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## SOME COMPLICATIONS OF TRANSFUSION, ENDOCRINE THERAPY AND OXYGEN ADMINISTRATION

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### COMPLICATIONS OF TRANSFUSION

**I**N NO FIELD has medical opinion reversed itself so completely as in that of blood letting versus blood replacement.

A short time ago while visiting the reconstructed colonial town of Williamsburg, one saw the tools of the old barber surgeons. A copy of a manuscript on the wall stated that George Washington was bled on several occasions during his terminal illness, without seeming benefit.

In this paper, I would like to emphasize some of the ills of blood replacement rather than withdrawal.

Due to the impetus given by life-saving

transfusions during the war, blood transfusion has become universally available in all parts of the country. This has not proved an unmixed blessing, however, for the dangers associated with blood transfusion have also been greatly multiplied thereby.

The factors which give rise to these dangers are as follows: 1) those associated with donor; 2) those associated with stored blood; 3) those associated with act of transfusion; 4) those associated with recipient.

#### 1. Factors Associated with Donor

1. Homologous serum jaundice.
2. Allergic reactions.

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3. Transmission of tropical and other infections.

The danger of transmitting the virus which causes jaundice is greater than may be realized, and is related to the incidence of the carrier state in the population. The incidence in the general population has been estimated as from 0.1% to 0.5%<sup>1</sup> to 0.35%.<sup>2</sup> In one Army Camp in the United States it was found to be as high as 5%.<sup>3,4</sup>

As one might expect the danger of transmission is greatest the more recently the donor has had jaundice, but some work in Germany suggests that even 6 years or more after having hepatitis, donors may transmit the virus to 3.6% of recipients. However, supposedly normal donors gave blood resulting in the same incidence of jaundice in the recipient.

Such figures indicate that a history of jaundice is an indication for rejection of a potential donor. The reported incidence of jaundice after blood transfusion may not seem excessive (0.8%, Liverpool; 0.5%, United States) if one were sure that each transfusion was life-saving or truly needed. However, "tonic" transfusions for mild anemias or other indefinite reasons undoubtedly contributes a significant number of cases of hepatitis because of the multitude of such unnecessary transfusions given.

Far more important, however, are the dangers from giving transfusions of plasma or serum. Most commercial supplies represent pooled plasma from many donors. It has been shown that a single infected donor may contaminate the whole pool, and the larger the pool of donors, the greater is the chance of such contamination.

The English<sup>2</sup> quote an incidence of jaundice in recipients of pooled plasma of 11.9%. Figures as high as 20% are quoted in the United States.<sup>3</sup>

It is important to stress the minute amounts of infected plasma which may give rise to infection in the donors. The small amount of plasma which may adhere to a hypodermic needle after giving an injection, may, if injected into a second individual, transmit the virus.

Thus, in all inoculation procedures separate or individual sterilized syringes and needles should be used for each patient. It is also important to have individual stilettes for drawing blood for hematologic examinations.

In one Army camp where a single syringe technique was in use for the administration of tetanus toxoid, 20% of the inoculated group developed jaundice.

## 2. Factors Associated with Stored Blood

1. Contamination (bacteria-pyrogens).
2. Free hemoglobin.
3. Incompatibility (technical and organizational).
4. Large transfusions of universal donor blood.

Contamination of stored blood is a hazard that can only be guarded against by constant vigilance.

Free hemoglobin may be excessive in blood which is stored too long or where warming has been too great or too rapid.

In this group of causes, the greatest dangers arise from technical errors by inexperienced technicians or by poor organization within an institution, whereby the blood consigned to one patient gets administered to another, in error.

## 3. Factors Associated with Transfusion<sup>5</sup>

1. Excess blood or too rapid administration.
2. Air embolism.
3. Thrombophlebitis.
4. Excess citrate.

Excess blood in certain pathologic states may lead to heart failure. This may also be brought about by too rapid administration which does not permit normal circulatory adjustments.

Where large amounts of stored blood are used, as in exchange transfusions, tetany may result from the excess citrate present. This must be guarded against by the administration during the procedure of calcium gluconate.

The other factors require no amplification.

#### 4. Factors Associated with Recipient

1. Antibodies.
2. Cardiac and renal insufficiency.
3. Anemia.
4. Miscellaneous: reagens, sudden unexplained death.

In cardiac and renal insufficiency, transfusions are dangerous because of the increased blood volume and hazard of precipitating pulmonary edema. The same may be true in simple anemia, a condition much more safely treated with iron.

Previous transfusions or other sensitizing procedures may make transfusions even with homologous types very hazardous. Only the most careful cross-matching and testing, e.g., indirect Coombs' test, should be employed in such cases.

Of particular interest to the pediatrician is the fact that a transfusion to a female child or adult may develop antibodies in that individual which may bring about the death of her children in the future from erythroblastosis.

Chown<sup>6</sup> has estimated that at least half of all transfusions given are unnecessary and that probably only 1% are actually life-saving; as he so aptly puts it in referring to Rh sensitization of women by transfusion: "Death holds his cards close to his belly and he plays them slowly; sometimes very slowly. So you forget. Or you don't know. You are no longer in the game, when Death plays his trump."

#### COMPLICATIONS OF ENDOCRINE THERAPY

Endocrinology, especially endocrine therapy, has been and is still today, one of those fields where the physician has often practiced more art than science. Perhaps this is not surprising in that the effects of endocrine action on bodily configuration has long been a preoccupation of the artist.

Time does not permit one to deal with the many facets of this problem, so I shall restrict my remarks largely to some of the problems associated with adrenal steroid therapy.

Good<sup>7</sup> has reviewed this subject recently and finds in a hospital series that 10% of patients receiving adrenal steroid therapy have complications. It is worth emphasizing that deaths have undoubtedly occurred from the use of these hormones.

The following is only a partial list of the ways in which death has been brought about:<sup>7-9</sup>

1. Decreased resistance of host to infection.
2. Suppression of signs of infection.
3. Adrenal failure due to atrophy.
4. Intestinal perforation and peritonitis.
5. Gastrointestinal hemorrhage.
6. Cardiac failure.
7. Status epilepticus.
8. Polyarteritis nodosa.
9. Unexplained sudden death.

In addition to a reduced resistance to infection, many infections become almost inapparent because of the lack of usual response. In pneumonia, for example, patients with gross pulmonary involvement and bacteremia may seem apparently well. Thus, while patients are receiving adrenal steroid therapy, one must be alert to minor manifestations as indicative of major infections, or patients will die unnecessarily.

It is now well recognized that various types of physical stress create an increased demand for adrenal steroid hormones. If the adrenal has been rendered quiescent through suppression of adrenocorticotropin by administration of cortisone, then stress in the form of an operative procedure, accident, or other trauma may precipitate acute adrenal insufficiency.

Where cortisone has been given over a period of time (20 days), intravenous adrenocorticotropin may require 4 days to restore adrenal activity. After prolonged suppression, the adrenal may remain relatively inactive and atrophic for many months. Salassa<sup>10</sup> reported a case of adrenal failure following operation 18 months after cortisone therapy had been discontinued.

Supplementary cortisone therapy should be considered in all patients who have had

a course of cortisone when undergoing major surgery.

Intestinal perforation and hemorrhage are rare but important complications of adrenal steroid therapy. They are most likely to occur if there is pre-existing disease of the bowel, e.g., regional ileitis or ulcerative colitis. They may, however, occur during the treatment of rheumatoid arthritis or other disorders unrelated to the gastrointestinal tract.

Cardiac failure may result from excess retention of sodium and water, especially if heart disease is already present.

Prednisone and prednisolone have less tendency to cause sodium retention but in large doses may do so. They have no other virtues and may exhibit the same tendency to cause perforation, hemorrhage and spread of infection as in the case of cortisone or adrenocorticotropin.

Prolonged use in the treatment of rheumatoid arthritis may lead to the development of polyarteritis nodosa. Kemper *et al.*,<sup>11</sup> reporting from the Mayo Clinic, found it present in 4 of 14 (29%) of patients coming to necropsy, while none was found in 38 patients who died without the benefit of cortisone.

On the other hand, there are numerous reports to suggest that polyarteritis nodosa is often improved by adrenal steroid therapy.

Unexplained deaths are also reported. We have had two such cases in our hospital. One child with subacute nephritis died suddenly about 2 hours after he had been examined and found to be progressing favorably. The blood pressure was not elevated and concentrations of electrolytes were normal a few hours prior to death. Necropsy failed to reveal anything other than the usual renal changes. A second child, receiving intermittent therapy for nephrosis, was brought for a check-up to the hospital. While the physician was talking to the parents, the child died. Necropsy revealed no cause for death.

While death from administration of adrenal steroids is rare, other major and

minor complications are not at all uncommon.

Psychoses, osteoporosis with spontaneous fractures, insulin-resistant diabetes and thrombo-embolic phenomena are amongst the more serious. Moon facies, hirsutism and acne are unimportant but common minor accompaniments of such therapy.

I should like to conclude this section with a couple of short quotations from a recent article by Good:<sup>7</sup> "In the light of the consideration offered herein, we think it improper to consider ACTH or cortisone as 'better forms of aspirin,' as slightly improved anti-histaminics, as adjuncts to the antibiotics in the general treatment of infection, or as agents to be used indiscriminantly in the treatment of disease," and, "However, the best method of reducing the frequency of serious untoward side reactions to cortisone and ACTH is for every physician to recognize these hormones as the potent pharmacologic agents which they are, and to use them only where they are clearly indicated, after having evaluated the potential hazard as well as the potential benefit to be derived from their clinical application."

#### COMPLICATIONS OF OXYGEN THERAPY

Oxygen as a therapeutic tool came into general use only after the First World War. Most drugs and therapeutic nostrums have been prescribed by doctors in carefully regulated dosage. Until recently such was not the case with oxygen. The severe damage to the eyes of premature infants caused by excess oxygen are too well known to bear repeating.

However, there is some danger that the pendulum may swing too far the other way. There are undoubted instances of severe cyanosis in the newborn where concentrations higher than 40% presently recommended, may be necessary. Probably the ultimate control of oxygen for the infant will not be the concentration in the ambient air of the incubator, but the concentration of oxygen in the circulation as measured by the oximeter.

Ill effects of excess oxygen administration are not confined to the premature. One has seen cases of status asthmaticus and cases of bulbar polio in which the administration of oxygen has proved fatal.

In such cases the inability to obtain an adequate respiratory exchange leads to a rising tension of carbon dioxide in the blood and eventually the respiratory center becomes unresponsive to this usually potent stimulus. The center is now dependent on anoxia as its sole stimulus to maintain the mechanics of respiration. Oxygen administration removes this stimulus and respiratory movements cease. Further accumulation of carbon dioxide results and frequently proves sufficiently injurious to the center that the center is permanently depressed and the patient dies.

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*Pediatrics* 1958;22;170

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