

# Hyper-IgM Syndrome: To Switch or Not to Switch?



by

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## Preliminary

Answer the following questions to ensure that you have the necessary background knowledge for completing the case study in class.

### Questions

1. Name the primary classes of antibodies and describe their structures.
2. In response to an antigen, which antibodies are secreted/produced first? Are all classes of antibodies found in the circulation at all times?
3. Which antigen receptors are present on the B cell? What is the sequence of B cell receptor isotype expression during the maturation process?
4. What are the mechanisms by which helper T cells stimulate B cell proliferation and differentiation?
5. What are the signals necessary to induce heavy-chain isotype-switching?
6. Explain why circulating lymphocyte count values alone would not necessarily provide evidence for or against a B cell deficiency.
7. Define the following terms: *neutralization*, *opsonization*, *agglutination* and *complement fixation*.
8. Considering the X and Y chromosomes, why are immune diseases more common in males than females?

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## The Case

Three year-old Adam presented with a fever and frequent episodes of coughing. He had a history of recurrent pneumonia and sinus infections since he was six months-old, but appeared to be of normal physical and mental function.

Adam's mother had brought him to the doctor's office for a fever that had started two days earlier. She had started him with liquid Tylenol and had hoped that his fever would go away, but Adam continued to have fever, poor appetite, and sporadic diarrhea. Adam was up-to-date on all vaccinations. When Adam's mother was questioned about her family history, she told the doctor that she was 36 years-old, and was healthy, while Adam's father was 42 years-old and had essential hypertension. Adam's sister was 10 years-old and in good health. Adam's maternal uncle had died as a child from an unknown infection.

No one in the household smoked or used any nonprescription drugs. Household chemicals including cleaning agents and pesticides were stored in child-safe cabinets. They had no household pets.

Adam's vital signs showed his blood pressure was 110/60 mmHg, his pulse 145 bpm, his respiratory rate 32–36 breaths per minute, his temperature 39 degrees Celsius, and his body mass index 14.0 kg/m<sup>2</sup>. The doctor noticed a flushed face with a tinge of cyanosis on his lips. Palpitations, dyspnea, and mild rales and rhonchi were noticed throughout both lung fields during his physical examination. Adam was placed on oxygen via nasal cannula at 2 L/min. After 5 minutes on oxygen, his oxygen saturation was obtained by a pulse oximetry and demonstrated 95% saturation.

Suspecting a hereditary immune disease, the doctor sent Adam (on oxygen) and his mother to the hospital lab for blood work. The blood was drawn for normal electrolyte, hemoglobin, hematocrit, WBC count and differential profile, antibody levels as well as prothrombin time (PT) and partial prothrombin time (PTT). Adam's mother was instructed to continue giving Tylenol (160 mg/dose, not to exceed four doses/day) until Adam's lab results were read.

The lab results revealed sodium concentrations of 135mEq/L, chloride 99mEq/L, potassium 4mEq/L, bicarbonate 22 mEq/L, blood urea nitrogen 15 mg/dL, creatinine 1.0 mg/dL, and glucose 90 mg/dL. Arterial blood gas values were PaCO<sub>2</sub> 36 mm Hg, PaO<sub>2</sub> 95 mm Hg, SaO<sub>2</sub> 97% and pH 7.44. His WBC counts were 4,500/mm<sup>3</sup>, platelets 140/mm<sup>3</sup>, hematocrit of 34, and hemoglobin 2.0% 12 g/dL. WBC differential shows Neutrophils 45%, Lymphocytes 40%, Monocytes 4%, Eosinophils 2.0%, and Basophils 1%. His serum immunoglobulins showed IgM 350 mg/dL, IgG 100 mg/dL, IgA 0, and IgE 0. Adam's PT was 11 sec and PTT was 62 sec.

The nurse contacted Adam's mother to let her know that the doctor had ordered a chest X-ray and bronchoscopy based on the lab results.

A pediatric pulmonologist, who happened to be in the hospital, was consulted who performed a bronchoscopy in the ER. *Pneumocystis jirovecii* was quickly identified. A nasal swab displayed gram positive cocci in chains. The lung lavage confirmed *P. jirovecii*. Chest X-ray showed diffuse pneumonia. The doctor diagnosed Adam with hyper-IgM syndrome and admitted Adam for observation.

Adam was treated with pentamidine nebulizer (300 mg) per protocol. Bactrim (40 mg/kg sulfamethoxazole and 8 mg/kg trimethoprim for 24 hours, given in two divided doses every 12 hours for 10 days) and immunoglobulin therapy (300 mg/kg of body weight every 3 to 4 weeks) was implemented. Blood work was to be repeated to follow immunoglobulin levels, blood cell counts, hemoglobin and hematocrit.

### Questions

1. List the abnormal findings, signs, and symptoms in this patient. Explain the cause(s)/mechanism(s) of each.
2. Explain the pathophysiology of hyper-IgM syndrome.

*Note:* Please include the questions along with your associated answers. Do not forget to cite your sources within your answers. Much of the needed information to answer these questions should be found in your responses to the eight questions in the Preliminary section.