Unneeded testing
continued from page 38

methods of looking for clonal B cell populations, including flow cytometry and immunohistochemistry.

This has been borne out in Mayo’s practice data. In immunoglobulin gene rearrangements ordered on 54 specimens (seven on peripheral blood, 47 on bone marrow), “It appeared to us that all of them were unnecessary.” In some cases, the tests were ordered in a context where there did not seem to be an underlying B cell disorder; in others, the lab already knew the B lymphocytes were clonal, thanks to flow cytometry.

For T cell receptor gene rearrangements in the peripheral blood, Dr. Kurtin and colleagues looked at 294 cases. This time, 171 appeared unnecessary. There were also 25 probable false-positives—exactly the 10 percent incidence that would be expected in elderly patients, he reminded his audience.

What about in bone marrow specimens? Of 172 cases, 136 T cell receptor gene rearrangement studies were unnecessary, he said, with 19 probable false-positives and 12 probable false-negatives.

No use in squirreling away these data. Dr. Kurtin and his lab colleagues shared their findings with their clinicians, and the response of one of the senior hematologists was striking: “These tests are dangerous for patient care,” he told the lab. “Why do you let us order them?”

After a telling pause in his AACR talk, Dr. Kurtin went on to say, “So our recommendation for T cell and immunoglobulin gene rearrangement is that they’re poor screening modalities.” The lab uses them only to resolve specific diagnostic problems posed by morphology and phenotyping.

The algorithm puts the reviewing hematopathologist in the driver’s seat. Mayo’s lymphoma disease oriented group approved several principles regarding test use:

- The reviewing hematopathologist needs to approve cytogenetic test requests for bone marrow evaluations for lymphoma.
- Ditto for lymphoma FISH tests (which can also be approved by a geneticist).
- A hematopathologist needs to approve all immunoglobulin and T cell receptor gene rearrangement requests on blood and bone marrow.

Next up: improving test use for chronic myeloproliferative neoplasms. In this case, there’s plenty of literature on the topic, Dr. Kurtin said.

With numerous genetic tests available, what’s the best way for labs to “string them together,” as Dr. Kurtin put it, to arrive at a diagnosis?

In response, he offered the case of a 71-year-old male with fatigue, and with no hematopoietic- megaly. He was anemic, with normal MCV, WBC, and platelet count, and elevated LDH.

A blood smear revealed abnormal teardrop-shaped red blood cells, which usually indicates fibrosis in the bone marrow, as well as circulating nucleated red blood cells. “You shouldn’t have the rookies in the blood,” Dr. Kurtin said. “You should just have the mature red cells in the blood.” The smear also reveals other “rookies”—circulating left-shifted granulocyte precursors—as well as small megakaryocytes.

What was going on? “It looks like the bone marrow is being replaced by something.”

The test menu is extensive:

- Bone marrow aspirate/biopsy
- Cytogenetic analysis
- JAK2 V617F mutation analysis
- JAK2 Exon 12 sequencing
- cMPL Exon 10 sequencing
- BCR-ABL FISH
- BCR-ABL PCR dx screen
- BCR-ABL p190 quant PCR
- BCR-ABL p210 quant PCR
- MDS FISH
- KIT D816V mutation analysis
- CHIC2 (FIP1L1/PDGFR alpha deletion FISH)

So was the physician’s order, which included the JAK2 V617F mutation analysis on both blood and bone marrow, and most of the other assays on this list.

This came with a hefty price tag. “That is about $5,000 worth of genetic tests,” Dr. Kurtin said.

He and his colleagues bore down. Their first question focused on the aforementioned JAK2 analyses on bone and blood. “If you go to the factory, do you get a higher rate of JAK2 mutations than if you look at the blood? And we looked at that,” continued on page 42