Relapses and Recurrences

Two cases which demonstrated that immunity to one type did not give immunity to a different type are described below. One case occurred in this epidemic; the other occurred a few years ago, and is included here because it shows the same thing happening in a more dramatic way.

Case 1.—This patient, one of the Type 18 cases of pharyngitis complicated by pain and effusion into the joints, had suffered in the previous term from pharyngitis and infection of the remains of a tonsil due to Type 12.

Case 2.—A few years before two cases of scarlet fever occurred within four days of each other—one due to Type 13, the other to Type 1. The Type 13 case was mild in character, but had a definite scarlatiniform rash. After about seventeen days both cases were found to be negative to the Dick test and were allowed to convalesce together. Three days later the case due to Type 13 developed a second attack of a more severe character, with intense sore throat and extensive rash. This patient's second swab revealed a Type 1 infection.

In connexion with the above two cases the paragraph below (Stimson, 1936) is of interest:

"Following 1 to 5 per cent. of cases of scarlet fever (the mild ones or those treated with serum, or particularly those with persistently positive Dick tests) relapses may occur from three to six weeks after the onset of the original attack, or recurrences of the disease at a still later period. The new attacks may be milder or more severe than the original one, and, though auto-reinfection is considered possible, are usually due to a new infection. Convalescent cases with persistently positive Dick tests should accordingly be kept separate from other convalescing scarlet fever patients."

It will be observed that in both these cases the type was different. The Type 12 case contracted a Type 18 infection after a lapse of about two months, and the Type 13 case was infected with Type 1 after barely three weeks. An interesting point is that although the Dick test was negative in the case of Type 13 it was no guarantee against cross-infection by Type 1, which was a more virulent strain. It is also interesting to note that the reverse cross-infection did not take place.

Conclusions

It seems reasonable to conclude that the production of the rash in this epidemic depended on two factors at least: first, on the individual reaction of the patient to each type and not to any variation in the character of the specific type; and, secondly, on the rash-producing properties of each individual type, which appeared to be greater in the non-epidemic strains.

Many, if not all, types of haemolytic streptococcus seem to be capable, in certain circumstances, of producing the rash of scarlet fever.

The production of the rash had no effect on the course of the disease, and these cases were almost without complication. It was therefore regarded as of no special significance. Epidemic quality was shown to a high degree in one type only, and the virulence of this infection remained low. Other types presented the usual low degree of infectivity.

A highly specific immunity was apparently set up on two occasions for individual types, as shown by second attacks by dissimilar types at short intervals.

Scarlet fever is a misleading term which suggests a distinction that does not exist between different haemolytic streptococcal infections.

REFERENCE

Stimson, P. M. (1936). *Common Contagious Diseases*, p. 122, London.

USE OF PLASMA OR SERUM AS A SUBSTITUTE FOR WHOLE BLOOD

BY

C. H. BEST, M.D.Toronto, D.Sc.Lond., F.R.S.

Professor of Physiology, University of Toronto

AND

D. Y. SOLANDT, M.D.Toronto, Ph.D.Lond.

Associate Professor of Physiology, University of Toronto

(From the Departments of Physiology and Physiological Hygiene, University of Toronto)

In the issue of the *Journal* for May 18 (p. 799) we reported the results of the use of concentrated serum in the treatment of traumatic shock in experimental animals. A preliminary account of further work in this field was presented at the Annual Meeting of the American Human Serum Association a few weeks ago.

It is apparent that there is considerable uncertainty over the relative merits of serum and plasma as substitutes for whole blood in the clinic. In our more recent experimental work serum and plasma have been used interchangeably. The results are identical. These materials are employed in experimental and clinical work for two main purposes: first, to provide fluid; and, secondly, to provide the serum proteins, which by their osmotic pressure retain fluid in the blood stream or attract it from the tissues. In so far as these two properties are concerned there is no significant difference between serum and plasma. The amount of fibrinogen in the plasma has a relatively insignificant effect on the production of osmotic pressure. In experimental work sera which produce undesirable reactions are discarded. In our experience most samples of normal or concentrated dog serum produce no undesirable reaction.

The Question of Reactions

When a substitute for whole blood is used clinically, however, the question of reaction-producing substances is of great importance. It can now be stated that normal serum, concentrated serum, and serum reconstituted after drying in the frozen state have been used in the treatment of many clinical cases without the occurrence of any serious reactions. These points were established by the findings of Thalhimer in New York, Levinson in Chicago, Drury and his collaborators in England, and our clinical colleagues in Toronto. It is true, however, that some groups of investigators reported very troublesome reactions when dried serum was used. These investigators quite naturally prefer dried plasma, and if complete uniformity of product were immediately necessary plasma might well be the choice. In the present circumstances, however, some of those who are preparing dried or concentrated serum and are encountering no serious difficulties may feel that it is unnecessary to make the change. Serum has certain advantages from the viewpoint of preparation, but, on the other hand, plasma is more readily available if material is to be obtained from blood banks.

In the project for supplying blood substitutes for military use, conducted in these departments in collaboration with Drs. Ridout, Chute, and Magladery, concentrated serum has been prepared from some 3,000 blood donors enlisted by the Canadian Red Cross Society. Dried plasma and dried serum will also be made available until a final decision is reached regarding the type or types of blood substitutes best suited to the various conditions under which they may be used.

We wish again to emphasize the point that plasma and serum free from reaction-producing substances are physiologically and therapeutically identical and may be used interchangeably. It will be regrettable if discussion of the relative merits of these two materials should in any way impede their production or inhibit their use under appropriate conditions.

Clinical Memoranda

A Note on Urinary Symptoms associated with Change of Environment

In October, 1939, some 200 students of King's College, London, were evacuated to Glasgow. Sooner or later in the first six months of their stay members of the King's College teaching staff and the attendant staff found that they had to rise frequently at night to pass urine. As the majority were affected it was considered worth while to send a questionary round the students. The same questionary was circulated among the Glasgow students so that a basis of comparison would be available.

The number of questionaries returned by Glasgow (G.) was 187, by King's College (K.C.) 143; the average age in G. was 20 5/12 years, and in K.C. 21 1/12 years. The groups seem to be reasonably similar. 26.8 per cent. of K.C. had to get up during the night to pass urine, whereas only 6.4 per cent. of G. required to do so. The difference —20.4 per cent., with a standard error of 4.1 per cent.— is undoubtedly significant. Examination of the replies to questions concerning the intake of beer, milk, and tea showed that the frequency of micturition was related only to tea. The question in this case was: "Do you take tea or coffee after 9 p.m.?" The replies can be summarized as follows:

	% Getting up at Night		Difference	Standard Error
	G.	K.C.		
137 take tea late	5.8			
50 who do not	8.0		2.2	4.3
126 take tea late		29.4		
16 who do not		0	29.4	4.1

It seems reasonable to conclude that the cause of the rising at night among the K.C. students was the taking of tea late in the evening. But why should it make 29.4 per cent. of K.C. get up and only 5.8 per cent. of G.? This is the real problem, and one to which we have no solution.

One cause of getting up at night ought to be referred to first. In very cold weather there is a greater tendency to micturate frequently. The climate in London, though warmer in the summer, is often colder in the winter than that of Glasgow; so that it can hardly be said that King's College students had come north to a more rigorous climate. In any case the weather during the last winter was colder than either group was accustomed to; it should, therefore, have affected both groups equally.

The water of London contains a very large amount of calcium and other salts compared with that of Glasgow. This is, so far as we are aware, the only striking difference between the two environments.

Three possible but highly speculative explanations may be put forward: (1) Tea made from Glasgow water, or the brands of tea used there, may contain relatively more caffeine or other diuretic material. (2) Glasgow water, having a very low mineral content, may be less laxative, and therefore more water must be excreted by the kidney on going from London to Glasgow. (3) The glomerular membrane of persons accustomed to hard water may allow of a greater filtration of water when soft water is drunk.

Which, if any, of these possibilities is important it is difficult to ascertain, the more so as it has not been found possible to determine whether there is an increased urine production or merely increased frequency of micturition.

The results are put forward here in the hope that others may have observed a similar state of affairs as a result of a change of environment, and that they may be able to shed some light on the problem.

G. H. BELL, M.B., B.Sc.
R. J. S. MCDOWALL, M.D., D.Sc.
Institute of Physiology, University of Glasgow.

A Case of Gonococcal Arthritis

The followng case may be of interest. It illustrates relapse after sulphapyridine therapy, and the subsequent development of acute gonococcal arthritis and toxic conjunctivitis, which did not respond to further dosage of sulphapyridine but reacted successfully to vaccine therapy.

CASE REPORT

A man aged 31 was admitted to the venereal diseases wards on March 5, 1940, with pain and swelling of joints and discharge from the eyes of three days' duration. The history revealed that six weeks before admission he had contracted gonorrhoea, for which sulphapyridine, totalling 35 grammes, had been given.

On examination both shoulders, the right elbow, ankle, and index finger were tender, hyperaemic, swollen, and showed limitation of movement. The conjunctivae were congested, and there was a sero-purulent discharge. The temperature was 100–101° F. A mucoid urethral discharge was present, and the urine was hazy in the first glass and slightly hazy in the second glass. Urethral smears revealed many pus cells, Gram-positive and Gram-negative organisms, and extracellular diplococci. Smears from the conjunctival sacs showed many pus cells but no organisms. The Wassermann and Kahn reactions were negative, but the complement-fixation test was strongly positive. Blood culture for gonococci was negative.

Sulphapyridine, 3 grammes daily for one week, followed by 2 grammes daily, was given, but no urethral irrigations were done. The urine cleared after three days. Boric irrigations 1/60 and protargol guttae 15% were given for the eye condition, which cleared after four days. Antiphlogistine poultices, glycerin and belladonna dressings, and radiant heat were applied to the joints.

Six days after admission to hospital the patient developed suicidal tendencies. The knees and right wrist subsequently became affected. Fluctuating temperatures continued. Examination revealed a slightly enlarged prostate gland. A course of prostatic massage was given, and prostatic secretion showed many pus cells but no organisms. As the patient failed to progress the sulphapyridine was discontinued after eleven days. A differential blood count showed 4% myelocytes, 0.6% eosinophils, 73.4% polymorphs, and 18.8% lymphocytes.

A graduated course of eight gonococcal detoxicated vaccine injections, totalling 93,000 million bacteria over a period of forty days, was prescribed. Good progress was made, and the pyrexia and joint conditions finally settled. Early massage and remedial exercises were given to the affected joints. The complement-fixation test at the end of the course of vaccine therapy was negative. The patient was discharged, following tests of cure, nine weeks after admission to hospital, and in view of the manifold joint affections showed very little residual wasting or stiffness.

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A. STERN, M.B., Ch.B.,
Temporary Medical Officer in Charge V.D. Dept., East Suffolk and Ipswich Hospital.