Knowledge of human blood types is necessary for successful transfusions.

Recognition that blood types have relatively simple inheritance patterns led to their use in paternity cases, forensics, and similar "identity" cases.

Blood typing relies on antigen-antibody reactions and thus requires some understanding of our immune system.

"Acquired immunity" refers to the fact that we can respond to invasion by a "foreign" organism only after exposure; our system is able to recognize "antigens" as foreign.

Antigens are molecules (usually proteins) that differ in some way from our own natural proteins. The proteins on one person's cell surfaces will usually be recognized as "foreign" to another individual which accounts for rejection in many organ transplant attempts. The system is also involved in recognition of aberrant cells that may lead to cancer. Compatible antigens and antibodies interact via "mutually attractive" 3-D surfaces, which can inactivate the antigen, or target it for destruction.

Our immune system is activated after birth; mother's milk contains a type of antibodies that can help protect the child.

Immune response is highly dependent on "white cells" (also called lymphocytes or leukocytes) that circulate in our blood and lymph systems.

3 types; B cells, T cells and macrophage interact to play key roles
see:  [http://www.cellsalive.com/antibody.htm](http://www.cellsalive.com/antibody.htm)

All are made in bone marrow

Each B cell, when activated, makes one specific kind on antibody, a protein that can recognize and bind to a specific antigen. Since the antibodies also circulate in the blood, the response is called a humoral response.

Each antibody consist of 4 protein chains, 2 heavy or H chains, and 2 light of L chains. Different B cells combine different components of the genetic information used to make these chains from a relatively small set of Immunoglobin genes. If the antibody that a B-cell makes "recognizes' an antigen, that B cell will, with assistance from T-cells, begin to multiply and excrete thousands of copies of the same antibody. Antibodies are classed according to the type of H chain they have:
<table>
<thead>
<tr>
<th>Immunoglobulin type</th>
<th>relative amounts</th>
<th>primary targets</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ig G (gamma)</td>
<td>80%</td>
<td>microbes</td>
<td>small, can cross placenta</td>
</tr>
<tr>
<td>Ig A</td>
<td>12%</td>
<td>microbes</td>
<td>in saliva, tears etc. to target before entry</td>
</tr>
<tr>
<td>IgM</td>
<td>7%</td>
<td>cell surfaces</td>
<td>includes blood cells</td>
</tr>
<tr>
<td>IGD</td>
<td>Tr</td>
<td>on B cell surface</td>
<td>needed for activation</td>
</tr>
<tr>
<td>IGE</td>
<td>Tr</td>
<td>“venoms”</td>
<td>high in allergic responses</td>
</tr>
</tbody>
</table>

After the invader has been targeted and destroyed, most B-cells die off, but some remain as “memory” cells to rapidly reactivate if needed.

T-cells "travel" to point of attack so are involved in "cellular immunity".
Helper T cells stimulate appropriate B-cells to activate by releasing cytokines
Cytotoxic (killer) T cells attach to "abnormal cells" (virus infected or tumor cells) and bore holes in the membrane;
Suppressor T cells help shut down the immune response
Memory T cells enable rapid re-responses

For a 3 dimensional image of antibodies, take advantage of the programs at:

http://www.umass.edu/microbio/chime/antibody/index.htm

Our specific blood types are also determined by antigens on red cell surfaces.

Only 3 of many systems will be described. Blood types A, B, AB, and O; result from the 3 alleles at one gene locus. Although it is actually more complex, Rh positive and negative can be considered as two alleles of one gene (rh negative is recessive) and blood types M, N, or MN result from M and N alleles of another gene.

ABO Blood Types (Groups) (Landsteiner, 1900)
Involve antigenic proteins on surface of red cells;
Are similar enough to plant protein fragments that can pass through walls of intestine that a person will make anti-A or Anti-B if non-self without being exposed to actual blood cells; must be verified before any transfusion!
Involve IgM antibodies, so no problem mother to fetus

<table>
<thead>
<tr>
<th>Blood type</th>
<th>Red Cell Antigens</th>
<th>Antibodies in plasma</th>
<th>Genotypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>A</td>
<td>anti-B</td>
<td>IA\text{A} or IAi\text{o}</td>
</tr>
<tr>
<td>B</td>
<td>B</td>
<td>anti-A</td>
<td>IB\text{B} or IBi\text{o}</td>
</tr>
<tr>
<td>AB</td>
<td>A &amp; B</td>
<td>none</td>
<td>IAIB</td>
</tr>
<tr>
<td>O</td>
<td>neither A or B (H)</td>
<td>ant-A &amp;-B</td>
<td>i\text{o}i\text{o}</td>
</tr>
</tbody>
</table>

A, B and O are alleles, A & B are codominant, O is recessive.
If red cells from an A person are mixed with plasma of a B, or vice versa, the cells will clump (agglutinate). In transfusions, red cells cannot be transfused to a recipient with antibodies already there! It is best to match perfectly as far as possible, but adding some antibodies to a mis-matched recipient is not as disastrous as adding cells. The A & B antigens differ by the addition of either a galactose-amine sugar (A allele) or galactose (B allele) to a cell surface protein (H)

**MN blood types (Landsteiner 1920s)**

Although it is not very important in transfusions, another antigen pair is useful in identification since both alleles are fairly common.

Persons may be type M, N, or MN depending on whether they have the genotypes (the blood type is shown in parenthesis):

**IM\text{M} (M), IN\text{N} (N) or IM\text{N} (MN)**

These are co-dominant alleles of a different immunoglobin gene than ABO
Some persons secrete the antigen in saliva, others do not, which is also a single gene trait.
**RH blood groups (Landsteiner, 1940s)**

Although there are several known alleles, we can consider this blood group like a case of simple dominance. Persons who are Rh\(^+\) have an Rh antigen on their red cell surfaces. People who are rh\(^-\) do not have the antigen, so they will make anti-Rh if they are exposed to Rh\(^+\) blood cells.

\[
\begin{align*}
\text{Rh}\,^+/- & = \text{Rh positive} \\
\text{rh}^-/\text{rh}^- & = \text{rh negative}
\end{align*}
\]

Accounted for some cases where a second transfusion failed even though the donor and recipient were matched for ABO type.

Is responsible for "erythroblastosis fetalis" or "blue babies"

The anti Rh is an Ig-G and crosses placenta

At birth of an Rh\(^+\) baby, an rh\(^-\) mother gets some Rh\(^+\) cells and makes anti-Rh, which can attack the red cells of the next Rh\(^+\) fetus; the problem gets worse with each Rh\(^+\) baby conceived.

Some protection was seen if there was also an ABO mismatch, which led to a solution.

Rhogam is now given to any rh\(^-\) negative mother following birth of an Rh-plus baby; Rhogam is anti-Rh so it "soaks up" the fetal cells before she mounts an immune response.

**Tissue transplants and HLA genes**

There is a set of 5 genes on human chromosome 6 that all code for proteins found on many tissues, including white cells, heart, kidney etc.

The genes are called HLA-A, HLA-B, HLA-C, HLA-D, and HLA-DR

Each of the 5 genes has many common alleles. There are 23 known HLA-A alleles, 47 HLA-B alleles 8 HLA-C alleles, 12 HLA-D alleles and 12 also for HLA-DR. No one allele of any of the genes is predominant among the human population.

The genes are so close together on chromosome 6 that they tend to be inherited as a "block". That is, whichever A, B etc. alleles are on one of the chromosome 6 partners will end up together in the egg or sperm after gametogenesis.

Any person will make antibodies and thus reject a tissue transplant if it contains any allele different from those that were inherited.
As an example, just using the HLA-A and B genes:

<table>
<thead>
<tr>
<th></th>
<th>Man's alleles</th>
<th>Wife's alleles</th>
<th>Child's alleles</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HLA-A</td>
<td>HLA-B</td>
<td>HLA-A</td>
</tr>
<tr>
<td>chrom 6#1</td>
<td>2</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>chrom6#2</td>
<td>1</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

The child will get one chromosome # 6 from each parent; in this case, neither parent could donate a heart or kidney etc. to the child, since mismatches would occur at both A & B HLA- loci. The matches do not have to be identical for all alleles present, just be sure that no allele not present in the recipient is present in the organ.

Corneas, heart valves and even bone evoke no or very minor immune responses. Autoimmune diseases such as rheumatoid arthritis (anti IgG) or Luous (anti DNA) occur when antibodies are made against "self".

Some HLA alleles are known to affect likelihood of other diseases, especially autoimmune diseases. Example, only 4% of people have B27, but 90%of people with ankylosing spondylitis have B27.