in the control group (Table II), it becomes clear that certain typical changes occurred after the end of the treatment. Thus about four months after the treatment finished considerable deterioration had occurred, consisting in particular of disappearance of the improvement obtained during the treatment, and also of the appearance of some new cases of deterioration. This indicates that in some cases improvement of certain senile features and prevention of further senile deterioration can be maintained only if treatment with the vitamins is continued. In spite of this relapse in a number of cases, however, in numerous others the improvement obtained by the vitamin treatment was maintained after its discontinuation. This was demonstrated by the clinical observations (Table I), the psychological test (Table III, Test No. 2), and the ergographic test (Table III, Test No. 4).

Experiments on deficient animals have shown that the specific effects of vitamins B and C do not last long after the end of the administration of these vitamins. Therefore it is most probable that the explanation of the lasting action of the vitamins in some of the senile patients lies in the disruption of those secondary vicious circles which are originated by pathological changes in different organs (e.g., sex glands, adrenals, gastro-intestinal canal, liver, etc.), changes in these organs in their turn being produced by the direct action of vitamin deficiency. These secondary pathological conditions, being specific for dysfunction of the affected organs, become additional to those caused by pure vitamin deficiency proper. Of course, when the effects of the discontinued vitamin treatment have worn off, the repair of the organ concerned disappears after some time and the secondary vicious circles return.

Summary

Forty senile patients were treated with vitamins B complex and C, the whole period of observation lasting for about a year. The condition of these patients was compared with that of 18 senile patients of a control group receiving dummy tablets. All patients were on a usual hospital diet not rich in vitamins.

Treatment with vitamins B and C, as with any other remedy, did not stop the biologically inevitable development of senility, and therefore did not affect those basic features which are specific for and present in even the most physiological type of senility.

By treating the aged people with vitamins, however, it was possible to prevent or improve, in some cases to a striking degree, certain of those senile features which could be considered as pathological, because they appear prematurely or in an extreme degree (e.g., muscular, cardiovascular, and mental deterioration) or which do not seem to be inevitable in normal physiological senility (e.g., dementia, insomnia, skin rashes and itchings, constipation).

During the period of observation improvement or disappearance (apparently not of a lasting nature) of some pathological senile features was observed in numerous cases, while a number of other cases were not improved by the treatment, and a few patients who had been free from certain senile features developed them during and notwithstanding the treatment.

In spite of the comparatively limited and modest results which aged people might expect from treatment with vitamins, it seems clear that in suitable cases the relief obtained in some pathological senile features might be considerable.

The results obtained provide strong support to the argument, repeatedly emphasized by several specialists in the modern science of nutrition, that the greatest care should be taken to prevent the occurrence of partial or latent vitamin deficiency, apparently widely spread in the population. This will result not only in the prevention of certain vitamin-deficiency diseases but probably also in the approach to a less pathological senility.

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THE VALUE OF BLOOD TRANSFUSION IN MALIGNANT DIPHTHERIA

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Judging by the lack of any published reports in English medical literature on the value of blood transfusion in malignant diphtheria, it would seem that this method of therapy has received little or no attention in this country. On the other hand, a review of the available literature goes to show that the subject has engaged the attention of certain Continental workers for some time.

Baar and Benedict (1933) treated 43 cases of malignant diphtheria with either "human serum" or blood transfusion. All the cases selected for treatment by transfusion were rigorously classified, nor were desperate cases with cardiac insufficiency discarded. Twenty-seven of the 43 cases recovered, giving a case mortality of 37.2%. The authors claimed that transfusion reduced the mortality rate of malignant diphtheria by one-half.

Moeller (1934) tried the method of giving blood in the proportion of 1/70 of the patient's weight. In all he transfused 19 cases: 5 were transfused late in the illness (6th, 7th, or 8th day), and of these four died; 2 were moribund on admission and died; of the remaining 12 cases, 7 survived. Moeller calculated the mortality rate at 41% in the transfused cases and at 66% in the non-transfused, but intimated that the number of cases was too small for any firm conclusions.

Darrow and Yannet (1935) emphasized the value of blood transfusion in malignant cases as a method of combating the

early toxæmic manifestations which in many respects were analogous to those of shock, and also in the maintenance of nutrition in those cases in which persistent vomiting precluded oral feeding.

The present investigation into the value of blood transfusion in malignant diphtheria was carried out during the 1940 epidemic of diphtheria in Swansea, which was characterized by the prevalence of malignant cases. The report is based on 40 malignant cases admitted to hospital between July, 1940, and January, 1941, of which 20 consecutive cases, admitted during the three months November, 1940, to January, 1941, were transfused.

Clinical and Therapeutic Considerations

It seems hardly necessary to recall here the clinical features of malignant diphtheria, since these are admirably described in modern textbooks on infectious diseases. We would mention briefly that the term "malignant" is applied to an unusually toxic form of diphtheria. The patient is as a rule apathetic and drowsy, and takes little interest in his surroundings. Locally there is extensive membrane, involving the tonsils, pillars, palate, and uvula, and extending on to the nasal mucosa, together with faucial and palatal oedema and redness, the oedema at times being so pronounced as to mask the real extent of the membrane. A profuse purulent or sanious nasal discharge is common and results in nasal obstruction and oral breathing. Swelling of the cervical glands and periglandular tissues is considerable. Fætor is marked. Haemorrhage into the skin and from mucous surfaces is not uncommon. As a rule such cases show a slow response to specific treatment with antitoxin. The mortality is often as high as 50%, and those patients that recover usually suffer severe paralysis.

Up to November, 1940, malignant cases were treated at this hospital upon the following lines:

1. Prompt administration of a large dose of concentrated antitoxin, intravenously if possible, and partly intramuscular.
2. Intravenous infusion of 10% glucose in saline.
3. Absolute rest in the flat position with the foot of the bed raised.
4. Glucose drinks by mouth, except in those cases in which vomiting was troublesome and persistent, when oral feeding was stopped and salines with 5% glucose administered rectally.
5. Strychnine daily.

In spite of intensive antitoxic therapy it was felt that its value in malignant cases was limited, and in November, 1940, it was decided to investigate the possibilities of blood transfusion. The first case transfused responded so well that it was decided to continue with the investigation, and during the ensuing three months until the subsidence of the epidemic towards the middle of January, 1941, in all 20 consecutive malignant cases were transfused. Apart from the substitution of blood transfusion for the intravenous administration of glucose and saline, the treatment of the 20 transfused cases was strictly comparable in all other respects to that given to malignant cases admitted before November, 1940.

Transfusion Technique

Transfusion was performed as soon as possible after the admission of the patient to hospital, and in each case the total volume of blood given was approximately one pint. Stored citrated blood was used throughout, and whereas 14 of the cases were grouped beforehand and received blood of the same grouping, this preliminary was omitted in the case of 6 desperately ill patients who were transfused with Group O blood. The apparatus used for giving the blood was the Medical Research Council's blood transfusion outfit, and owing to the collapsed nature of the veins it was found necessary in each case to cut down on the vein. The blood was given cold, and in order to avoid over-

loading an already embarrassed myocardium the rate of flow was slow, the average duration of transfusion in the 20 cases being two hours.

Plan of Investigation

The object of this paper is to compare the results obtained in respect of 20 transfused cases (test series) with a similar number of consecutive cases of malignant diphtheria treated by the orthodox method outlined above, and which were admitted during the four months July to October, 1940 (control series). It is proposed to compare the results in the two series of cases with regard to the following criteria: mortality rate, immediate response to treatment, incidence and severity of complications, and total duration of stay in hospital.

Since the validity of such a comparison might easily be influenced by such factors as (1) the real extent of malignancy in individual cases and the amount of antitoxin administered, (2) the age and sex distribution of the patients, and (3) the duration of the disease before admission to hospital, these must first be briefly considered.

All the cases were under the direct supervision of one of us (I. P.) throughout, and they all received the same nursing attention. All were rigorously classified on admission, and their malignancy may be gauged from the fact that the total amount of antitoxin given in the test series and control series averaged 110,000 and 112,000 units per case respectively. In no single case was the total dosage of antitoxin under 100,000 units. That the two series were fairly comparable regarding age and sex distribution can be seen from Table I. Table II gives the day of disease on admission, and it will be noted that whereas all the cases in the control series were admitted on the second and third days, 5 in the test series were admitted later than the third day of illness.

TABLE I.—Age and Sex Distribution

Age	Test Series		Control Series	
	Males	Females	Males	Females
3-4 years	1		1	1
4-5 "		1	1	2
5-10 "	4	9	6	1
10-15 "	2	2	2	5
15-20 "		1		1
Total	7	13	10	10

TABLE II

	Day of Disease on Admission				
	1st	2nd	3rd	4th	5th
Test cases		6	9	4	1
Control cases ..		10	10		

Results

Mortality Rate.—Out of the 20 cases treated by blood transfusion in the test series there were 2 deaths, giving a case mortality of 10%, whereas in the control series there were 7 deaths and a case mortality of 35%. Of the 2 patients who died in the test series, one was moribund on admission and died the same day, a few hours after transfusion. The second died during the sixth week of the illness. At this time the patient was suffering from pharyngeal paralysis, and death occurred from cardiac failure as the result of an unfortunate attempt to institute nasal feeding. In the control series 5 patients died of profound toxæmia during the first week, while the other two fatalities were due to cardiac failure during the second week. Table III gives the number of deaths at different age periods.

TABLE III

Age	Test Series		Control Series	
	Cases	Deaths	Cases	Deaths
3-4 years	1		2	
4-5 "	1		3	2
5-10 "	13	2	7	2
10-15 "	4		7	3
15-20 "	1		1	
Total	20	2	20	7

Immediate Response to Treatment.—A noticeable feature of the test series was the rapidity with which most of the cases responded to treatment as compared with the control series. It was noted in most of the transfused cases that during the days immediately following the giving of the blood the patient's apathetic and drowsy aspect was transformed into a bright and keen appearance, and the nasal discharge, the periauritis, and the membrane rapidly cleared up, whereas such a rapid clinical improvement was not so prominent in the control series.

Complications.—As regards the incidence and severity of complications in the recovered cases, the test series followed a more favourable course: of the 18 cases that recovered 4 were uncomplicated; the other 14 developed a total of 33 complications. In the control series all 13 recovered cases developed complications, with a total of 44 complications. Although complications of a mild character were common to both series, the more severe types, including cardiac irregularities, pharyngeal paralysis, and severe peripheral neuritis, were more prominent in the control series (Table IV).

TABLE IV.—Complications in Recovered Cases

	Test Series No.	Control Series No.
Recovered cases	18	13
Uncomplicated recovery	4	0
Complicated recovery	14	13
Complications :		
Mild { Precocious palatal paresis		1
Palatal paresis	8	5
Paralysis of accommodation	1	
Facial paresis		1
Squint	2	2
Absent or sluggish reflexes	8	10
Severe { Pharyngeal paralysis	3	7
Weakness and wasting of limbs		2
Second week cardiac failure	1	3
Late cardiac irregularities	1	4
Albuminuria	6	9
Secondary cervical adenitis	1	
Otitis media	2	
Total complications	33	44

The incidence of paralysis in both test and control series is approximately equal, being 55% and 60% respectively. When, however, the severer forms of paralysis are considered alone it is found that they predominate in the control series, their incidence in this group being 35% as compared with 15% in the test series.

Duration of Stay in Hospital.—Table V gives the duration of stay in hospital of the recovered cases. Transfused cases made a more rapid recovery, the average duration of stay being 10 weeks as compared with an average duration of 13 weeks in the control series.

TABLE V.—Length of Stay of Recovered Cases

Weeks :	8	9	10	11	12	13	14	15	16
Test cases	6	3	3	2	1	3		1	6
Control cases		2	3		1				

Reactions following Transfusions.—Among the 20 cases transfused 3 developed a mild febrile reaction with a rise of temperature up to 100° F. soon after the giving of blood. In only one case was a definite rigor encountered.

Comments

In the 40 cases of malignant diphtheria under review it appears that following the introduction of blood transfusion, on the whole, the immediate clinical response of the patients to specific therapy was accelerated. Not only was the case mortality reduced from 35% to 10%, but there was a decided decrease in the incidence of the severer forms of paralysis, and the duration of stay in hospital of recovered cases was appreciably reduced. Admittedly the number of cases transfused is small, and we fully realize that in such circumstances the results are open to serious criticism. Nevertheless, we maintain that the results are sufficiently encouraging to warrant further investigation into the possibilities of blood transfusion in the treatment of malignant diphtheria.

Summary

The available literature on the use of blood transfusion in malignant diphtheria is reviewed.

The main clinical features of malignant cases are outlined.

The present investigation deals with a series of 40 consecutive cases of malignant diphtheria. The first 20 were treated in the usual orthodox manner; in the others treatment was supplemented with blood transfusion.

The transfusion technique adopted is described with special reference to the form of apparatus used, and the type, volume, and rate of administration of the blood.

The results obtained in the two series are compared, and it is suggested that the results for the transfused series are sufficiently encouraging to merit further investigation into the value of blood transfusion as a therapeutic measure in malignant diphtheria.

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J. S. Simmons (*South. med. J.*, 1941, **34**, 62) states that early in 1940 the Surgeon-General requested that the chairman of the Division of Medical Science of the National Research Council should appoint committees composed of civilian leaders in the various medical specialties to advise the U.S. Army concerning its emergency problems. Another important health measure was instituted in February, 1940, when the Public Health Service was authorized to co-operate with the Army by improving sanitation and disease control in civilian areas adjacent to military stations and concentrations. The Surgeon-General has also obtained the assistance of the American Medical Association in classifying the medical personnel of the country and determining the availability of physicians for service in civil life and in the Army. The paper contains brief notes of the procedure applicable to (1) immunization of all military personnel against small-pox, typhoid and paratyphoid, and tetanus; (2) immunization against localized outbreaks of endemic disease such as scarlet fever; (3) immunization against uncommon and dangerous diseases to which the troops might be exposed at home and abroad—such as yellow fever, cholera, plague, and typhus.