epitope between amino acid residues 32 and 79. Hence, p53 protein over expression as detected immunohistochemically indicates a mutation in the p53 domain of missense type or stabilization of the wild type by either cellular or viral products or the presence of DNA damage by a physical or chemical agent.6-8

Furthermore, from the work of Cavenee, White and Vogelstein on colon, and brain tumors, 6,8 it is widely believed that cancer development will involve mutations and overexpression of several genes. It is not surprising that recent emphasis to study several oncogene expressions that effect the cell at several subcellular levels is becoming more popular.10,11

With these facts in hand, we were not surprised by our finding that several cellular products and oncogene over expressions can serve as auxiliary tools in diagnostic cytopathology and surgical pathology as well. However, it should not at any time substitute morphologic discipline, as message that we hope did not escape our readers.

AIZEN J. MARROGI, MD
Department of Pathology and Laboratory Medicine
 Tulane University Medical Center
 New Orleans, Louisiana

REFERENCES

Ethylendiamine Tetraacetate Acid-Associated Leukoaagglutination

To the Editor—we read with great interest the recent report of Deol and colleagues describing EDTA-associated leukoaagglutination.6 We recently had two patients whose peripheral blood smears showed clumping of leukocytes. The first patient was a 38-year-old male with alcoholic cirrhosis who subsequently died of liver failure. The CBC results were as follows: WBC 10,200/mL; HGB 10.2 g/dL; HCT 33%; MCH 34.9 pg, MCV 113.1 fL; MCHC 30.8%, RDW 16%; and nucleated red blood cells 5/100 WBC. His peripheral smear showed clumping of granulocytes in which bands and segmented neutrophils 13%; lymphocytes 33%; monocytes 8%; eosinophils 4%; RBC 2.92 million/μL; HGB 10.2 g/dL; HCT 33%; MCV 113.1 fL; MCH 34.9 pg, MCHC 30.8%, RDW 16%; and nucleated red blood cells 2/100 WBC. His peripheral smear showed clumping of granulocytes in which bands and segmented neutrophils surrounded more immature granulocytes and/or monocytes. The second patient was a 24-year-old female with toxic shock syndrome whose peripheral smear showed clumping of bands and segmented neutrophils. Her CBC revealed: WBC 22,400/μL; myelocytes 3%; bands 53%; segmented neutrophils 36%; lymphocytes 5%; monocytes 1%; eosinophils 2%; RBC 2.65 million/μL; HGB 8 g/dL; HCT 22.4%; MCV 84.6 fL; MCH 30.1 pg; MCHC 35.5%; RDW 15%; and nucleated red blood cells 5/100 WBC. In both patients, the leukoaagglutination was transient and self-limiting. No apparent cause was found for the leukoaagglutination.

Clumping of leukocytes in the peripheral blood had been described previously in several case reports. Neoplastic lymphocyte clumping was reported in a patient with chronic lymphocytic leukemia by Bizzaro and colleagues2 in 1991 and in splenic lymphomas with circulating villous lymphocytes by Juneja and coworkers3 in 1992 and Imbing and associates4 in 1995. As pointed out by Deol and colleagues, this phenomenon of leukocyte clumping does not only occur in malignant lymphocytes but with benign lymphocytes as well. EDTA is not the only anticoagulant that causes leukoaagglutination. The phenomenon has also been reported with other anticoagulants such as heparin5 and citrate.6 It may also occur with more than one anticoagulant in the same patient. Some investigators have reported that the abnormality is corrected by dilution of the patient serum, but in others, dilution of the serum may worsen the phenomenon.6,7 An IgM autoantibody has been postulated as the probable cause of this in vitro event but in most of the reported cases, the presence of IgM could not be demonstrated.8 In some cases, platelets are agglutinated whereas in others, only erythrocytes, lymphocytes, and/or granulocytes are affected. The only thing that appears to be common to all the reported cases is the association of the event with room temperature.

Therefore, we conclude that EDTA-induced leukoaagglutination is a phenomenon caused by more than one cold agglutinin. Its importance lies in its potential to cause spurious blood count results, thereby causing unnecessary panics and expenses to both physicians and patients. More studies are needed to identify and characterize the culprit autoantibodies.

FAUSTO D. IMBING JR, MD
PATRICK A. ADEGOYEGA, MD
EDDYE MCLUCAS, MT
TAREK ELGHETANY, MD
Division of Hematopathology
Department of Pathology
The University of Texas Medical Branch
Galveston, Texas
REFERENCES


The Authors' Reply

To the Editor—We thank Dr. Imbing and his colleagues for their letter confirming the description of band and segmented neutrophils surrounding immature granulocytes in a blood film from one patient, and clumping of neutrophils in another patient. We assume that these blood films were prepared from EDTA-anticoagulated blood, although this is not stated in their letter. Their conclusion that EDTA-induced leukoagglutination is a phenomenon caused by more than one cold agglutinin needs explanation. First, in our experience the vast majority of cases of leukocyte or platelet agglutination in EDTA-anticoagulated blood will be corrected by collection in sodium citrate or heparin anticoagulant and are not corrected by warming the EDTA blood sample tube. We certainly do agree that some cases are not corrected by sodium citrate or heparin and are corrected by warming to 37 °C. These cases are undoubtedly caused by cold agglutinins, and such cases have been reported in the literature as secondary to cold agglutinins.1-3 We concluded our article with the admonition that if agglutination persists upon collection in sodium citrate or heparin anticoagulant, a cold agglutinin should be suspected.

INDERJIT DEOL, MD
Department of Pathology
Texas Tech University
El Paso, Texas

ANTONIO HERNANDEZ, MD
Department of Pathology
Kaiser Permanente
Los Angeles, California

ROBERT V. PIERRE, MD
Department of Laboratories and Pathology
LAC/USC Medical Center
Los Angeles, California

REFERENCES


Corrections

"In the Pathology Patterns October supplement 1995 (Chmiewleski SA. Advances and Strategies for Glucose Monitoring. Am J Clin Pathol 1995; 104(Suppl)S59-S71), there was an error on p S61. The sentence should have read: "The most recent American Diabetes Association Consensus Conference5 set a goal of ±15% total error at glucose concentrations ranging from 30 to 400 mg/dL."

In the article by Goldstein et al, "Histologic Spectrum of Cryptogenic Chronic Liver Disease and Comparison With Chronic Autoimmune and Chronic Type C Hepatitis in the November issue (Am J Clin Pathol 1995; 104: 567-573), the legend for Figure 5 should have read, "CCLD needle biopsy with portal lymphoid aggregate. Note the histologic similarity with hepatitis C." We regret the errors and any confusion they may have caused.