Reminder - One of you should complete this sheet after the group has arrived at its answers.

Diagnosis: (Check one.)

- Normal immune system
- Granulocyte deficiency
- Complement deficiency
- Deficient cell-mediated immunity
- Humoral immune deficiency
- Combined immunodeficiency

2. Data consistent with the diagnosis. (Underline that data which you feel was of crucial importance.)

3. Data irrelevant for making diagnosis:

4. Data inconsistent with the diagnosis.

5. Brief description of expected lymph node histology.
6. One of the photomicrographs below illustrates normal lymph node architecture, and the other shows the abnormalities expected in this patient. Identify the abnormal lymph node and describe the abnormalities that you can see on it.
THE CORRECT GROUP ANSWERS ARE ON THE FOLLOWING PAGES. DO NOT LOOK AT THEM OR REMOVE THEM UNTIL YOUR GROUP HAS DISCUSSED AND FILLED OUT THE ANSWERS ON THE GROUP ANSWER SHEET.
Correct Group Answers

1. *Diagnosis:* Deficient antibody-mediated immunity.

2. *Data consistent with the diagnosis.* *(All were consistent, but there were far more data than necessary to make the diagnosis.)*

a) History and evidence of recurrent infections (especially extracellular bacterial infections) were highly suggestive.

b) The following are indications of normal cell-mediated immunity (CMI). Any one of the first three would be reliable proof of normal CMI, since you would have *firsthand* information. Item 4 is a laboratory test and, like all laboratory tests, is subject to error. Item 5 relies on *secondhand* information and should be evaluated according to your trust of the mother.
   1. Poison ivy rash (this is a cell-mediated hypersensitivity reaction, so its presence its indicative of normal CMI)
   2. Positive mumps skin test, which is also indicative of normal CMI.
   3. Positive skin test with tetanus toxoid. Although not everyone immunized with tetanus toxoid develops cell-mediated immunity to this antigen, this is a very informative skin test since most individuals have been immunized with tetanus toxoid, and as such a negative result can be considered as indicative of cell-mediated immunity deficiency (although clearly not sufficient, by itself, to make the diagnosis). In this patient there was documented exposure to tetanus toxoid, with no detectable humoral immunity, but with a positive skin test, that his cell-mediated immunity was not deficient.
   4. Normal numbers of total T lymphocytes, as well as of the helper (CD4+) and cytotoxic/suppressor (CD8+) subpopulations
   5. History of normal course of mumps and chickenpox infections. (Recovery from both are thought to be dependent upon T-lymphocyte function.)

c) **Two** of the following indications of deficient antibody production were necessary:
   1. Low serum IgG (< than 0.5 g/L).
   2. No detectable antibody to tetanus and diphtheria toxoids.
   3. No detectable neutralizing antibody to poliovirus.
   4. No detectable antibody to pneumococcal polysaccharide type 3.
   5. No detectable antibody to mumps virus.
   6. No detectable antibody to type A RBC.
   7. No detectable antibody response to *Haemophilus influenzae* PRP *(spike in graph is artifactual, see below).*
   8. Low numbers of CD19+ B lymphocytes in peripheral blood.

Items 1 and 6 are the two most readily available assays and together would indicate deficient antibody production.

Item 7 is most significant from the functional point of view, but was it necessary in light of all the other data? Incidentally, did you see the laboratory error in the data? There is no way that antibody can rise suddenly three weeks after a booster and drop back to low levels two to three days later.

d) The scanty tonsillar tissue was a clue but not definitive data, and the normal number of lymphocytes in the blood ruled out lymphopenia. These were not crucial data.
Correct Group Answers (cont.)

e. Data that rule out other diagnoses:

1) High neutrophil count (ruling out a diagnosis of agranulocytosis).
2) Normal NBT reduction assay, which rules out a diagnosis of chronic granulomatous disease.
3) Normal values for the CH50 hemolytic complement assay, ruling out a complement deficiency.

3. Irrelevant Data

1) History of broken leg.
2) Lack of anti-B antibody in serum (patient is type B and therefore could not have anti-B antibody).
3) Negative PPD skin test (no history of tuberculosis).

4. Inconsistent Data

1) The lab error mentioned in 2c(7) above.

2) Failure of PHA stimulation. The radioactivity count values for the patient lymphocytes are so low that a lab error is immediately suggested. On retesting, the patient gave normal PHA stimulation. A variety of errors could have accounted for this result, e.g. the patient's cells were accidentally exposed to a toxic substance, the cell count was grossly inaccurate, or thymidine was inadvertently omitted from the patient's cultures.

5. Lymph Node Histology

Rather than multiple prominent germinal centers characteristic of a stimulated lymph node, you would probably see few, if any, germinal centers (i.e. no follicles, where B-cells are normally located) but no marked deficit in the cortex (site of localization of T-cells).

6. Photomicrograph Identification

A. Patient's lymph node    B. Normal lymph node

Having finished the problem, each student should answer the questions on the posttest, then discuss the answers with the other group members.