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Hyperplastic Areas, Hyperplastic Nodules, and Hyperbasophilic Areas as Putative Precursor Lesions[1]

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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 endoplastic 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.

[1] Introduction to Session on Liver, at the Conference "Early Lesions and the Development of Epithelial Cancer," October 21 to 23, 1975, Bethesda, Md.

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