Volume 32, No. 6
June 1970

THE JOURNAL OF Anesthesiology
THE AMERICAN SOCIETY OF ANESTHESIOLOGISTS, INC.

Editorial Views

The AABB Reference Laboratories

WHEN KARL LANDSTEINER discovered the ABO blood groups about 70 years ago he predicted that many additional blood group factors would be found. He concluded that when a sufficient number of blood group factors were known an individual's blood group pattern would probably be found to be as peculiar to him as his fingerprints. The rapid accumulation of knowledge of human blood groups and blood group immunology over the past decades seems to indicate that Landsteiner's prediction will hold true. This means that completely matched blood for transfusion can be obtained only from the recipient himself as donor or from an identical twin.

Fortunately, nature has provided extensive leeway in blood transfusion therapy regarding individual type specificity. Transfused erythrocytes which have not been damaged by storage normally survive in a recipient for their normal life span (*i.e.*, 100 to 120 days) if they are not attacked by specific blood-group antibodies. Except for the naturally-occurring anti-A and anti-B isoagglutinations, blood group antibodies usually are found only in individuals in whom they have been produced in response to earlier transfusion or pregnancy.

The abilities of individuals to produce blood group antibodies vary, for reasons that are not known. Patients with certain diseases, such as disseminated lupus erythematosus or rheumatic fever, have high incidences of sensitization to erythrocytic antigens in transfused blood. Although the incidence of sensitization in otherwise-normal patients is quite low, the increasing use of blood transfusion has been followed by a parallel increase in the number of sensitized recipients. The antibodies will, in most cases, destroy subsequently transfused erythrocytes containing the corresponding antigens. Therefore, compatible blood lacking the specific antigens must be selected for future transfusions.

Blood for transfusion is routinely classified by ABO and Rh_0 (D) typing only. Therefore, single or multiple antibodies that do not correspond to either of these basic blood groups can create major problems in blood bank laboratories. Frequently, many hours, sometimes days, are spent in frantic searches for compatible blood.

The Reference Laboratories Program of the American Association of Blood Banks (see Literature Brief on page 572) was organized 12 years ago as a special service to assist blood banks with special problems in blood group antibody identification and to help them in their search for donors with compatible blood.

The special problems created by the multiplicity of blood group antibodies have been of two general types. The first is due to single antibodies directed against one of the "high-frequency" antigens. Since these antigens are present in the erythrocytes of almost every possible donor, it is extremely difficult to find a person who lacks the same antigen as that to which the patient is sensitized. We know about 40 of these "high-frequency" antigens, many of which, such as k (Cellano), Tj^a (P), Lu^b, Vel, and Yt^a, have created major prob-

lems in blood transfusion therapy. Steadily increasing numbers of people whose blood cells lack these "high-frequency" antigens have been located and registered with the Rare Donor File of the American Association of Blood Banks. Today, therefore, the problem of locating compatible donors in these cases has become relatively easy compared with an almost impossible task only ten years ago.

The second general problem with blood-group antibodies occurs when patients have become sensitized to a number of different blood group antigens. It is not unusual today for a patient to have as many as five different blood group antibodies. The task of finding compatible blood lacking all of these antigens can be very difficult, since the random incidence of donors whose blood cells lack a specific combination of antigens is the product of the occurrences of all the antigens multiplied together. For example, approximately 15 per cent of random blood donors lack the Rh_0 (D) antigen (*i.e.*, its incidence = 0.15 or 15 per 100 random donors). A single antibody to this antigen does not normally present a major problem, even though Rh_0 (D)-negative blood is seldom in plentiful supply.

If a patient were to have antibodies to more than one antigen, each with the same incidence as Rh_0 (D), the incidence of donors lacking all the antigens simultaneously would be:

Number of Antibodies (each 0.15)	Combined Incidence	Incidence among ABO-compatible Donors
1	0.15	15 per 100
2	0.15 × 0.15	23 per 1000
3	0.15 × 0.15 × 0.15	34 per 10,000
4	0.15 × 0.15 × 0.15 × 0.15	51 per 100,000
5	0.15 × 0.15 × 0.15 × 0.15 × 0.15	75 per 1,000,000

Extensive experience over the past several years has shown clearly that group O frozen blood cells, freed of their plasma anti-A and anti-B isoagglutinins, can be used safely for transfusion into patients with any ABO blood group. This experience, combined with the observations that multiple antibodies usually include one or more in the Rh–Hr system, leads to the selection of three basic categories of group O donors:

For patients with antibodies:

1) group O rr (dce/dce)	anti-D, anti-C, anti-E
2) group O, R_1R_1 (DCe/DCe)	anti-c, anti-E
3) group O, R_2R_2 (DcE/DcE)	anti-C, anti-e

Since anti-Kell and anti-Duffy^a (Fy^a) are also very common antibodies, donors in these categories are further selected for lack of these antigens. These special categories of blood are additionally tested for as many as possible of the known blood group antigens. The greater the number of missing antigens, the more useful the blood is for transfusion to patients with multiple blood group antibodies.

During the past years several techniques for freezing blood have been developed. About half of the 28 AABB Reference Laboratories blood banks are now able to freeze blood and process it for transfusion. While blood collected in conventional anticoagulant preservative solutions can be stored for only three weeks, frozen blood cells can be stored for years, then prepared for transfusion. For the AABB Rare Donor Program this has the obvious advantage that a relatively small number of donors lacking the "high-frequency" antigens, or those with the above-mentioned blood group combinations, can provide a sizable number of units of frozen erythrocytes by donating their blood four or five times a year to one of the AABB depots for frozen blood.

Since the majority of the AABB centers have identical blood freezing and processing systems, rare types of frozen blood can be shipped in dry ice from one center to another and be processed only if actually needed.

During the 12 years that the Reference Laboratories Program of the American Association of Blood Banks has been in operation, many hundreds of units of rare types of blood have been shipped to blood banks throughout the United States and also as far away as Australia and New Zealand. The goal of the program is to make certain that all blood banks and transfusion services can receive the necessary help to solve their problems with blood group antibody identification, and to secure adequate supplies of compatible blood for patients in need of transfusions.

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Drugs

PENTAZOCINE VS. MORPHINE The d- and l-isomers of pentazocine were compared with morphine for analgesia and other effects in two randomized, double-blind assays involving 889 treatments of 478 patients. Most of the analgesics were given for postoperative pain. Responses to 60 mg/d-pentazocine were less than that to 5 mg morphine. Relative potency of l-pentazocine, based on measurement of effects for as long as 255 minutes, was found to be 0.55 to 0.40 (25 to 29 mg approximately equal to 10 mg morphine). Sedation and sweating were common with the l— isomer. It appears that analgesia resides principally in the l— isomer. (*Forrest, W. H., and others: Analgesia and Other Effects of the d— and l— Isomers of Pentazocine, Clin. Pharmacol. Ther. 10: 468 (July) 1969.*)

ANALGESICS AND MAO INHIBITORS The monoamine oxidase inhibitors, iproniazid and tranylcypromine, potentiated the acute toxicity of meperidine, morphine, pentazocine and phenazocine in mice. The increased toxicity of meperidine previously has been related to the inhibition of a hepatic microsomal MAO enzyme system, a system not important in the detoxification of the other analgesia studied. There was no correlation between changes in brain and hepatic MAO activity and the increased meperidine toxicity. The acute toxicity of pentazocine was enhanced in spite of normal blood pentazocine levels. On the other hand, the increased toxicity of all the analgesics studied correlated well with increased brain levels of 5-hydroxytryptamine but not with the other monoamines, norepinephrine and dopamine. (*Rogers, K. J., and Thornton, J. A.: The Interaction between Monoamine Oxidase Inhibitors and Narcotic Analgesics in Mice, Brit. J. Pharmacol. 36: 470 (July) 1969.*)

ANTIPYRETIC-ANALGESIC DRUGS The antipyretic effect of aspirin and related drugs on the temperature-regulating region of the hypothalamus is a central one. The analgesic action is predominantly peripheral, probably occurring at receptors in nerve terminals. The anti-inflammatory effect is also peripheral, but may be mediated by axon reflex inhibition. (*Keele, C. A.: Sites and Modes of Action of Antipyretic-analgesic Drugs, Proc. Roy. Soc. Med. 62: 535 (June) 1969.*)