CPRA and Its Importance in Organ Transplantation

Background Information

Antibody: A protein molecule produced by the immune system in response to a foreign body, such as virus or a transplanted organ.

HLA stands for Human Leukocyte Antigen. HLA antigens are substances, usually a protein, found on the surface of our cells that stimulate the production of antibodies.
These antigens are referred to with a letter and a number such as A2 or B23.

Each person's HLA make-up is unique. You inherit it from your parents. If something foreign is introduced into your body, your immune system recognizes the foreign intruder and mounts an antibody attack against it. In the case of an organ transplant, the body will recognize the HLA antigens on the transplanted organ as not being the same as its own, and form specific antibodies against those particular HLA antigens.

HLA is important in organ transplantation for two main reasons:

First, a body may reject any transplanted organ (eg, kidney, pancreas, heart, lung, liver, and intestine) because the recipient's immune system recognizes the organ as foreign and initiates a rejection response (this can be in the form of antibody production) which could eventually destroy the organ.
Patients receive anti-rejection drugs after a transplant to prevent antibodies from forming.

Second, because of previous medical events, some patients have already developed antibodies to specific HLA antigens. For example, if a candidate has developed a specific antibody to the HLA antigen A2, that person is said to be "sensitized" to the A2 antigen. If a donor organ that displayed the A2 antigen were placed in that candidate, there may be an immediate rejection response (**a hyperacute response**) which would lead to the rejection of the transplanted organ.

Now for the good news

It is not easy to become sensitized to human HLA antigens. Most people waiting for a transplant (around 80%) are not sensitized. Patients can become sensitized to HLA antigens because of:

- Pregnancies. About 30-50% of women with three or more pregnancies will develop HLA antibodies. In some women the antibodies could be present for just a short time (weeks to months), while in others they may persist for many years.
- Blood transfusions. About 50% of patients who receive multiple transfusions will develop antibodies. Today, most patients who require blood transfusions receive filtered blood, which decreases the chances for a patient to become sensitized.
- Previous transplant. About 90% of patients develop HLA antibodies within two weeks of a failed graft. However, by the time the patient is relisted (some will have "lost" their antibodies.
- Viral/bacterial infections. There are some reports that patients with virus infections develop HLA antibodies, although this is relatively rare.

What is PRA?

PRA stand for Panel Reactive Antibodies. In order to determine whether or not a patient already has any specific HLA antibodies, a lab specialist will test a patient's blood (serum) against lymphocytes (white blood cells) obtained from a panel of about 100 blood donors. These 100 donors represent the potential HLA makeup for a donor from that area. Percent PRA (%PRA) is the number of reactions within that panel. If a candidate's serum does not react with any of the donor samples, the candidate is not sensitized and has a PRA of 0. If a candidate's serum reacts in 80 out of 100 samples, the patient has a PRA of 80%. Theoretically, that means that if a donor becomes available from that donor pool, the recipient would experience acute rejection 8 out of 10 times. That patient might have to wait a very long time until a compatible donor becomes available. This is why the kidney allocation algorithm gives patients with a PRA of 80% or higher, 4 additional points.

Why we need to refine PRA?
There's a problem with PRA. We might know that a patient will have a reaction 80% of the time, but we don't know what they are reacting to. However, technology has advanced to the point that in most cases the specificity of an antibody produced by a patient can be identified. For example, a patient could develop antibodies to A2 and A24. In this case A2 and A24 may be considered **unacceptable antigens** (mismatches) for this patient. If the patient were transplanted with a kidney that had A2 and/or A24, it could be rejected hyperacutely. Transplant centers enter these unacceptable antigens for their candidates. That way a potential donor with the unacceptable antigen will not even be considered for that candidate. Entering unacceptable antigens for candidates increases the efficiency of organ allocation by screening off incompatible donors.

What is CPRA?

We also know the number of times A2 and A24 appear in our national donor pool. This means we can calculate the likelihood that the recipient and donor would be incompatible. This would be known as the **CPRA** or the Calculated Panel Reactive Antibodies. The system will calculate the CPRA using the unacceptable values that have been entered for a candidate**.** To determine the CPRA value, the computer system will use an established formula and HLA frequencies derived from the HLA types found in more than 12,000 donors.

When a transplant coordinator enters the unacceptable antigens for a patient, the CPRA calculator automatically calculates the CPRA value. Whenever a transplant coordinator updates a patient's unacceptable antigens, the system will automatically recalculate the value. Candidates with a CPRA value of 80% or higher will receive points in the kidney allocation formula.