

Hyperplastic Areas, Hyperplastic Nodules, and Hyperbasophilic Areas as Putative Precursor Lesions¹

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By way of introduction to the session on liver, I would like to orient the audience very briefly to the current thinking on precursor lesions in liver carcinogenesis. As you are no doubt aware, the liver has been a favorite object for studies in chemical carcinogenesis. This has led naturally to a faster development of concepts than in some other organs. Included in this is the delineation of reasonably clear-cut new hepatocyte populations as presumptive precursors, either immediate or remote, for liver cancer. There are now known 4 hepatocyte populations that seem to be involved in liver carcinogenesis. These are: (a) hyperplastic or enzyme-deficient areas, islands, or foci; (b) early hyperplastic nodules; (c) late hyperplastic nodules (neoplastic nodules); and (d) hyperbasophilic foci.

The properties of these hepatocyte populations that have been described are outlined below.

- I. Properties of hyperplastic areas (1, 11, 15, 22, 26-29, 36, 39-44, 48).
 - A. Low or deficient in
 1. Glucose-6-phosphatase
 2. Nucleotide polyphosphatase ("ATPase")
 3. β -Glucuronidase
 4. Serine dehydratase
 5. Glycogen phosphorylase
 - B. Decreased breakdown of glycogen
 - C. Disturbance in iron uptake or metabolism
 - D. Contain cells in mitosis
- II. Properties of hyperplastic nodules—early or late (2-4, 6, 7, 10, 12-18, 20, 21, 23, 25, 30-34, 37, 38, 45-47, 49)
 - A. Disturbances in carbohydrate metabolism
 - B. Loose open chromatin structure
 - C. Altered DNA appearance
 - D. Resistance to cytotoxic action of carcinogens or hepatotoxins
 - E. Slow cell proliferation
 - F. Abundant smooth endoplasmic reticulum
 - G. Disturbance in iron uptake or metabolism
 - H. PN antigen
 - I. Organized in 2 or more cell thick plates, tubules, etc.
 - J. Early: differentiated with maturation to adult-like liver and loss of preneoplastic antigen
 - K. Late: little or no differentiation or maturation
- III. Properties of hyperbasophilic foci (5, 8, 9, 19, 24, 25, 35)
 - A. Hyperplastic nodule—at least 1 site of origin
 - B. Decrease in RNase and DNase activities

C. ATPase activity over whole cell surface histochemically

D. Ultrastructurally resembles liver cancer

It is generally believed that all 4 hepatocyte populations are precursor lesions for liver cancer in many instances. These and many other aspects will be covered in detail in the following presentations.

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