index 1.05; the van den Bergh test was negative. The Price-Jones curve is now within normal limits, with a mean diameter of 7.014 μ .

Discussion

The striking feature of this case was the persistence of a reticulocytosis of over 30% for at least forty-eight hours in a patient who had received no treatment and the difficulty in diagnosis that this finding caused. Such a reticulocytosis, taken in conjunction with the apparently rapid onset and a history of other attacks and of jaundice, seemed to indicate haemolytic anaemia. Against this the presence of glossitis was one small point, but the negative findings of the special investigations and the subsequent findings of complete achlorhydria threw further doubt on the original diagnosis. Finally, the reticulocyte response to a test dose of liver extract associated with a rise of red cell content indicated an absence of haemopoietic factor. Such a response would be exceptional in any of the haemolytic types of anaemia. In fact, all the findings seem to indicate a diagnosis of pernicious anaemia in spite of such an unusual reticulocytosis.

Little mention is made in the literature regarding the number of reticulocytes present during the relapse phase. Sturgis and Isaacs (1938) state that spontaneous crises are sometimes seen with 7 to 8% of reticulocytes. Whitby and Britton (1939) note that occasionally pronounced reticulocytosis is present, but do not give figures. A rapid survey of other relevant publications failed to throw any light on the problem. The marked reticulocytosis in this case, following a submaximal dose of the intrinsic factor, should be due to the reaction of a young and comparatively healthy bone marrow, which has not yet become exhausted in the effort to keep up the supply of corpuscles from inadequate material. The same amount in an older person would, no doubt, only have given the reticulocytosis that is usually noted during remissions (7 to 10%).

It is interesting to speculate on the reason why this patient, accustomed to a regular and adequate diet, should suddenly relapse and with apparently equal rapidity begin to regenerate her red blood corpuscles. While we know that absence of the intrinsic factor leads to the development of pernicious anaemia, there is no definite knowledge as to the factors that lead to its disappearance. It is frequently suggested that the stomach in persons completely achlorhydric is especially disposed to gastritis, which will eventually lead to the suppression of the intrinsic factor. The history in this case supports such an idea. Dental sepsis, often put forward as an aetiological factor in earlier days, no doubt caused some degree of gastritis to initiate the first relapse. The last relapse, ushered in as it was by nausea, vomiting, epigastric pain, and jaundice, is very suggestive of gastritis with an associated "duodenitis." The relapses would then be due to a suppression of the intrinsic factor and the remissions be due to improvement in the gastritis, with a consequent return to a more normal diet and the reappearance of a small amount of intrinsic factor (cf. pernicious anaemia of pregnancy). The diagnosis of gastritis is not altogether unjustified, as for a short period after starting liver therapy the patient had nausea, vomiting, and epigastric discomfort which were relieved by a simple bismuth mixture, and also on one or two occasions since her discharge from hospital she has had short bouts of epigastric discomfort.

Summary

A case of pernicious anaemia in a young married woman aged 30 is reported. The patient presented the unusual feature of reticulocytosis of 33.4% in the absence of any previous treatment.

Administration of liver extract gave complete relief of symptoms and restored the blood picture to normal.

Good health has been maintained on a fortnightly dose of 2 c.cm. of anahaemin.

I wish to thank Prof. W. H. Wynn for permission to report this case and for his criticism and advice in preparing the manuscript; also Dr. T. W. Lloyd and Dr. A. L. Peeney for their detailed blood examinations and help in the diagnosis of this case.

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Medical Memoranda

Acquired Immunity to Blood Transfusion Reactions: A New Phenomenon

Reactions occurring during the transfusion of blood are for clinical purposes commonly divided into two main groups: haemolytic and non-haemolytic. The onset of the reactions is similar, but as a rule the former becomes progressively worse for hours or days, and often ends fatally; while the latter, alarming though it may appear, usually expends itself within an hour, leaving no observable evidence of permanent damage. It is with the latter type that this paper is concerned.

It has been our experience that the recipient, having suffered this reaction, is for some time immune to further reaction to the same blood. Hence the transfusion may with complete safety be resumed soon after subsidence of the response.

FIRST OBSERVATIONS

Our first observation of this kind was made on a male Hindu aged 18 to whom a transfusion was given following amputation of a leg after a crush injury. Fifty c.cm. or so of 5% glucose solution alone was first used, and then the blood was started at the rate of about 50 drops a minute. When 150 c.cm. of blood had run in, the patient developed a severe chill, the pulse became rapid and thready, and there was marked pallor. The transfusion was discontinued promptly, the foot of the bed was elevated on shock-blocks, and hot-water bags and blankets were applied. One c.cm. of adrenaline was injected intramuscularly. The reaction, which was most violent, ran its course and subsided completely within an hour. A careful check was made of the blood, but no error was found either in the grouping or in the cross-agglutination tests. Also, the citrate solution had to be considered, although our intravenous solutions had produced no such symptoms in some hundreds of administrations. Accordingly, 50 c.cm. of the glucose-saline solution was given by vein to each of three otherwise healthy fracture patients, and 20 c.cm. of 3.8% citrate solution was injected intravenously in two other afebrile individuals. None of these subjects developed chills or fever, nor was there any significant variation in the pulse rate as a result of the injections. The reaction observed in our patient was therefore purely from the blood, and was characteristic of the non-haemolytic type, being in general essentially the same as the others of this type which we had seen here and elsewhere.

THE HYPOTHESIS OF ANAPHYLAXIS

Because of its typical character this case was chosen to test a hypothesis which had occurred to us: that the reaction is anaphylactic in nature. If this were an anaphylactic response the patient had very likely become desensitized, and it should be possible, therefore, to continue the transfusion without further response. Accordingly, some five hours after the patient's recovery the transfusion was resumed, the blood being run into the vein very slowly, while careful watch was kept for any untoward symptoms. The transfusion was completed without the slightest reaction.

With this as a precedent, in every other case of transfusion shock since then—twelve in all—we have merely interrupted the transfusion long enough to permit complete recovery from the reaction and to check the cross-matching. In all cases the readministration of blood to a total of about 500 c.cm. proceeded without event.

The following table summarizes the essential details of the cases:

Case	Age	Sex	Group	Amount of Blood before Reaction	Interval between Transfusion
				c.cm.	hours
1	18	M	B (III)	150	5½
2	55	M	B	25	3½
3	18	M	B	70	15
4	28	M	B	70	3
5	27	M	B	400	5
6	22	M	B	350	21
7	17	M	B	200	5½
8	10	M	B	120	5½
9	28	M	B	150	22
10	35	M	B	150	7½
11	3½	M	O (IV)	70	22
12	37	M	B	250	8

CONCLUSIONS

We can find in the literature no satisfactory explanation for the non-haemolytic reactions—that is, where, as here, fresh blood is used. Impurities in the rubber tubing, particles of old blood left in the needle, the use of blood from a donor in the post-prandial period, are among some of the explanations given. Such reasons seem inadequate, for we do not observe reactions from saline and glucose injections when the same apparatus as that used for blood transfusions is employed, and our blood donors were all drawn from the local prison, where the rule prohibiting the taking of food before the giving of blood is strictly enforced.

The symptoms of this type of reaction to blood transfusion are certainly very similar to those of anaphylactic shock in general. And our finding that soon after recovery the transfusion could be resumed without response suggests to us that these reactions are indeed anaphylactic in nature. Accordingly, *the reaction is to be considered a process of desensitization*. We do not venture to guess the nature of the antigenic substance.

Of the twelve cases reported, eleven belonged to Group B (III), and all the patients were males. (Our patients are limited to this sex entirely.) The predominance of Group B in the transfusion reactions here seems to be only a coincidence. Five Group B patients not mentioned had no reaction at all to transfusion. There have been reactions of this kind in only two cases belonging to Group O (IV), one of which is reported here (Case 11). In the other case a direct transfusion was given and was not repeated, so no mention of it is made above.

The practical importance of this phenomenon is self-evident. Blood which has caused such reactions need not be discarded, our experience showing that after checking the cross-agglutination the transfusion may be resumed safely soon after the recipient has recovered from the reaction.

We are indebted to Dr. C. M. Van Allen, chief surgeon of the Bikaner State Hospital, for his guidance and kind criticism.

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M. J. Reuter and R. Nomland (*Wisconsin med. J.*, 1941, 40, 196), who record three personal cases in women aged 52, 56, and 72, state that cutaneous metastatic cancer may be associated with inflammatory signs. The clinical features are closely allied to the inflammation of erysipelas, but there is no chill, fever, prostration, or leucocytosis. The diagnosis is difficult and a biopsy is usually required. As inflammatory metastatic carcinoma secondary to primary cancer of the breast is common, any inflammatory lesion of the skin of or about the breast which does not subside in two or three weeks warrants a biopsy for diagnosis. Histologically the inflammatory signs are due to extensive lymphatic blockage by cancer cells which causes oedema.

Reviews

PLANNING FOR HEALTH

National Health Services and Preventive Methods for Improving National Health. By Dame Janet Campbell, M.D., and H. M. Vernon, M.D. (Pp. 46. 9d.) London: British Association for Labour Legislation.

In his introduction to this pamphlet of the British Association for Labour Legislation its chairman, Mr. H. Graham White, M.P., says: "We must prepare for a real extension of national health insurance (including dependants of the insured), a reorganization of our hospital system, and a change in the position of the medical profession in the community." As to the first two of these aims there is a considerable measure of agreement; what the third means is not at all clear. In the first of his *Collected Addresses* the late Wilfred Trotter, comparing the profession of medicine with those of the Church and the Law, describes it as having, unlike them, "had no direct influence in the work of government. It has therefore had to submit to its duties being piled up as occasion arose with no resource for securing a due compensation of privilege and immunity. . . . The result is that it finds itself of all professions the least in command of social prestige, the least privileged, the most exposed, and the hardest worked. I do not think it is to be deplored. It has put medicine in the very small class of professions in which it is possible for men and women to pursue the dying ideal that an occupation for adults should allow of intellectual freedom, should give character as much chance as cleverness, and should be subject to the tonic of difficulty and the spice of danger." A profession of which this could be said by one of the wisest of its members may well be watchful of proposals ostensibly intended to change its position in the community; and his statement affords criteria by which the desirability of any profound changes may well be tested.

The pamphlet under review is definitely designed to promote some such changes. It is not a joint production of its authors in the ordinary sense, but consists of two independent essays—one by Dame Janet Campbell on "National Health Services," the other by Dr. H. M. Vernon on "Preventive Methods for Improving National Health." The latter is a useful contribution, setting out clearly a number of facts relative to social and industrial health, and showing that "there are at our disposal many simple preventive measures, not dependent on medical aid, which, if adopted, will cause a considerable rise in the average standard of health and physique in the nation." The facts will probably be familiar to a majority of readers, but it is to be hoped that there will be others to whom they will afford a fresh stimulus to action. Two opinions expressed are particularly noteworthy: that "occupational environment is not nearly so important a factor in controlling the health of the nation as social environment"; and that "of all the social conditions met with in the home maternal care comes next in importance to nutrition and counts for more than the standard of the housing." If to these be added a third—that every responsible individual can largely determine his own environment—we have some valuable guides towards reform.

Dame Janet Campbell's essay has a more direct bearing upon the position of the medical profession. Here again the facts of the situation are set out clearly, though they are now quite familiar to most readers. So are the defects of the present medical provision. But in this connexion the author is not quite accurate or fair. She underestimates both the curative and preventive work of the general practitioner, though admitting his potentialities for good; and it