surprising that the majority of case reports in the literature refer only to the allergic donor (*Lancet* editorial, 1941). Although the role of the allergic recipient is mentioned sometimes in discussions on allergic transfusion reactions (Polayes and Lederer, 1932; Kilduffe and De Bakey, 1942) only one case report of an allergic recipient developing a transfusion rash was found in the literature (Stewart and Bates, 1938). Böttner (1924), Brem *et al.* (1928), and Price (1934), considering the sensitiveness of the recipient as the cause of transfusion reactions, do not refer to urticaria and related syndromes, but to febrile reactions. Duke and Stofer (1924), who are also frequently quoted as having observed an allergic reaction in a sensitive subject after transfusion, do not describe a typical allergic syndrome, but a coma.

Nothing is known of the character or source of the atopic substances in human serum. The fact is notable that fresh autoserum failed to react even in highly serum-sensitive subjects, and positive skin reactions were observed only with isosera or with serum from pools. The same observation was made by Chant and Gay (1927) in a fairly large series of cases. This may indicate that the reacting substances are foreign to the human body. Furthermore, it is interesting that a serum-sensitive person does not respond equally strongly to different human sera.

Levine and State (1942) claim that the soluble A and B substances produce the positive serum reaction and the serum rashes. No confirmation of their observations has yet been published. Nor was it obtained by the results of the present skin tests with A and B sera.

There is some reason to believe that the presence of extraneous atopens—e.g., food or inhalants—in the transfused serum may be the cause of the serum reactions in sensitive subjects. In this respect Walzer's and Freeman's researches are noteworthy. Walzer (1927) sensitized small areas of normal skin passively with serum from persons who were highly food-sensitive. When the normal recipients, on the following day, ate the corresponding food, the sensitized site responded promptly by producing a wheal and an erythema. This proved the absorption of food atopens from the non-allergic digestive tract. The absorption of pollen atopen from the non-allergic mucous membrane of the nose was shown by Freeman (1925) in a similar way.

3. *Desensitization.*—In the present series 10 out of 11 serum-sensitive subjects, after recovery from a transfusion rash, showed a condition of desensitization on re-transfusion. Thus, on repetition, the administration of serum caused no urticaria or only the slightest rashes in subjects who had reacted previously. The reaction to the first serum transfusion cannot be due to nervous excitement, as several cases had preliminary saline transfusions without reaction. The refractoriness may only be temporary. It was, however, still present in several cases transfused three months after desensitization had been established. The refractory state of transfused atopic subjects resembles the desensitization in anaphylaxis, since sensitive animals surviving a sufficiently strong dose of their antigen do not react to a second dose of the same antigen. That the desensitizing effect can also be produced by whole blood was shown by Young (1942). She investigated the reactions of three subjects who responded with a transfusion rash when receiving blood for the first time. When blood of another donor was used for repetition of the transfusion a rash developed again. On the other hand, when using the same donor's blood for a second time no reaction occurred. Apart from these cases no definite reports on desensitization by transfusion could be found in the literature. Concurrently with the change of reaction to serum there occurred in bronchial asthmatics a marked improvement of the general condition and a decrease of or even a freedom from asthmatic attacks. This may be due to immunological changes. On the other hand, it may be due entirely to psychological factors, as it cannot be denied that transfusion with "normal serum" means in practice for every patient some psychological impression.

Summary

Pooled human serum, dried and then reconstituted, when used for skin tests gave positive reactions in 77% of atopic subjects, but in only 20% of non-atopic. Sera from single individuals also gave

positive reactions in the same recipient. Autoserum failed to react. The skin-reacting properties of serum were independent of the group-specific substances.

On transfusion, such serum caused "allergic" reactions in 14 out of 17 atopic recipients, but in none of the 21 non-atopic.

On repeated transfusion in 14 atopic and in 14 non-atopic cases no sensitization occurred.

On repeated transfusion, desensitization was observed in 10 out of 11 serum-sensitive atopic cases.

In the course of the follow-up of patients who received serum transfusions a number of cases of homologous serum jaundice were observed. In some of the cases the hepatitis was mild (Loutit *et al.*, 1944), in others as yet unreported acute hepatic necrosis occurred. Further attempts at desensitization of allergic patients with human serum, therefore, are not at present advised in this country.

I wish to thank Dr. A. N. Drury for suggesting this line of research and Dr. J. L. Livingstone and other members of the E.M.S. medical staff of Sectors 8 and 9 for their co-operation in investigations of patients under their care. I am especially indebted to Dr. J. Loutit, Director of the S.W. London Blood Supply Depot, for his great help and interest at every stage of this study.

REFERENCES

- Böttner, A. (1924). *Dtsch. med. Wschr.*, **50**, 599.
 Brem, W. V., Zeiler, A. H., and Hammack, R. W. (1928). *Amer. J. med. Sci.*, **175**, 96.
 Chant, E. H., and Gay, L. N. (1927). *Johns Hopk. Hosp. Bull.*, **40**, 63.
 Coca, A. F., Walzer, M., and Thommen, A. (1931). *Asthma and Hayfever in Theory and Practice*, Chas. C. Thomas, Springfield, Ill.
 Colonel, W. J. (1943). *U.S. Nav. med. Bull.*, **41**, 1356.
 Duke, W. W., and Stofer, D. D. (1924). *Med. Clin. N. Amer.*, **7**, 1253.
 Freeman, J. (1925). *Proc. roy. Soc. Med.*, **18**, Laryngol. Sect., 29.
 Györgi, P., and Witebsky, E. (1929). *Münch. med. Wschr.*, **76**, 195.
 Hoxworth, P., and Skinner, C. (1941). *Arch. Surg.*, Chicago, **42**, 321, 480, 498.
 Kilduffe, R. A., and De Bakey, M. (1942). *The Blood Bank and the Technique and Therapeutics of Transfusions*, H. Kimpton, London.
Lancet (1941). **2**, 163.
 Levine, M., and State, D. (1942). *J. Amer. med. Ass.*, **120**, 275.
 Loutit, J. *et al.* (1944). In the press.
 Polayes, S. H., and Lederer, M. (1932). *J. Lab. clin. Med.*, **17**, 1029.
 Price, A. S. (1934). *Rev. Gastroent.*, **1**, 192.
 Stewart, W., and Bates, T. (1938). *Lancet*, **1**, 319.
 Walzer, M. (1927). *J. Immunol.*, **14**, 143.
 Wiener, A. S., Oremland, B. H., Hyman, M. A., and Samwick, A. A. (1941). *Amer. J. clin. Path.*, **11**, 102.
 Young, R. E. S. (1942). *Amer. J. Surg.*, **55**, 607.

INCIDENCE OF BLEEDING GUMS AMONG R.A.F. PERSONNEL AND THE VALUE OF ASCORBIC ACID IN TREATMENT

BY

W. P. STAMM, M.B., B.S.
Wing Commander

T. F. MACRAE, D.Sc., Ph.D.
Wing Commander

AND

SIMON YUDKIN, Ph.D., M.B., M.R.C.P.
Flight Lieutenant

(R.A.F. Institute of Pathology and Tropical Medicine)

Reports appearing in medical journals recording good results obtained by the treatment of various forms of gingivitis with ascorbic acid led to a very large consumption of that substance in the Royal Air Force for the treatment of all forms of bleeding gums. An investigation was therefore carried out between October, 1941, and May, 1942, to discover the incidence of bleeding gums in the R.A.F. and to assess the value of ascorbic acid in the treatment of this condition.

Experiment 1

This experiment took place at three R.A.F. stations during October and November, 1941. At each station all personnel available were examined, except those already taking ascorbic acid, those being treated for acute ulcerative gingivo-stomatitis, and those with no teeth. About two-thirds of those examined were airmen; the remainder were airwomen and soldiers, with a few officers, sergeants, and naval personnel. The majority of subjects in this and later experiments were between the ages of 18 and 25. All those included in this experiment had been living on Service rations for six months or more. An estimation was made of the ascorbic acid content of the airmen's food during the experimental period and in the early spring of 1942.

Methods

The gums of the lower jaw were examined for bleeding after digital massage. Three degrees of bleeding were recognized and noted: (a) bleeding just perceptible at one or two points after firm massage; (b) bleeding more easily produced or bleeding from several points; (c) bleeding apparent on inspection or at the slightest touch. Where gums showed bleeding, ulceration and redness were also looked for, being classified as "absent," "present," or "marked."

Alternate members of the group with bleeding gums were given ascorbic acid tablets and dummy tablets flavoured with tartaric acid. The dose of ascorbic acid was 200 mg. daily for 7 days, followed by 100 mg. daily for 14 days; the dummy tablets were similar in appearance and taste, and were given in similar numbers. Distribution of the tablets was conducted under the supervision of section N.C.O.s, to whom each man had to report daily. The tablets had to be chewed and swallowed in the presence of the N.C.O.s, who kept records of attendances. The dental officer at each station was supplied with a list of those in the experimental group and was asked not to carry out any dental treatment on them during the period of the test.

At the end of the experimental period of three weeks all subjects given ascorbic acid and dummy tablets were re-examined. The original notes were not available to the examiner, so that he could not be influenced by his previous observations or by a knowledge of which tablets had been given. After examination each individual was asked whether he had noticed any improvement or deterioration during treatment. For various reasons not connected with the experiment about 27% of the subjects were not available at the second examination.

The ascorbic acid content of the food as served to the airmen in the messes was determined by the dichlorophenol-indophenol technique (Harris and Oliver, 1942) during one week of the experimental period at each station. The average weight of each item consumed by the personnel in their messes at each of the 28 meals served during the week and the ascorbic acid content per unit weight of each of these items at the time of serving were determined. The average intake of ascorbic acid per airman at each station was calculated from these data. This determination of the ascorbic acid intake was repeated at the same stations in March, 1942, in order to discover the degree of seasonal variation.

Results

The total number of personnel examined at the three stations was 1,791, and 344 of these had some degree of bleeding of the gums—a percentage of 19.2. The incidence varied between the stations and between different classes at the same station, but not to any significant extent (Table I).

TABLE I.—Incidence of Bleeding Gums at the Various Stations and in the Different Classes of Personnel. (Experiment 1)

Station	Number Examined	Number with Bleeding Gums	Percentage with Bleeding Gums
1	521	101	19.4
2	708	111	15.7
3	562	132	23.5
Total ..	1,791	344	19.2

Class of Personnel	Number Examined	Number with Bleeding Gums	Percentage with Bleeding Gums
Airmen ..	1,191	215	18.0
Airwomen ..	271	57	21.0
Sergeants ..	68	22	32.4
Officers ..	10	3	30.0
Army ..	215	45	20.9
Navy ..	36	2	5.5
Total ..	1,791	344	19.2

Of those with bleeding gums 250 completed the test—119 receiving ascorbic acid and 131 dummy tablets. Table II summarizes the effects of the two treatments on the bleeding, ulceration, and redness of the gums. There was no significant difference between the effects

TABLE II.—Effect of Treatment with Ascorbic Acid on Bleeding, Ulceration, and Redness of Gums. (Experiment 1)

	Treated with Ascorbic Acid				Treated with Dummy Tablets			
	Im- proved	No Change	Deterior- ated	Total	Im- proved	No Change	Deterior- ated	Total
Showing No. bleeding	43	61	15	119	53	64	14	131
% ..	36	51	13	—	40.5	49	10.5	—
No. showing ulceration	3	19	1	23	10	14	1	25
No. showing redness	36	42	8	86	51	33	8	92

produced by ascorbic acid and by the control tablets; the apparent better effect of the latter tablets was probably due to chance.

Ulceration developed during the experiment in 5 of the 119 treated with ascorbic acid and in 9 of the 131 given dummy tablets; redness developed in 6 of the ascorbic acid group and in 9 of those receiving dummy tablets. The effects of the treatments were worked out for each station and for each class of personnel, but as the results showed no significant difference the details have been omitted. Subjective feelings of improvement usually bore no relation to the objective signs, but when there was any marked change in the degree of bleeding this had usually been noticed when the teeth were being cleaned.

The results of the estimations of ascorbic acid intake are summarized in Table III. The average daily intake of the airmen was about 26 mg. each during the autumn and 17 mg. during the early spring.

TABLE III.—Average Daily Intake of Ascorbic Acid by Airmen in their Messes at Three R.A.F. Stations. (Experiment 1)

Station	First Series of Tests (Autumn)		Second Series of Tests (Spring)	
	Test Period	Ascorbic Acid Intake (mg. per man daily)	Test Period	Ascorbic Acid Intake (mg. per man daily)
1 ..	8/10/41 to 15/10/41	25.5	3/3/42 to 9/3/42	19.0
2 ..	21/10/41 to 28/10/41	27.0	11/3/42 to 17/3/42	15.2
3 ..	5/11/41 to 12/11/41	24.8	19/3/42 to 25/3/42	16.3
Average :		25.8		16.8

The main cause of the difference between the ascorbic acid intake in the autumn and that in the spring was the ascorbic acid content of the potatoes. Potatoes contributed an average of about 11 mg. of ascorbic acid per man daily in the autumn, but only about 6 mg. in the spring. Potatoes were the most important source of ascorbic acid in the autumn, but in early spring greenstuffs provided the largest amount. Taking the two test periods together, potatoes and greenstuffs contributed about equal amounts, and between them supplied about three-quarters of the total ascorbic acid, the remainder being derived from root vegetables, the small amounts of fruit served, jam, and a number of less important sources.

Experiment 2

At another R.A.F. station 571 airmen were examined and treated for bleeding gums during April, 1942. The same methods were used as in experiment 1, except that special note was made of the presence of "sponginess" of the gums and that the dosage of ascorbic acid was slightly different; in this second experiment 150 mg. was administered daily for 20 days. The dietary history of the personnel of this station differed from that of the personnel of experiment 1, as the men had received Service rations for periods of only one to six weeks before the beginning of the experiment; previously they had lived in civilian billets and received civilian rations.

Results

The number with bleeding gums was 122—an incidence of 21.3%. The effects of the treatments of all cases of bleeding gums are given in Tables IV and V. Those with and without "sponginess" of the gums have been separated into two groups, and the effects of the two treatments have been worked out for each group. Six of those with bleeding gums failed to complete the experiment.

TABLE IV.—Effect of Treatment with Ascorbic Acid on Bleeding Gums. (Experiment 2)

Treatment	Improved		No Change		Deteriorated		Total
	No.	%	No.	%	No.	%	
Ascorbic acid	17	25	37	54	14	21	68
Dummy tablets	22	46	14	29	12	25	48

TABLE V.—Comparison of Effects of Treatment on Bleeding Gums with and without "Sponginess." (Experiment 2)

Treatment	"Sponginess" Present					"Sponginess" Absent				
	Improved		Deteriorated or no Change		Total	Improved		Deteriorated or no Change		Total
	No.	%	No.	%		No.	%	No.	%	
Ascorbic acid	9	33	18	67	27	18	44	23	56	41
Dummy tablets	8	47	9	53	17	23	74	8	26	31

Again the dummy tablets were rather more effective than the ascorbic acid, but the difference was not statistically significant. Improvement was shown by a significantly larger proportion of those showing no "sponginess" compared with those with "sponginess" present, but the better results were independent of the form of treatment.

Experiment 3

This experiment was carried out during April and May, 1942, at the same station as experiment 2, as part of a more general nutritional survey. Six hundred airmen, other than those taking part in experiment 2, were examined three times at intervals of three weeks, and at each examination the presence or absence of bleeding gums was noted. After the initial examination the men were divided into several groups, which were given different vitamin supplements and control tablets.

Results

The incidence of bleeding gums on initial examination was 20.3%—a figure similar to those found in the two previous experiments. The results of treatment with ascorbic acid and other vitamin supplements showed no significant difference. It therefore seems justifiable to consider the observations made on the 600 airmen as a whole.

There was almost exactly the same percentage showing bleeding gums at each examination, and the distribution of the degrees of bleeding was similar on each occasion (Table VI). On the other hand, only 57 of the 122 who showed bleeding at the initial examination did so at each of the two subsequent examinations.

TABLE VI.—Number with Bleeding Gums at Three Examinations of 600 Airmen at Intervals of Three Weeks. (Experiment 3)

	Degree of Bleeding*			Total	
	a	b	c	Number	% of 600
1st examination ..	53	50	19	122	20.3
2nd " ..	42	53	16	111	18.5
3rd " ..	52	53	13	118	19.7

* The degrees are defined in the account of experiment 1.

At the second examination the gums of 48 subjects (39% of the original 122) had stopped bleeding entirely—about the same percentage as showed improvements in experiments 1 and 2—but at the same time 37 of the rest of the 600 had started to bleed. Similarly, at the third examination 34 had stopped bleeding, while 41 had started. It is thus apparent that there is a considerable normal variation irrespective of treatment.

It was observed in this experiment, as in experiment 2, that those gums with "sponginess" tended to remain unchanged from one examination to the next. The majority of those who showed improvement during the test period had fairly firm, pale gums with only a little bleeding on massage. Neither type showed greater improvement with any particular treatment.

Discussion

In frank scurvy, swollen spongy bleeding gums are a characteristic sign. Most investigators who have treated bleeding gums with ascorbic acid have reported improvement in at least a portion of those affected, and have inferred that bleeding gums may be an early sign of ascorbic acid deficiency (Roff and Glazebrook, 1939; Campbell and Cook, 1941, 1942; Blockley and Baenziger, 1942; Stuhl, 1943; Kent, 1943).

There is no evidence from the early descriptions of scurvy (Hakluyt, 1600; Lind, 1753) that the gums began to bleed before the other signs and symptoms were seen; and during the investigations on experimental human scurvy by Crandon, Lund, and Dill (1940) the gums did not become swollen and haemorrhagic before other signs of scurvy appeared. Work by Burrill (1942) showed no relationship between low blood plasma vitamin C levels and the presence of gingivitis, and McNee and Reid (1942) found patients with sore bleeding gums to be no more "unsaturated" than others.

In the present experiments estimation of the intake of ascorbic acid showed that even in the autumn, when it might be expected to be high, the amount in the food served to the airmen on three R.A.F. stations was about 25 mg. daily, or slightly less than the amount considered desirable by the Health Organization of the League of Nations (30 mg. daily). The ascorbic acid intake during the spring was little more than half that recommended. Subsequent experiments on other stations have

confirmed that the average between these spring and autumn figures is representative of the average figures throughout the year on most R.A.F. stations. It might reasonably be expected, therefore, that if gingivitis were an early sign of ascorbic acid deficiency a noticeable proportion of those with bleeding gums would have shown improvement with ascorbic acid treatment.

In all three experiments the gums of those treated with ascorbic acid showed no greater improvement than those of the control groups, and the incidence of bleeding gums was remarkably constant (about 20%), although the subjects of experiments 2 and 3 had been living on civilian rations in billets until a short time before those experiments. The opinions of patients as to the efficacy of the treatments were found to bear no relation to the objective signs. Those gums which were not "spongy" tended to improve more than those with "sponginess," but the improvement was irrespective of the type of treatment.

Observation of 600 subjects in whom there was a 20.3% incidence of bleeding gums at the first examination showed that there is a large normal variation in the condition of gums, although the total incidence of bleeding gums remains very constant. This may well be the explanation of the apparent success in treatment with ascorbic acid which has been so often reported.

It seems justifiable to conclude that in Royal Air Force personnel in this country ascorbic acid is valueless in the treatment of bleeding gums, and the incidence of bleeding gums is not related to the ascorbic acid intake. This does not exclude the possibility that other subjects living under different dietary conditions might benefit from treatment with ascorbic acid.

Summary

The average amount of ascorbic acid present in the food served to airmen at three R.A.F. stations was 25.8 mg. per man daily during October and November, 1941, and 16.8 mg. during March, 1942.

On examination of 2,962 personnel, 588 (19.8%) were found to have some degree of bleeding of the gums, a similar incidence being found in the autumn and spring and at each of the four stations where the investigations were carried out.

No greater improvement in the gum conditions was obtained by treatment with ascorbic acid than with dummy control tablets.

Observation of 600 personnel over a six-weeks period showed that there was a large normal variation in the degree of bleeding of the gums, irrespective of treatment.

Those having "sponginess" as well as bleeding of the gums showed no greater improvement with ascorbic acid treatment than with dummy tablets, although there was less normal variation in their condition.

Patients' personal opinions as to the efficacy of treatment bore no relation to the objective signs.

We are indebted to Dr. Bradford Hill for the statistical analysis of the results, and wish to thank the officers, airmen, and other personnel at the stations where the experiments were carried out for their co-operation.

REFERENCES

- Blockley, C. H., and Baenziger, P. E. (1942). *Brit. dent. J.*, **73**, 57.
Burrill, D. Y. (1942). *J. dent. Res.*, **21**, 353.
Campbell, H. G., and Cook, R. P. (1941). *British Medical Journal*, **1**, 360.
— (1942). *Brit. dent. J.*, **72**, 213.
Crandon, J. H., Lund, C. C., and Dill, D. B. (1940). *New Engl. J. Med.*, **223**, 353.
Hakluyt, Richard (1600). *The Principal Navigations*.
Harris, L. J., and Oliver, M. (1942). *Biochem. J.*, **36**, 155.
Kent, B. S. (1943). *Lancet*, **1**, 642.
Lind, J. A. (1753). *A Treatise of the Scurvy*, Edinburgh.
McNee, G. Z. L., and Reid, J. (1942). *Lancet*, **2**, 538.
Roff, F. S., and Glazebrook, A. J. (1939). *J. roy. nav. med. Serv.*, **25**, 340.
Stuhl, F. (1943). *Lancet*, **1**, 640.

Several English cities are likely to benefit from Mr. William Eichholz's £100,000 legacy for the development of the Alfred Eichholz Memorial Clinic in London and of the blind professional masseur generally. The National Institute for the Blind, which administers the clinic, hopes to use some of the money to open similar clinics in provincial centres. When the Institute founded the Eichholz Clinic in 1931 Mr. Eichholz paid all the cost of its establishment and equipment as a memorial to his late cousin, Dr. Alfred Eichholz of the Board of Education. He became an enthusiastic admirer of the ability of its blind staff. All the new clinics in the Provinces will be staffed by blind physiotherapists trained at the Institute's school. This was enlarged last year to meet the training needs of war casualties in the Forces and among civilians.