Type II Hypersensitivity: Summary

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TYPE II hypersensitivity was described as a histopathologic observation by Gell and Coombs in 1963. Later, it was demonstrated to be due to antibodies binding directly to cell surfaces or to proteins and tissues that surround and connect cells together. Typically, IgG (primarily subclasses 1, 2 and 3, but not 4) and IgM antibodies are involved, followed by activation of the complement system, which results in holes through cell membranes that can cause cell damage and death. Normally, this is one of the mechanisms of the immune system to protect against invading microorganisms.

Type I hypersensitivity, involving IgE and the activation of mast cells, contrasts with type II hypersensitivity. The former causes true allergic disease, whereas the latter causes cell and tissue injury commonly seen in autoimmune diseases. Thus, type II hypersensitivity is not a true allergy. Type II hypersensitivity is also known as direct-antibody cytopathology or cell cytotoxicity. The Table lists diseases for which type II hypersensitivity is thought to be involved, along with the target cells or tissues and clinical manifestations.

Under normal circumstances, an infusion of intravenous immune globulin (IVIG) can cause a slight decline in the recipient's hematocrit (the ratio of the volume of red blood cells to the total volume of blood), with clinical indicators that some hemolysis has occurred. Likewise, the platelet count may fall slightly in some recipients of IVIG. Usually, these are mild reactions and not considered to be clinically relevant, and specific antibodies causing the issues cannot typically be found. Yet, if a person has somewhat compromised kidney function, and even if the adverse reaction is considered to be mild, hemoglobin from lysed red blood cells could actually result in acute renal failure. This reaction is very rare, but awareness of this complication is needed to minimize potential morbidity from otherwise normal infusions of IVIG.

Furthermore, there may be risks for type II hypersensitivity reactions from IVIG infusions since offending antibodies may be present from some plasma donors. Since autoimmune diseases with autoantibodies are actually quite common (thought to occur in 5 percent to 8 percent of people), autoantibodies may also be considered quite common in potential plasma donors. It is reassuring that the screening process for plasma donor selection not only helps prevent transmission of infectious diseases such as hepatitis C and HIV, but also helps prevent those with significant autoimmune disorders from donating. Even if a plasma donor has made specific autoimmune antibodies, but has not been excluded from donating, that plasma will be mixed with as many as 10,000 other units of plasma, greatly diluting most significant autoimmune antibodies. Therefore, even though it is theoretically possible infusion of autoimmune antibodies could result in a reaction in IVIG recipients, the safeguards in place make this unlikely to occur.

Nevertheless, IVIG infusions should not be cavalierly performed. Medications need to be available, along with personnel who can help, if a reaction occurs. Further, if a severe reaction occurs, the IG brand and lot number must be reported to the U.S. Food and Drug Administration so appropriate evaluations can be performed (for example, to determine if a significant autoimmune antibody is present in that specific lot). If that is the case, the lot could be removed from use to prevent others from having severe reactions or worse.

Next time, we will begin with a discussion of the type III hypersensitivity reaction. IG

Table. Clinical Manifestations of Some Examples of Type II Hypersensitivity Reactions

Disease	Target	Clinical Manifestation(s)
Acute rheumatic fever	Heart tissue	Myocarditis
Autoimmune hemolytic anemia	Red blood cells (RBC)	RBC hemolysis/anemia
Autoimmune thrombocytopenia	Platelets	Low platelet count/bleeding
Goodpasture syndrome	Lung and glomerular basement membranes	Hemoptysis (coughing up blood)/ hematuria (blood in the urine due to kidney injury)
Graves' disease	Thyroid stimulating hormone receptor	Hyperthyroidism
Hemolytic disease of the fetus and newborn	Rho or D antigen (Rh or Rhesus factor)	Severe anemia/cardiac problems/ hydrops fetalis
Myasthenia gravis	Acetylcholine receptor	Muscle weakness or paralysis
Pemphigus vulgaris	Desmosomes (protein complex for attaching cells to each other)	Loss of cell contact resulting in tissue layer separation and large blister formation
Pernicious anemia	Intrinsic factor	Anemia due to the lack of absorption of vitamin B12
Transfusion reaction	ABO mismatch/other RBC antigens	Acute hemolytic anemia
Type 1 diabetes mellitus	Islet cells of the pancreas	Diabetes (high blood glucose levels)
Vasculitis due to ANCA	Cytoplasmic proteins in neutrophils	Vasculitis (inflammation of blood vessels)