TRANSFUSION IN THE DESPERATE PNEUMONIAS COMPLICATING INFLUENZA

PRELIMINARY REPORT ON THE SUCCESSFUL USE OF TOTAL IMMUNE CITRATED BLOOD

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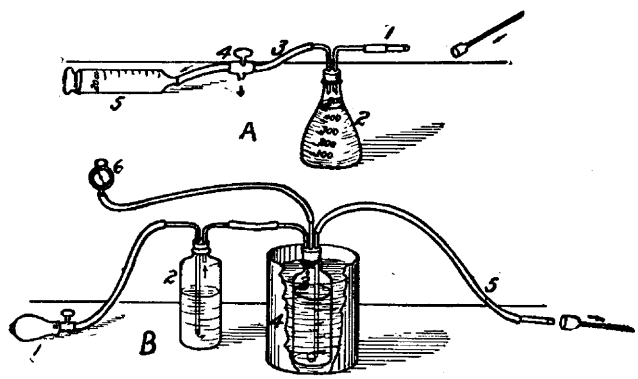
The problems presented to the medical personnel supervising the care and treatment of the selected seriously ill civilian employees of the Mare Island Navy Yard were many. These cases represent a small percentage of the total illness of the community, since many of those not seriously attacked went to their homes and did not report to the emergency hospital; and our allotment was principally composed of neglected patients who did not do well with home treatment together with a small proportion of men who had no home or who were taken so suddenly and severely ill that they were unable to get home. The general status of the large majority of patients, with a resultant failure of accepted care and treatment, was most discouraging. The average patient was of the lower type as regards mentality, morality and personal hygiene, and in the main was physically deficient. A large proportion of the patients had been ill and without even simple care for from two to eight days before admission. Fifty per cent. of the pneumonia patients had been ill for four or more days and presented a uniformly low white blood count, from 2,000 to 4,000, extreme toxic cardiopathies with vasomotor palsy, cyanosis, depressed respiratory activity, no localization of the pneumonic process, delirium and tremendous acidosis, with greatly deficient or absent urinary chlorids—conditions that remained uncorrected by the usual care and the desperate efforts of alkalinization by intravenous, subcutaneous and colonic routes, and the stimulation of leukocytosis by the intravenous injection of magnesium sulphate and other supportive measures.



Apparatus for transfusion: *A*, receiving apparatus: 1, receiving tube with very short rubber connection (all paraffined); 2, 500 c.c. Ehrlenmeyer flask (paraffined); 3, suction tube for partially exhausting air from flask; 4, two-way stopcock; 5, 20 c.c. syringe; *B*, apparatus for giving blood to recipient: 1, bulb and valve (from sphygmomanometer); 2, wash bottle (containing mercuric chlorid, 1:500); 3, delivery bottle for citrated blood; 4, vessel containing water at temperature of 43 C.; 5, delivery tube; 6, pressure gage (to measure rate of flow and pressure).

Previous work and excellent results by others with the use of serum from convalescent influenzal pneumonia patients suggested its use to us. However, the difficulty of keeping serum properly, and the uncertainty of testing the old serum as regards compatibility, made it inconvenient to our circumstance. The value of immune serum having been established, no objection to the use of total blood could be seen. The added advantages theoretically to be gained by the use of total blood are:

1. The increased coagulating power caused by the introduction of blood platelets. It was found that in advanced cases the coagulability of the blood was markedly decreased, and was undoubtedly an important factor in allowing this type of pneumonia to progress to a fatal termination.

2. The fact that additional immune bodies are contained in the leukocytes, as first advanced by Metchnikoff and later shown by practical application. Cases progressing to a fatal termination have shown an increasing leukopenia down to 2,000 and lower. We therefore decided to try transfusion of total blood of persons convalescent from two days to six weeks (height of immune content of blood) from pneumonia complicating influenza.

The simplicity, the safety and the brilliant results have been most encouraging.[1] In thirteen cases of the desperate type described, the following brief observations have been noted: Four patients, two of whom had been ill for more than ten days and were at the time moribund, died. Of the remaining nine, all showed definite localization of the pneumonic process with progressively increasing leukocytosis and resolution, rapid clearing of cerebrospinal, respiratory, cardiovascular and renal disturbances, diminished acidosis, and normal temperatures for from twenty-four to seventy-six hours.

We are using from 200 to 400 c.c. of blood at a dose and repeating in from twelve to twenty-four hours if marked results are not obtained. With improved technic we are using it early in the course.

TECHNIC

The usual delirium of the patient, the absence of a surgically clean place for work, and the occasional delay suggested the citrate method as the more practical. The work in emergency wards and tents demanded special care as regards avoidance of infection. This technic has made the procedure safe and simple:

The donors are persons who have had a definite influenza accompanied by a definite pneumonia; the time of selection is from three days to six weeks of convalescence (height of immune body content). Donors are selected from our own patients and from those in surrounding districts. Donors must be subjected to the Wassermann test and clinical examination for syphilis. The donor's and the recipient's blood is tested for isohemolysins and iso-agglutinins.[2] We have found several incompatibilities. All preliminary tests having been made, the blood is taken with a paraffined receiving apparatus from the veins about the anticubital fossa with the usual surgical technic. The apparatus shown in the accompanying illustration allows no exposure of blood to infected

1. Detailed case reports and statistics are to follow in a future report.

2. Compare Kolmer, J. A.: Practical Text-Book of Infection. Immunity and Specific Therapy, with Special Reference to Immunologic Technic, Ed. 2, Philadelphia, W. B. Saunders Company, 1918.

air. The paraffined receiving flask minimizes the danger of coagulation. A 1 or 2 per cent. solution of sodium citrate in physiologic sodium chlorid solution is used.

The blood is transferred to the closed apparatus for delivering the blood to the recipient. A vein is chosen on the arm and the usual technic followed. The pressure gage is of extreme value to control rate and pressure of flow. The citrated blood is kept at proper temperature by a water bath, as shown in the illustration. Exclusive of laboratory tests, it takes approximately forty-five minutes to perform a complete transfusion, taking and giving.

ERYTHEMA MULTIFORME

A CLINICAL AND LABORATORY STUDY OF FORTY-SEVEN CASES

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A definite cause may be ascribed to certain cases of the clinical entity that we call erythema multiforme. The rôle of certain drugs, antitoxins and serums has long been recognized. Cases developing following the ingestion of stale meat, fish, oysters, etc., have been seen sufficiently often to warrant the assumption of direct causation, theoretically being due to the absorption of products of decomposition, bacteria or their products. It would seem that a few reported cases have been due to uterine irritation, a neurosis, etc. Parker and Hazen studied a group of cases occurring in the course of such diseases as typhoid and diphtheria, and were inclined to favor a toxic theory. The theory of absorption of intestinal toxins has long been prominent in the literature. Lain, Chipman and others have recently associated erythema multiforme with focal infections about the teeth, tonsils and accessory air sinuses. Mahon, Vidal and others, from a purely theoretical standpoint, believed a number of cases to be of bacterial origin. Corlett reported a case following a gunshot wound in which a streptococcus was found. Epidemics have been reported by Gaul, Herxheimer, Duhring and others.

I wish to report certain phases of an endemic form of erythema multiforme at Camp Travis, Texas, during the months of February and March, 1918. In all, forty-seven cases were seen, the cutaneous pictures of which varied through all grades with mild erythematous lesions to those showing all manner of individual lesions or a preponderance of vesicular and bullous lesions on skin and mucous membranes. In most of the cases with extensive skin involvement the onset of the disease was heralded by a mild chill or chilly sensations, followed by a febrile reaction that continued over a period of from fourteen to twenty-one days. The temperature curve was irregular but showed a tendency to an evening rise and a morning remission, all ending by lysis. Many of the patients observed had a rise of temperature for two or three days only, the highest recorded temperature being about 100. Several had no abnormal temperature. There were purpuric lesions in approximately 10 per cent. of the cases. Only two gave a history of an attack prior to enlistment, while ten of the forty-seven returned to the hospital with a second attack, one with a third. We early began to investigate every patient that was admitted to the hospital. Careful physical examinations failed to reveal anything noteworthy except that nearly all had hypertrophied and mildly inflamed tonsils. Several had open wounds, the result of recent vaccinations.

LABORATORY FINDINGS

All the urines were practically normal. A few showed a transient albuminuria.

The feces were negative.

In the red cells of the blood there was no change; in the white cells, a moderate leukocytosis, rarely over 11,000.

The hemoglobin was normal.

The differential count showed that the leukocytosis was due to an increase in the polymorphonuclears.

Blood cultures, taken at different times during the course of the disease, were all negative, as were cultures from vesicular and bullous lesions.

Throat swabs showed all the organisms usually found.

Cultures from deep tonsillar crypts showed in thirty cases a hemolytic streptococcus as the predominating organism. Superficial swabs were negative for this organism in the same cases. In nine cases a pyogenic streptococcus was found. In two cases in which the throat and tonsils were negative, the hemolytic streptococcus was isolated from recent vaccination wounds.

At the same time that the cases under consideration were being studied, there was in Camp Travis an epidemic of streptococcic respiratory infections, in the greater number of which the *Streptococcus hemolyticus* was recovered.

Repeated attempts to obtain pure cultures of the *Streptococcus hemolyticus* on defibrinated blood agar failed, and no growth was obtained on plain plus reaction agar.

Serum from infected individuals did not agglutinate the organism.

The opsonic index gave us no information.

It was noted that with the clearing of the exanthem we were unable to obtain the streptococcus with the same facility from the tonsil crypts, but that in those cases with second attacks the organism could again be found. Believing that this organism was possibly the cause of this particular group of cases, acting by elaboration of toxins from a focus in the tonsils, all patients in whom the streptococcus was found were referred for tonsillectomy as soon as the exanthem, temperature, etc., had subsided. In none of these cases was there a recurrence.

CONCLUSIONS

The presence of an endemic form of erythema multiforme, presenting, in addition to the cutaneous manifestations, certain phenomena common to all the acute infectious diseases, makes plausible an infectious theory of etiology. The presence of a hemolytic streptococcus deep in moderately inflamed tonsils, coupled with what scant knowledge we have of the pathogenicity of this particular organism, lends color to the theory. Absence of organisms in the blood stream and skin lesions would seem to indicate the action of toxins generated in a focus of infection rather than a localization of organisms in the skin. The results obtained by tonsillectomy in streptococcus carriers is not conclusive on account of the small number of cases, but it is at least suggestive.

Symptomatic Treatment.—This form of therapy—often disdainfully characterized as "merely symptomatic"—represents, in my view, the very acme of the medical art.—B. Fantus, M.D.