Liver biopsy in 2000. The pathologist’s view
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In spite of tremendous progress in virology and molecular biology with numerous applications in noninvasive diagnostic methods, at the end of this millennium liver biopsy still remains the gold standard by which other modalities to evaluate the liver are judged (1).

In the year 2000...as before...the pathologist has to remain aware that the diagnostic usefulness of liver biopsy changes over time (2). He or she may expect to be less often confronted with pathology of acute hepatitis, and problems of differentiation between intra- and extrahepatic cholestasis, and other conditions such as hemangiommas and focal nodular hyperplasia; these diagnostic problems will be resolved by the clinician with other methodologies such as serology and imaging techniques. Instead, he or she may expect to be less often confronted with pathology superimposed on the main clinical suspicion (3). For these goals, as in the past, an intelligent collaboration between clinician and pathologist is imperative. As such medical teamwork is still rather the exception than the rule, further integration of pathology into clinical medicine will remain a necessity in the next millennium.

Besides the classical indications and methods of examining and reporting liver biopsies, the pathologist active at the turn of the millennium should pay particular attention to actual and future needs. The following lines mention a nonexhaustive enumeration of some general examples.

Liver biopsy will remain useful in chronic liver diseases, as noninvasive methods for assessment of liver fibrosis remain inadequate (4). However, for the pathologist this implies that grading of disease activity and staging of disease progression should be specified as much as possible, and not only in chronic hepatitis (5). In the appropriate setting, grading and staging can be achieved with the use of semiquantitative scoring systems (6). As the number of new drugs of potential use in liver disease will undoubtedly increase, there will be a growing need for further refinement of semiquantitative scoring procedures for comparison of pre- and post-treatment states. With further progress in computer-assisted analysis and digital display, automated and interactive image analysis will become of greater diagnostic importance. Presumed first applications are quantitation of liver fibrosis and pattern recognition diagnosis of liver cirrhosis.

Refinements of biopsy techniques will render the biopsy procedure less dangerous, also in view of tumor spread in case of liver malignancy (7). As a result, the pathologist will have to deal more and more with early and premalignant changes in liver tumor pathology; this will in parallel increase his/her role in patient care and surveillance. An example is the investigation of “irregular regeneration” in chronic viral hepatitis C (8). The diagnostic yield of liver biopsy will further be increased by application of immunohistochemistry and in situ hybridization. Further work is needed to increase the number of new applications and to improve the reliability of existing ones (e.g., in situ demonstration of viral antigens in viral hepatitis C, and search for markers of autoimmune hepatitis).

Introduction of immunostains in various diagnostic areas leads to better yields in finer diagnostic precision. Examples are immunostains for “bile duct-type” cytokeratins in chronic cholestatic liver disease, and demonstration of proteins in endoplasmic reticulum storage disorders (9).

Thoughtful application of immunostaining and electron microscopy may assure original results, like recognition of hitherto unrecognized tumor entities (10). As was the case before, one may guarantee that liver biopsy will reveal an unexpected diagnosis (11), or unveil additional pathology superimposed on the main clinical suspicion (3).

Above all, pathologists should continue to use their inventiveness in order to meet the challenge of the future and to maintain the position of liver histopathology as the gold standard and cornerstone in the diagnosis of liver disease.

References