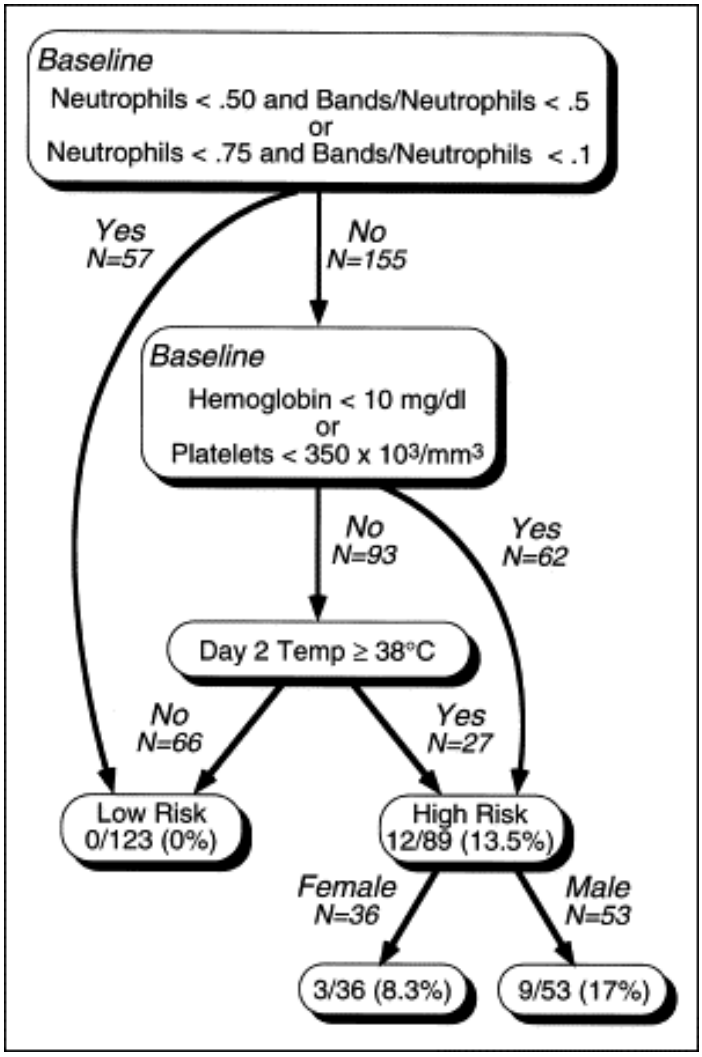
7.1 Predicting coronary artery aneurysms in children with Kawasaki Disease

Kawasaki disease is an acute febrile illness in children of unknown cause that includes a rash, conjunctivitis, inflammation of mucous membranes of the mouth, swollen lymph nodes and swelling of hands and feet. Affected children are treated with intravenous immunoglobulin (IVIG) to prevent coronary artery aneurysms, the most serious complication of the disease. Using data from the intervention groups of two randomized controlled trials of IVIG, Beiser et al(Beiser et al 1998) developed an instrument to predict which children with Kawasaki disease would develop coronary artery aneurysms. The predictive instrument they developed is shown below:



From Figure 1. Beiser AS, et al. Am J Cardiol. 1998 May 1;81(9):1116-20. ***Need Permission***. Neutrophils (also known as polymorphonuclear leukocytes) are one kind of white blood cell. Bands are immature neutrophils. "Neutrophils < 0.5" means that, based on the white blood cell count differential, less than 50% of the white cells are neutrophils. "Bands/neutrophils < .5" means that, of all the neutrophils, fewer than 50% are bands.

a.) At first it might look like Figure 1 was created with classification tree software, such as the rpart routine from the statistical package R. What features of the figure suggest it was not simply the product of classification tree analysis?

b.) Assume you are treating a child like those included in the study. His initial complete blood count shows a hemoglobin of 11.2 g/dL, 600,000 platelets and 13,000 white blood cells/mm^3, with 8,000 (61.5%) neutrophils of which 1,000 (1000/8000 = 12.5%) are bands. On day 2 of the illness his temperature is 38.1° C. Would you classify him as high- or low- risk ?

c.) Now imagine the patient is at low risk. Does this mean you don't need to treat him with IVIG? Why or why not?

d) In a study such as this, it is important that the clinical prediction rule be validated on a group of patients separate from the group used to derive it. The abstract of the study states:

"The instrument was validated in 3 test data sets…[it] performed similarly in the 3 test data sets; no patient in any data set classified as low risk developed coronary artery abnormalities."

However, the methods section states:

"We developed many such [sequential classification] processes, each using a different combination of risk factors…Instruments that performed well on the development data set were validated using each of the 3 test data sets."

Is there a problem here? If so, what is it and how would it affect the results?