TRANSFUSION IN PELLAGRA

A REVIEW OF TWENTY CASES *

H. P. COLE, M.D.

MOBILE, ALA.

August 4, 1908, I employed the first transfusion in the terminal stages of pellagra. Encouraged by the immediate improvement and rapid recovery in this patient, in collaboration with Dr. Gilman J. Winthrop, I have since transfused nineteen additional patients in the terminal stages of the disease.

Whereas we are unable to draw positive conclusions from this number of cases, we believe that certain valuable deductions may be derived from the statistics which they present. We have endeavored to preserve a spirit of scepticism and unbiased judgment throughout our investigations, and to draw accurate conclusions from the data presented.

Transfusion has been resorted to only in cases in the last stages of pellagra, or steadily retrograding under prolonged and careful treatment by approved therapeutic measures. To illustrate the type of cases in which transfusion has been employed, it is sufficient to state that two patients were moribund at the time of operation, and one patient died on the railway train twenty minutes before arriving at Mobile for transfusion.

	Cases
Transfused	20
Females, aged 22-53.....	16
Males, aged 3-42.....	4

We note that the females (16, or 80 per cent.) were four times as numerous as the males (4, or 20 per cent.).

	Cases
Recoveries (60 per cent.).....	12
Deaths (40 per cent.).....	8
Relapse (8.3 per cent.).....	1

This relapse occurred two years after recovery in an institutional patient exposed to reinfection.

	Cases
Temporary improvement followed by death.....	2
No improvement following transfusion.....	6
Complications incompatible with recovery.....	2

Patient 1, a male, aged 42, whose case was complicated with tuberculous peritonitis, showed temporary improvement for several days, but died one month after the operation.

Patient 2, a male, aged 3, showed distinct improvement following transfusion, but died eight days later from intestinal perforation.

	Cases
Complications presenting insufficient flow of blood, followed by death.....	2

In Case 1 the only available donor permitted insufficient transfusion through a severe degree of arteriosclerosis. In Case 2 inadequate operative surroundings and a neurotic 14-year-old boy as the only available donor permitted insufficient transfusion.

	Cases
Patients moribund at operation followed by death..	2

It will be noted that four of the eight cases in which death resulted might well be excluded, for the following reasons: Two patients received an inadequate amount of blood at transfusion and two were moribund at the time of operation. Excluding these four cases, the mortality rate would be 25 per cent. as compared with 40 per cent. in the entire series. Considering the grave mortality rate in the type of patients on whom transfusion was performed, we can but feel that our mortality rate of 40 per cent. in the entire twenty cases compares most favorably with the mortality (80 to 90 per cent.) in this type of cases treated by other therapeutic procedures. We have been unable to observe that transfusion was a direct factor of death in any of the cases; the deaths followed in periods of from three hours to one month after operation. One patient mani-

fest symptoms of cocaineism, necessitating a termination of transfusion at the end of fifteen minutes. This patient, however, made an excellent recovery from pellagra. Neither hemolysis nor agglutination, thrombosis nor embolism, have been observed in any of the cases.

Of the recovered patients (seventeen) there were: females, eleven (68.8 per cent), and males, one (25 per cent). We note a far greater percentage of recovery in the females. All the recovered patients presented distinct and severe lesions of pellagra; there were marked emaciation, asthenia, anemia, reflex excitability, and in many cases grave mental changes. Severe pellagra erythema, stomatitis, and diarrhea were present in a majority of the cases. Within a few days after transfusion there was either alleviation or disappearance of all the symptoms of pellagra; there was a rapid disappearance of the pellagra erythema, stomatitis and diarrhea, and also a gradual alleviation of the mental and nervous symptoms. In several cases there was an astonishing improvement in the patient's mental condition, shortly following operation. In all cases there was rapid increase in the patient's hemoglobin index, a rapid return of body strength, a return of digestive faculties, and an increase of body weight. All the recovered patients gained from three to eight and one-half pounds in the first week following transfusion; one patient gaining thirty-four pounds within eleven weeks. All the recovered patients have returned to a normal condition within from one to four months after operation; several are in better physical condition than they have presented for years. The patient relapsing two years after transfusion was living in an institution and was constantly exposed to pellagra, and it is fair to assume that this case may be considered a re-infection, rather than a relapse.

It is but just to state that all approved therapeutic procedures were employed in the recovered cases, both previous to and following the operation. As these procedures were employed without beneficial effect previous to the operation, it is fair to assume that they were unimportant factors in the recoveries after transfusion.

We have been unable to ascertain a constant clinical sign that would indicate a certainty of recovery following transfusion. A moribund state of the patient and complication of pellagra with pathologic conditions contra-indicate the employment of transfusion. The necessity of resorting to transfusion can be ascertained only on the appearance of positive signs of retrogression under approved institutional and constitutional therapeutic agents.

A majority of the patients referred for transfusion have recovered through hygienic, supportive treatment, not necessitating the employment of transfusion.

Transfusion, itself a delicate procedure, should be attempted only by those experienced in the technic, with a full knowledge of the dangers of the operation, and in adequate surroundings for its performance, and with the proper post operation treatment.

In these transfusions we have endeavored to employ donors who have lived in the same environment as the recipients, assuming that such donors who have not contracted pellagra possess a certain degree of immunity.

Transfusion was resorted to from donors who had recovered from pellagra in three cases; recovery occurred in one case (33 1/3 per cent.). This case relapsed two years following transfusion.

Transfusion was made from donors who had never had pellagra in seventeen cases; recovery ensued in eleven cases (64.7 per cent.).

* Read before the Southern Surgical and Gynecological Association, Nashville, Tenn., Dec. 15, 1910.

We may assume that there is, at least, no preference of a donor who has had pellagra over a donor who has never had pellagra.

Transfusion was resorted to from donors who were relatives of the patient, but who had never had pellagra, in seven cases. Recovery occurred in three cases (42.8 per cent.).

Transfusion was made from donors who were not relatives and who had never had pellagra in ten cases; recovery in eight cases (80 per cent.).

Here we may assume, at least, that there is no ground for preference of the use of a relative over the use of a non-relative.

We are unable to state from the statistics available that there is any immune principle transferred by transfusion. It is probable that any beneficial results obtained may be attributed to the relief of the existing anemia, permitting the patient's organism to approach its normal functional activities and thus to combat the progress of the disease.

CONCLUSIONS

In transfusion in twenty cases of pellagra, we have found no ill effect resulting to the patients directly from the operation. We may safely resort to transfusion in the severe type of case, steadily retreating under approved therapeutic procedures.

We have noted no advantage in the employment of a donor who has recovered from pellagra as compared with the donor who has never had pellagra.

There is apparently no advantage in the use of a relative for a donor as compared to the use of a non-relative.

The recoveries (60 per cent.) following transfusion in the grave type of cases, compares most favorably with the recoveries (10 to 20 per cent.) in the same type of cases in which other therapeutic measures are employed.

The employment of transfusion in the terminal stages of pellagra must be undertaken with a full knowledge of the difficulties and dangers of the operation. Without careful selection of the cases and unprejudiced conclusions, this procedure will fall into an undeserved ill repute.

202 Conti Street.

EXPERIMENTAL POLIOMYELITIS IN MONKEYS

NINTH NOTE: IMMUNITY PRINCIPLES; EFFECTS OF HEXAMETHYLENAMIN (UROTROPIN); EARLY DIAGNOSIS; VIRUS-CARRIERS*

SIMON FLEXNER, M.D.

AND

PAUL F. CLARK, Ph.D.

NEW YORK

In previous publications,¹ we have shown that an attack of experimental poliomyelitis protects against reinfection with the virus of the disease, and that the blood of monkeys and of persons who have recovered from the acute effects of epidemic poliomyelitis contains neutralizing principles for the virus on which their immunity must be considered to depend. The immunity principles have been shown to reside in the blood-serum and are, therefore, probably of the nature of antibodies. The course of epidemic poliomyelitis in its acute stage

is not known to be influenced by any form of medication, whence it follows that it is a self-limiting process, as are so many of the infections; and at present we must view this condition of self-limitation as being determined by the elaboration within the body, under the influence of the virus of the disease, of substances of the nature of antibodies, the so-called immunity principles.

IMMUNITY PRINCIPLES IN ABORTIVE CASES

What have come to be designated abortive cases of epidemic poliomyelitis are now playing an important part in the discussion of the mode of transmission of the disease. Our knowledge of this class of cases is still very imperfect, and doubt even exists of their occurrence at all. Until greater refinement and accuracy are introduced into diagnosis, this doubt must continue to arise. It is desirable, therefore, to present evidence that bears on the occurrence of this type of the disease.

It is possible by means of neutralization tests to determine in a given instance whether an attack of poliomyelitis was or was not suffered, and this independently of the circumstance whether or not paralysis was present. The test is made by mixing the blood-serum with the filtered virus, incubating the mixture at 37 C. for a few hours, and injecting it into a monkey. Normal human serum has no power to neutralize the virus, while the serum from recovered cases of poliomyelitis possesses this power. Dr. Richard Stein, of New York, kindly supplied us with the blood taken from a patient suspected of having passed through such an abortive attack, in which the neutralizing immunity principles were demonstrated. This method does not provide a means of diagnosis, but it is of value in establishing the occurrence of abortive cases of epidemic poliomyelitis.

DISTRIBUTION OF IMMUNITY PRINCIPLES

Up to the present, the immunity principles have been established to exist in the blood of men and monkeys who have passed through the acute stage of the disease. We have already emphasized the lesions of the leptomeninges that result from infection with the virus of poliomyelitis and the changes, corresponding to them, that take place in the cerebrospinal fluid. It is of interest to ascertain whether or not the immunity principles exist in the cerebrospinal fluid, whether or not they may originate there, and, hence, whether or not the control of the lesions of the meninges and the nervous tissues is in any degree dependent on such a local production. We are enabled to determine these points by reason of the circumstance that the secretion of antibodies from the blood into the subdural space and the cerebrospinal fluid takes place, under normal conditions, practically not at all. Should they be found there, they must either have arisen locally, or have been secreted there from the blood because of abnormalities that increase the permeability of the blood-vessels.

We have examined a number of specimens of the cerebrospinal fluid obtained from patients at various periods after the disappearance of the acute stages of poliomyelitis, but at times when paralysis of one or more extremities still persisted. In some instances, the blood and cerebrospinal fluid were taken simultaneously and both tested for neutralizing power. The results are instructive. During the first one or two months, the immunity principles may exist both in the blood and in the cerebrospinal fluid, but, even at this early period, the principles demonstrated to be present in the blood have not always been detected in the fluid. At later

* From the Laboratories of the Rockefeller Institute for Medical Research.

1. The previous work is summarized and discussed by one of us (Flexner) in *THE JOURNAL A. M. A.*, Sept. 24, 1910, p. 1105.