Special Section

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Introduction

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This conference assembled an international group of nearly 200 research-minded gastroenterologists in the renowned Gewandhaus of Leipzig to update the current status and discuss future perspectives of novel topics relevant to clinical gastroenterology and hepatology. The topics were presented by 33 experts in 8 different sessions on diseases of the stomach and duodenum, liver and bile ducts, pancreas, jejunum and ileum, cancer, diagnostic procedures, and two sessions on treatment. Two lunch poster sessions allowed young investigators to present their data.

Concepts on the pathophysiology and treatment of peptic ulcer diseases of the stomach and duodenum have been fundamentally changed by the discovery of gastric mucosal infection with the pathogenic bacterium, Helico-bacter pylori. Dr. Thomas Kirchner, University of Erlangen, showed how H. pylori induces chronic gastritis, clonal expansion of B lymphocytes and occasionally even malignant B-cell lymphoma of the stomach. Nearly 75% of gastric lymphomas may be curable in the early stage just by the antibiotic eradication of H. pylori. Dr. John DelValle, University of Michigan Ann Arbor, reviewed the mechanisms of hormonal and paracrine regulation of gastric acid secretion and showed how gastric acid secretion is stimulated by lymphokines released in response to the infection with H. pylori. Dr. George Sachs, University of California Los Angeles, who developed the gastric proton pump inhibitor drugs, presented data on the induction of gastric mucosal H+K+-ATPases by H. pylori. The sequence of events leading from H. pylori antral gastritis to duodenal ulcer disease was analyzed by Dr. Peter Malfertheiner, University of Magdeburg. He also evaluated the epidemiology of H. pylori gastritis and forecast the impact of improved sanitation and future vaccination on the decline in prevalence of H. pylori infection and consequently on the reduction in the incidence of peptic ulcer disease, gastric lymphoma and carcinoma. An evolving concept in the physiology and pathophysiology of liver cell regulation is the finding of Dr. Dieter Häussinger, University of Düsseldorf, that the degree of osmotic cellular swelling regulates the state of activation of the cell cycle, protein synthesis, carbohydrate metabolism and biliary secretion of liver parenchymal cells. The signal of osmotic swelling is transduced by activation of G proteins, tyrosin kinases and mitogen-activated protein kinases. Dr. Alan Hofmann, University of California San Diego, reported on recently cloned plasma membrane transport proteins of the liver cell and how, on a molecular basis, they can account for several cholestatic disorders. The current understanding of the pathogenesis of cholesterol gallstone disease and the overall futile attempts to prevent the recurrence of gallbladder stones after successful nonsurgical therapy have been critically analyzed by Dr. Thomas Holzbach, Cleveland, Ohio.
Nevertheless, the lack of simple prophylactic strategies leaves the treatment of gallbladder stone disease to the surgeons. Dr. Hubert Blum, University of Freiburg, summarized that chronic viral hepatitis B and C are cured by standard interferon-\(\alpha\) therapy in only about 30% of cases. Recent phase-I clinical trials on combination therapy of new antiviral drugs, mainly nucleoside analogs, with interferon-\(\alpha\) show promise with regard to doubling the cure rates. The hepatitis G virus recently isolated by differential molecular cloning is about as prevalent as the hepatitis C virus in patients with chronic liver diseases or persons at risk of parenteral infections. However, con-

The model of the exocrine pancreatic acinar cell has served to promote the basic cell biology of signal transduction, exocytosis, secretion of proteins, growth and replication of epithelial cells (Dr. John Williams, University of Michigan Ann Arbor). Autodigestion by the pancreas is induced in the pancreatic acinar cell by missorting of digestive enzyme precursors into lysosomes which activate these enzymes to digest membrane phospholipids and destroy cellular organelles (Dr. Michael Steer, Harvard Medical School, Boston, Mass.). The programmed suicide, apoptosis, of the pancreatic acinar cell has turned out to be an important mechanism in the protection from acute pancreatitis. Dr. Guido Adler, University of Ulm, reviewed several novel specific inhibitors that enable the manipulation of the complex neurohumoral regulation of the exocrine pancreas. These inhibitors, however, have not proven effective in the treatment of acute pancreatitis, as they cannot interrupt the autodigestive process once it has been started. Dr. Jean-Charles Dagorn, University of Marseille, demonstrated that pancreatic acinar cells secrete heat-shock proteins in response to inflammatory stimuli, a fundamental mechanism of cell protection for which the entire spectrum of actions has not yet been defined. New therapeutic strategies should now arise from the advances made in the cell physiology of the exocrine pancreas. The neurohormonal regulation of intestinal motility and pancreatic exocrine secretion was reviewed by Dr. Eugene DiMagno, Mayo Clinic, Rochester, Minn. Several novel peptide hormones have been characterized from endocrine and paracrine cells in the small bowel; some of
them have therapeutic potential (Dr. Wolfgang Schmidt, University of Kiel). For example, the peptide, GLP-1, can in part correct the disordered secretion of insulin and glucagon in type-II diabetes mellitus. Dr. Ulrich Fölsch, University of Kiel, reviewed the growth regulation of the intestine and pancreas by growth factor peptides, e.g. IGF-1, which holds therapeutic promise for the management of short bowel syndrome. The concepts on the pathogenesis of chronic inflammatory bowel disease have greatly advanced over the past few years (Dr. Martin Zeitz, University of Saarland, Homburg). In Crohn’s disease the response of the TH1-helper-type lymphocytes prevails with resulting granulomatous inflammatory reaction, whereas in ulcerative colitis the TH2-type response of helper lymphocytes induces mixed lymphocytic and granulocytic infiltrates and autoantibody formation. Intestinal bacteria may trigger the pathogenic immune response, because the lymphocytes in ulcerative colitis are sensitized specifically against bacterial antigens of the intestinal microflora. Furthermore, transgenic mice with disruption of lymphokine genes express ulcerative colitis pathology only when exposed to intestinal bacteria.

In the field of gastrointestinal oncology, minimally invasive endoscopic procedures have been introduced for therapy of early gastric cancer in Japan. Dr. Tetsuichiro Muto, University of Tokyo, demonstrated how early gastric carcinomas of ≤ 20 mm diameter can be removed by endoscopic mucosectomy. In all likelihood (> 95%) early gastric carcinomas of this small size have not yet undergone metastatic spread. However, these patients are predisposed to other carcinomas, e.g. of the bronchial tree, the colon, liver, prostate or breast. This suggests some genetic predisposition to cancer formation and mandates follow-up examinations. Enormous progress has been made in the molecular biology of carcinogenesis which has been reviewed for pancreatic carcinoma by Dr. Wolf Schmiegel, Ruhr University of Bochum, for colonic cancer by Dr. Young S. Kim, University of California San Francisco, and for hepatocellular carcinoma by Dr. Michael Manns, University of Hannover. New ways are being explored to characterize specific mutations of oncogenes, tumor-suppressor genes and DNA mismatch repair enzyme genes with the aim to assess the individual risk for cancer in cancer family syndromes, thereby offering prophylactic surgical strategies to high-risk individuals, and to predict the individual risk of disease recurrence after curative surgery. Adjuvant chemotherapy after resection of colonic carcinoma in tumor stages II and III has made it possible to double the rate of definitive cure. Only minor progress has been made in the palliative management of advanced gastro-intestinal cancers. New experimental data hold promise for future gene therapeutic approaches to cure cancer even in advanced stages. Diagnostic procedures in gastroenterology have now reached technical perfection in endoscopic and most endosonographic tools as outlined by Dr. Friedrich Hagenmüller, Hamburg, and Dr. Thomas Rösch, Technical University of Munich. Further progress can be expected in the miniaturization of endoscopes and in the development of minimally invasive endoscopic procedures with laser technology and endosonographic localization techniques. Some diagnostic endoscopic techniques, such as colonoscopy and endoscopic retrograde cholangiography, will soon be replaced in part by alternative virtual reality CAT and magnetic resonance imaging techniques. In the near future major emphasis will be on

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outcome research to define reliable and cost-efficient diagnostic and therapeutic strategies. Dr. Christian Wittekind, University of Leipzig, reviewed the booming developments that have occurred in immune histochemistry diagnostics since the advent of monoclonal antibody technology. This has led to immunochemical characterization and typing of carcinomas, malignant hematopoietic cells, lymphomas and melanomas, and enabled the demonstration of specific hormone receptors of therapeutic relevance on malignant cells. A new area of RNA and DNA in situ hybridization techniques has now begun which is presently revolutionizing the diagnostics of genetic and viral diseases.

Dr. Burkhard Goeke, University of Marburg, presented an overview of the wide array of molecular diagnostic tools under exploration for diseases of the liver, pancreas and gastrointestinal tract. He especially stressed novel approaches to predict prognosis and therapeutic response from in vitro tests on malignant cells.

Two sessions were dedicated to the standards and perspectives of treatment of gastrointestinal diseases: new strategies for the design and evaluation of new drugs of the cell receptor agonist and antagonist classes (Dr. Robert T Jensen, National Institutes of Health, Bethesda, Md.); current status of immunosuppressive therapy (Dr. Jürgen Schölmerich, University of Regensburg); the present onset and perspectives of gene therapy (Dr. Marshall Kaplan, Harvard Medical School, Boston, Mass.); the current status of endoscopic invasive procedures for upper gastrointestinal bleeding (Dr. Wolfgang Fleig, University of Halle); the place of extracorporeal shock wave litho-tripsy in the therapy of gallstones and pancreatic stones (Dr. Tilman Sauerbruch, University of Bonn), and the benefit of lasers for ablation of vascular and malignant neoplasias and for photodynamic therapy of malignant tumors (Dr. Jürgen F. Riemann, Ludwigshafen). New trends and established procedures were assessed for minimally invasive abdominal surgery (Dr. Karl-Hermann Fuchs, University of Würzburg) and for organ-preserving surgery of the liver, biliary tract and pancreas (Dr. Waldemar Uhl, University of Berne).

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