# Chronic Myelogenous Leukemia and Other Myeloproliferative Disorders: Review Questions

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## QUESTIONS

Choose the single best answer for each question.

**Questions 1 and 2 refer to the following case.**

A 37-year-old woman presents to her physician with complaints of weight loss, night sweats, and left upper quadrant abdominal pain. On examination, she appears thin and pale and has mild tachycardia, no lymphadenopathy, and a tender spleen tip palpable 8 cm below the costal margin. Results of laboratory tests reveal a leukocyte count of $120 \times 10^3/\mu L$, with a marked left shift and basophilia. Her hemoglobin level is 9.5 g/dL, and her platelet count is decreased at $97 \times 10^3/\mu L$. Chronic myelogenous leukemia (CML) is suspected.

1. **Which of the following tests would be most helpful in confirming this patient's diagnosis and determining the optimal initial treatment?**
   (A) Bone marrow biopsy and aspirate with cytogenetics
   (B) Peripheral blood cytogenetics
   (C) Peripheral blood fluorescence in situ hybridization (FISH)
   (D) Peripheral blood neutrophil alkaline phosphatase staining
   (E) Peripheral blood polymerase chain reaction (PCR)

2. **Testing confirms a diagnosis of CML. The patient is referred to a bone marrow transplant center, where human leukocyte antigen–typing of the patient and her 3 siblings is immediately initiated. In the meantime, the patient should begin which of the following therapies?**
   (A) Acute myelogenous leukemia (AML) induction chemotherapy
   (B) Hydroxyurea
   (C) Imatinib mesylate
   (D) Interferon-α
   (E) Supportive care with transfusions of packed erythrocytes and random donor platelets only

3. **A 75-year-old man with a history of hypercholesterolemia and type 2 diabetes develops transient speech problems and right arm weakness; however, these symptoms resolve en route to the hospital. On examination, his vital signs are normal and his spleen is markedly enlarged. His erythrocyte count is slightly elevated, and his platelet count is $1150 \times 10^3/\mu L$. Increased numbers of megakaryocytes and normal cytogenetics on a bone marrow biopsy confirm a diagnosis of essential thrombocythemia (ET). What is the best initial treatment for this patient?**
   (A) Interferon-α
   (B) Hydroxyurea and aspirin
   (C) Anagrelide and aspirin
   (D) Imatinib mesylate
   (E) Aspirin only

4. **A previously healthy, active 55-year-old man presents with complaints of a mild headache and pruritus that occurs after bathing. He appears flushed and has mild splenomegaly. His hemoglobin level is 22.2 g/dL, and his platelet count is $540 \times 10^3/\mu L$. Results of other laboratory tests are normal. Further testing confirms the diagnosis of polycythemia rubra vera. What is the optimal initial therapy for this patient?**
   (A) Hydroxyurea and low-dose aspirin
   (B) Phlebotomy
   (C) Phlebotomy and high-dose aspirin
   (D) Phlebotomy and low-dose aspirin
   (E) High-dose aspirin alone

*(turn page for answers)*

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## ANSWERS AND EXPLANATIONS

1. **(A) Bone marrow biopsy and aspirate with cytogenetics.** This patient almost certainly has CML, a condition defined by the presence of Ph chromosome (t[9;22] resulting in BCR-ABL gene fusion). The presence of weight loss, painful splenomegaly, and most importantly anemia and thrombocytopenia suggest that this patient's CML may have entered the accelerated phase, which is characterized by increasing numbers of blasts in the blood and/or bone marrow as well as the acquisition of additional clonal cytogenetic abnormalities beyond the Ph chromosome. FISH or PCR performed on either peripheral blood or bone marrow samples are probe-based tests that look specifically for the BCR-ABL fusion but will not detect other cytogenetic abnormalities. Standard cytogenetics are sufficiently sensitive for detection of Ph chromosome and will also identify other clonal aberrations. A bone marrow sample allows simultaneous assessment of cytogenetics and the percentage of bone marrow blasts; thus, it is more informative in this case than peripheral blood cytogenetics testing. Although a low peripheral blood neutrophil alkaline phosphatase score distinguishes CML from other myeloproliferative conditions, it is not sufficient to confirm the diagnosis.
2. **(C) Imatinib mesylate.** This patient requires treatment for her CML. Transfusions are unlikely to be beneficial because the symptoms she is experiencing are not likely related to her moderate anemia and mild thrombocytopenia. Hydroxyurea, interferon-α, and imatinib can reliably control leukocytosis, thrombocytosis, and splenomegaly caused by CML. Interferon-α and imatinib can also induce cytogenetic responses, which has been associated with improved survival; however, hydroxyurea therapy almost never induces a cytogenetic response. A large, multicenter, randomized trial comparing imatinib with a combination of interferon and cytarabine demonstrated that patients with chronic phase CML are much more likely to attain a complete cytogenetic response when treated with imatinib (76% versus 14.5%) and with markedly less toxicity.[1] Patients with accelerated phase CML can also have major cytogenetic responses when treated with imatinib, although a higher dose than that used for chronic phase CML is necessary,[2] underscoring the importance of accurately characterizing this patient's disease status. AML induction therapy would not be considered here unless the bone marrow biopsy unexpectedly revealed that the patient was in the terminal blast crisis phase of CML.
3. **(B) Hydroxyurea and aspirin.** Hydroxyurea is a well-tolerated oral agent used to control high platelet counts and splenomegaly in patients with ET and other myeloproliferative conditions. Using hydroxyurea to keep the platelet count below $600 \times 10^3/\mu L$ in patients at high risk of thrombotic events has been shown to reduce the risk of thromboses substantially.[3] Aspirin alone will not reduce the platelet count. However, the addition of aspirin is appropriate in patients with platelet counts over $1000 \times 10^3/\mu L$ and/or symptoms of a thrombotic event. Aspirin can also help alleviate symptoms of erythromelalgia, which is common in ET but is not present in this case. Anagrelide has been used as an alternative to hydroxyurea but may be less effective at preventing thrombotic complications and has been shown to have a less tolerable side-effect profile eg, headaches, palpitations, orthostatic symptoms). Interferon-α, although effective at controlling blood counts, is not nearly as well tolerated as hydroxyurea and also has the disadvantage of subcutaneous administration. Although imatinib has been shown to have some effect against other myeloproliferative conditions, its usefulness in ET is unproven.
4. **(D) Phlebotomy and low-dose aspirin.** The mainstay of therapy for polycythemia rubra vera is regular phlebotomy to keep the hematocrit below approximately 45%. This intervention will alleviate symptoms related to increased viscosity. A randomized study has shown the addition of 100 mg/d of aspirin significantly reduces the risk of developing thrombotic and cardiovascular events in polycythemia vera patients.[4] Higher doses of aspirin in this patient group have been associated with an unacceptably high frequency of gastrointestinal bleeding. Because neither splenomegaly nor thrombocytosis are problematic at present, hydroxyurea therapy is not warranted.

## REFERENCES

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