 (14%)	Nil
Marked anorexia present	6 (18%)	Nil	3 (20%)
Mild nausea present	4 (12%)	2 (14%)	2 (13%)

Toxicity

In the dosage used (30 mg. a day) prochlorperazine is remarkably free from toxic effects. In higher doses it may cause slight drowsiness and interference with accommodation (Gray, 1957), and in doses of more than 60 mg. a day confusion, dizziness, and fainting have been reported (Friend and McLemore, 1957). The manufacturers describe more bizarre forms of toxic effects occasionally encountered with very large doses, but none of these occurred in the trial described.

In this series it is difficult to evaluate whether any drowsiness encountered was due to the drug used or to the effects of irradiation. Apart from the occurrence of slight drowsiness in a small number of cases, there was no evidence of any undesirable constitutional side-effects in any of the patients treated.

Regular blood examinations showed no appreciable change in the cell count that could not be attributed to irradiation except in one case. This was a female patient aged 72 receiving post-operative irradiation following a

local mastectomy for carcinoma of the breast. The total white-cell count dropped to 1,200 after one week of irradiation and treatment with prochlorperazine. After about two weeks at this level there was a gradual return to normal, in spite of continuing both the irradiation and the prochlorperazine.

No other toxic effects were encountered.

Summary and Conclusions

In a controlled trial involving 45 patients receiving therapeutic irradiation, prochlorperazine has been found significantly more effective in relieving radiation sickness than pyridoxine or inert tablets.

The following conclusions may be drawn from the small series described: (1) Prochlorperazine is more effective in relieving the toxic symptoms of irradiation than pyridoxine or an inert tablet. (2) In the dosage of prochlorperazine used (10 mg. t.d.s.) there were no material side-effects; marked drowsiness as occurs with so many other anti-emetic drugs was not seen. (3) For maximum benefit it is best to begin giving prochlorperazine with the first exposure to irradiation, or at least as soon as possible after the onset of symptoms.

I thank Dr. I. Churchill Davidson for allowing me to conduct this trial on his patients and for his helpful suggestions and criticisms.

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Preliminary Communications

"Debricin": A New Agent for Wound Debridement

The presence of necrotic tissue in an open wound is an obstacle to healing. Infection persists, granulations are slow to appear, and epithelization is delayed. For small and superficial sloughs, routine treatment with local antiseptics and rest for the affected part usually provide sufficient help for the natural reparative processes to allow healing to occur within a reasonably short period of time. When a slough is of greater extent in depth or size, healing by this means is slow and may extend over many weeks, and it may also prevent the early application of a skin graft in suitable cases. For this reason, surgical excision of deep and extensive sloughs is often preferred, and may be combined with immediate skin-grafting.

Another way of tackling this problem is to rely on one of a variety of enzymatic preparations, application of which accelerates the removal of necrotic tissue and sloughs, which are broken up by proteolytic digestion; thus the period of healing or of wound preparation prior to a plastic procedure is greatly shortened. This approach has been investigated by others. Morani (1953) reported great improvement in six cases of chronic sloughing lesions using a trypsin preparation. A mixture of trypsin and chymotrypsin was used by Reiser, Roettig, and Curtis (1953), who found very rapid clearance of sloughs in similar lesions. Prueter, Stein,

Drum, and Kalz (1957) applied a preparation of chymotrypsin only and reported excellent response in 75% of a series of 60 patients.

Shelby, Taylor, Garnes, and Prigot (1958) used "viokase," a preparation of whole pancreatic extract, with similar success on 125 patients. Spittler and Parmenter (1954) reported their general impression of the use of a mixture of streptokinase and streptodornase on sloughing war wounds, and were also greatly impressed by the rapidity of slough clearance with these agents. "Debricin" was used by Douglas, Ferriday, and Gaughran (1958) in an experimental study on removal of necrotic tissue in guinea-pigs subjected to a standardized type of burn and found it greatly superior to five other enzyme preparations of similar nature.

PRESENT TRIAL

A short trial of debricin was therefore organized to assess its value in relation to the rapidity of disappearance of necrotic tissue and sloughs in suitable patients. Debricin is a protease extracted from fig latex and presented as a lyophilized (freeze-dried) powder, containing the active ingredient, which immediately before use is dissolved in a vegetable gum with suitable preservatives and buffers. This fig protease is a highly specific lytic agent with a pronounced effect on fibrin, denatured elastin, and denatured collagen, but no effect upon living or even partially denatured tissues. It is available in two strengths—1% and 7.5%.

During the period of the trial, all in- and out-patients whose lesions were of a suitable nature were included, irrespective of whether previous treatment had been given. All sites were included, and the pathology of the lesions ranged from traumatic necrosis to chronic ulceration. Size, aetiology, and total duration of each

lesion were recorded to provide the clinical background to the individual case. Previous treatment consisted most frequently of various combinations of commonly used antibiotics, local applications of eusol, and similar antiseptic solutions, and supporting bandages and rest for the affected part. Infection of the whole lesion was estimated in the general clinical sense of this term and was divided into three degrees of severity. Two types of slough were recognized: partial-thickness skin necrosis (group A), and full-thickness skin necrosis with or without additional necrosis of the superficial layers of the subcutaneous tissues (group B). The duration of the sloughs is stated separately, as in some cases these were of more recent occurrence than the primary lesion. Treatment consisted in the application of debricin directly to the slough, the whole wound then being covered with a simple dry gauze dressing.

In order to present suitable control cases, it would have been necessary to provide for each debricin-treated case one of similar aetiology, duration, size, and depth to be treated with standard methods only. Perusal of the tables of treated patients shows that among the entire series it would have been difficult to find similar cases for this purpose. Therefore as adequate controls could not be obtained they were omitted, and assessment of the results was made on the extent of clearance of slough after five days' treatment. Where treatment continued for longer, the time factor was also taken into consideration.

RESULTS

Tables I-III summarize the case details and results, the latter being graded as follows: Poor=little or no effect after five days' treatment. Moderate=50% or less slough clearance after five days' treatment. Good=75% or more slough clearance after five days' treatment.

Thirty-three lesions were treated in a total of 31 patients. Though the criterion for assessment of the usefulness of debricin was taken to be the percentage of slough clearance after five days of daily applications, the treatment period is actually longer in those out-patients who were seen only at intervals of several days. The results in these cases have therefore been judged on the total number of applications of debricin required to remove the necrotic tissue, as the total time of treatment was not the deciding factor. There were therefore 18 good results, eight moderate results, and seven poor results. However, in two of the last group treatment was discontinued after one application of debricin owing to the rather severe local discomfort.

Adverse Reactions.—Only local pain was complained of, and no generalized reactions occurred. The former could not be correlated with the degree of inflammation present, or any other local or general factor. In only two cases was it severe enough to stop further treatment, the remaining patients often stating spontaneously at the end of treatment that their discomfort had been negligible in comparison with the satisfactory result achieved. In no case was there any evidence that debricin had any adverse effect on healing.

SUMMARY AND CONCLUSIONS

Thirty-three open wounds and ulcers were treated with debricin to help with the rapid removal of sloughs and necrotic tissue. The disappearance of necrotic tissue from this type of lesion without the use of such an enzyme preparation is usually slow and delays healing. The best results in this trial were obtained on sloughs which, by the nature of the lesion, were moist and soggy when treatment was begun. Conversely, dry

TABLE I.—*Lesion*

Sites		Duration		Pathology	
Arm	3	0-7 days	5	Abrasions	9
Hand	1	8-14	4	Ischaemic necrosis	5
Finger	1	15-30	4	Stasis ulcer	15
Leg	26	30+	20	Infection	3
Face	1			Irradiation necrosis	1
Chest wall	1				

Previous Treatment		Infection		Size	
Antibiotics	13	Heavy	11	< 1 sq. in. (6.45 cm. ²)	9
Local antiseptics	19	Moderate	15	< 4 " (25 ")	11
Bandage/rest	23	Slight	7	> 1 " (6.45 ")	5
				> 4 " (25 ")	7
				Not known	1

Figures in all three tables indicate number of cases.

TABLE II.—*Slough*

Type		Duration		Size	
Group A	5	0-7 days	7	< 1 sq. in. (6.45 cm. ²)	13
" B	28	8-14	8	> 1 " (6.45 ")	12
		15-30	2	> 4 " (25 ")	8
		30+	13		
		Not known	3		

TABLE III.—*Treatment and Results*

Treatment		Duration		Additional Treatment	
Debricin 1%	22	0-7 days	27	Antibiotics	1
" 7.5%	11	8 days+	6	Local antiseptics	2
				Bandage/rest	24

Results		Adverse Reactions	
Good	18	Slight pain	7
Moderate	8	Severe	1
Poor	7	Pain and itching	1

and leathery sloughs were most resistant to digestion with debricin. In one case the continued presence of pus may have been the reason for the poor result. On the basis of this series of cases, debricin is a valuable adjunct to the standard methods of treatment of this type of lesion both in hospital and in out-patient practice. In successful cases removal of necrotic tissue and healing are greatly accelerated.

We thank the nurses of St. Mary's Hospital, who carried out the treatment of these patients, and Messrs. Johnson & Johnson for providing the debricin.

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Medical Memoranda

Prophylactic Ergometrine

It has been established that the prophylactic use of ergometrine in the second stage of labour reduces the incidence of post-partum haemorrhage (Lewis, 1956); but a recent letter to this *Journal* suggests that many still believe ergometrine used in this way inevitably results in an increased rate of manual removal of the placenta. This belief appears to persist in spite of a number of reports to the contrary (Davis and Boynton, 1942; Shaw, 1949; Kimbell, 1954). The series of cases here recorded adds to the weight of evidence in favour of the prophylactic use of ergometrine.

Table I shows the incidence of post-partum haemorrhage and the manual removal rate at Perivale Maternity Hospital from 1954 to 1957. There was a

TABLE I.—Incidence of Post-partum Haemorrhage and Manual Removal Rate

	1954	1955	1956	1957
No. of deliveries	1,010	1,123	1,190	1,292
Post-partum haemorrhage:				
No. of cases	75	80	51	49
Rate	7.4%	7.1%	4.3%	3.9%
Manual removal of placenta:				
No. of cases	14	21	19	14
Rate	1.3%	2.1%	1.6%	1.1%

noticeable decrease in the incidence of post-partum haemorrhage in 1956 and 1957 compared with the preceding years, without any alteration in the rate of manual removal of the placenta. Since 1951 0.5 mg. of ergometrine has been given intravenously with the birth of the anterior shoulder to patients predisposed to post-partum haemorrhage—namely, patients with a history of post-partum haemorrhage, those with a haemoglobin of less than 10.4 g./100 ml. at the onset of labour, patients expecting the fifth or subsequent baby, those with hydramnios or multiple pregnancy, after an ante-partum haemorrhage or prolonged labour, and if operative intervention had been necessary. From

the beginning of 1956 all patients not so treated, and delivered in alternate weeks, were given 0.5 mg. of ergometrine together with 1,000 units of hyaluronidase intramuscularly with the crowning of the head. The remainder of the patients were not given ergometrine unless undue bleeding occurred either before or after delivery of the placenta. The results are shown in Table II. The difference in incidence of post-partum

TABLE II.—Results of Treatment

	1956	1957	Total	Incidence
No. of deliveries	1,190	1,292	2,482	
No. of post-partum haemorrhages	51	49	100	4%
No. of manual removals	19	14	33	1.3%
Ergometrine given in the 2nd stage:				
No. of cases	464	590	1,054	
P.P.H.	9	16	25	2.4%
Man. Rem.	9	8	17	1.6%
No ergometrine until after delivery of the baby:				
No. of cases	726	702	1,420	
P.P.H.	42	33	75	5.3%
Man. Rem.	10	6	16	1.1%

haemorrhage in the two-year periods 1954–5 and 1956–7 is statistically significant ($P < 0.001$). The difference between the number of post-partum haemorrhages occurring in patients treated either with or without ergometrine in 1956 and 1957 is also statistically significant ($P < 0.001$). These figures are in fact of greater significance, since the group of patients treated with ergometrine includes those predisposed to post-partum haemorrhage. Further, the patients who were not given ergometrine during the second stage were given it before the delivery of the placenta if the amount or rate of blood loss caused concern. The manual removal rate is almost identical in all four years ($P 0.8-0.7$).

The series shows that there is no increase in the manual removal rate if ergometrine is used prophylactically in the second stage of labour; and these figures confirm the work of Lister (1950), Daley (1951), and Kimbell (1954). To save blood is of prime importance, and the prophylactic use of ergometrine, particularly in patients who are prone to have a post-partum haemorrhage, certainly does this, as well as shortening the duration of the third stage of labour (Shaw, 1949) without increasing the hazards to the mother.

It is agreed that occasionally, when ergometrine has been given during the second stage, the placenta and membranes may be trapped by the closing cervix; but by practising the Brandt-Andrews manoeuvre, if necessary supplemented by the inhalation of amyl nitrite, cervical spasm can be overcome and the separated placenta delivered from the cervix or vagina.

Since these results have become available, ergometrine is being used routinely in the second stage of labour for all patients delivered in Perivale Maternity Hospital.

I would like to thank Miss A. M. Dickins for permission to publish these figures.

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