
'Understanding the Development of Pancreatic Cancer Will Emerge from Basic Research'

An Interview with Prof. Hans G. Beger

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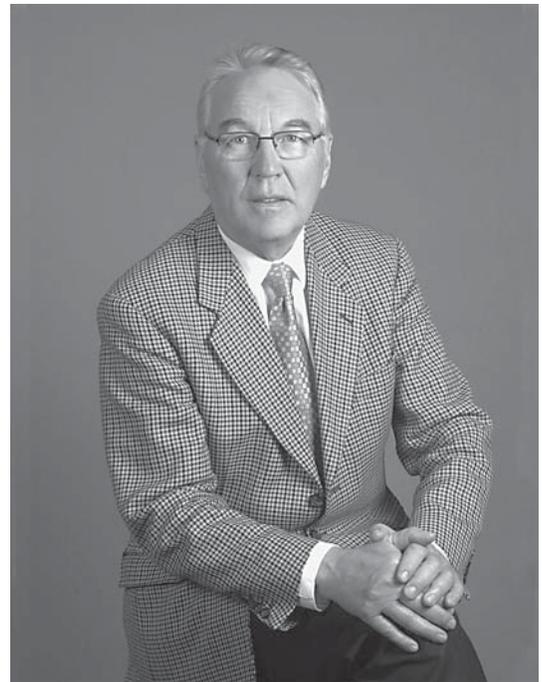
Abstract

Prof. Hans Beger is a worldwide-recognized pancreatologist in the treatment of pancreatic diseases. He led the way in pancreatic surgery with the development of a classic intervention: the Beger procedure for the treatment of chronic pancreatitis. In this interview for *Pancreatology* Prof. Beger shares his life experiences as a scientist in pancreatic research.

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M.F.-Z.: What initiated you to work in pancreas research in the first place?

H.B.: My interest in the pancreas was first stimulated by Dr. Emil Sebastian Bücherl, Chairman and Professor of Surgery at the Free University of Berlin, who always referred to the pancreas as the only easily accessible organ in the human body. During my residency, clinical observations such as systemic complications of pancreatitis also contributed to the development of my interest for this organ and generated many a hypothesis at the time. As senior resident at the Free University of Berlin I saw patients suffering from severe acute, necrotizing pancreatitis in the intensive care unit. The risk of the autodigestive tryptic capacity of the pancreas was frequently demonstrated in patients suffering from this condition; they mostly died despite intensive care management. Autopsy



analyses together with the pathologist Prof. Volker Becker frequently revealed an extended necrotic process in the retro-peritoneum as a possible cause of the multi-systemic organ failure. In consequence, we started to identify patients who may benefit from surgical debridement. In

cooperation with the Radiology Department, we measured the preoperative amount of necrosis and, intraoperatively, the wet weight of the dissected necroses.

In addition to my clinical experience, my interest in pancreatic research was also fuelled by my studies on binding and elimination of insulin from the liver at the Surgical Department in Berlin. In these experiments we measured the insulin clearance of the liver in diabetic patients, most of whom were suffering from chronic pancreatitis. Many of the patients with chronic alcoholic pancreatitis who received surgical treatment suffered from a suppression of insulin secretion. Almost every patient with chronic pancreatitis we operated had an inflammatory mass at the head of the pancreas. These observations lead to the proposition that Kausch-Whipple resection in chronic pancreatitis was unnecessary due to the benign characteristics of this disease and the lack of involvement of the stomach, biliary tree and duodenum. At the same time, experiments in dogs undergoing a subtotal pancreatic head resection with preservation of the arterial and venous blood supplies and of the duodenum, body and tail of the pancreas resulted in the development of a procedure that can be done without disturbing the arterial supply to the duodenum – if we preserve the dorsal capsule of the pancreas and resect the pancreatic head, including the uncinate process up to the intrapancreatic segment of the common bile duct. I learned from these animal experiments that it is unnecessary to perform a major oncological resection of the pancreatic head in human chronic pancreatitis. In the animals the anastomosis between the jejunum and the left pancreas was ensured as a way of binding the pancreatico-jejunostomosis with the jejunal loop, which was deprived of mucosa for a length of 2–3 cm. To our surprise, no fistulation developed in the animals.

M.F.-Z.: You have pioneered pancreas research in so many directions. At the end of the day, what has given you most personal satisfaction?

H.B.: I get a lot of satisfaction from my experience in pancreatology, but I have to confess that the successful translation of ideas that were generated by clinical observations in the intensive care unit and in the operating room into successful animal experiments and patient treatments gives me great pleasure. Still today, the successful bedside application of experimentally tested ideas is a major source of satisfaction in my professional life. For example, in necrotizing pancreatitis we observed that one-staged necrosectomy with drainage initially did not resolve the systemic complications. At that time we measured only a few cytokines but many prostaglandins and

endotoxines in the systemic circulation and in the drainage fluid. As a consequence of finding high concentrations of these biological active compounds in the postoperative period, we added a system of closed lesser sac lavage to surgical debridement, which we had learned from nephrologists using peritoneal lavage. This application of combined surgical and postoperative lavage procedures resulted in a dramatic decrease of morbidity and hospital mortality in many patients.

Similarly, we have been able to demonstrate the preservation of GI tract functions after a subtotal resection of the pancreatic head conserving duodenum, stomach, spleen, common bile duct and 60–70% of the pancreas in animal experiments as well as in a clinical setting at the Department of Surgery at the Free University in Berlin. It continues to give me enormous satisfaction that surgeons the world over are able to perform duodenum-preserving pancreatic head resection in hundreds of patients, enabling them to maintain their careers and have pain-free lives.

It is also a constant personal satisfaction to experience – particularly during the numerous hours in the research laboratory and operating theatres during day and night time – personal relationships with surgical colleagues who accompanied my research time. These personal relationships are still alive today.

M.F.-Z.: Based on your experience as mentee and mentor, can you comment on the value of mentorship for the development of a new investigator?

H.B.: During my career as a surgical scientist I was fortunate to have, from the beginning, a mentor who supported my interest in surgical research with intelligence and generosity. Throughout my career as an academic surgeon I experienced pleasure and satisfaction to motivate students and residents for surgical research projects, to support their career with a research fellowship in internationally established research institutions and to guide their career as academic surgeons. In my experience mentoring is one of the most precious tasks of a chairman; good mentoring usually results in a very successful career of the mentee and a life-long friendship.

M.F.-Z.: What is the best advice you received during your career? What is your advice to the young investigators that are beginning in the field of pancreas research?

H.B.: ‘Do not observe a patient with your textbook in mind, but with intelligence and awareness of the individual pattern of a disease.’ Dr. Ben Eiseman in Denver gave this advice many times during our rounds in the intensive care unit and in the operating theater.

Once a clinical observation has led to a hypothesis, focusing on the research topic is important for the success of a young investigator. In addition, for the last 10–15 years I tried to guide young colleagues to start with basic science research; I believe that the major contribution in understanding the pathogenesis of pancreatic diseases will come from this field. It is extremely important for a young investigator to become familiar with the methods used in research projects. In spite of a well-established section of molecular oncology with highly competent technicians, each investigator needs a trainee period to acquire reliable competence in the use of basic science methods before starting his research project.

M.F.-Z.: What do you think are the big questions that need to be answered in pancreatology?

H.B.: As a clinical surgeon I think the biggest challenge in pancreatology is how to manage pancreatic cancer patients on the basis of individual treatment options and to translate surgical and oncological skills into a survival benefit with preserved quality of life. Since many institutions worldwide are able to perform resection for pancreatic cancer without hospital mortality, oncologic surgical treatment contributes significantly to a survival benefit. However the majority of patients presently do not come to treatment in a stage of resectability of the cancer. Understanding the development of pancreatic cancer will emerge from basic research; take the knowledge regarding early neoplastic lesions that is now emerging from the definition of PanIN in the pancreas. The big

question is: How can we detect early PanIN II and PanIN III lesions to prevent the development of advanced pancreatic cancer?

In patients suffering from inflammatory diseases of the pancreas major questions include:

- How does alcohol change the integrity of pancreatic acinus cells? What is the first hit causing pancreatitis?
- In severe acute, necrotizing pancreatitis, which patient may benefit from medical treatment, including antibiotics, rather than undergoing surgical necrosectomy? There is some evidence that antibiotic treatment changes the complicated course of severe acute pancreatitis.

M.F.-Z.: What do you think is the major need that a journal like *Pancreatology* should fill?

H.B.: The future of *Pancreatology* is certainly connected with publishing high-quality scientific papers from clinical and basic research. Particularly in this day and age, when fundamental new knowledge from basic research is almost constantly changing our understanding of the field, good overview articles are extremely important. They should be written by clinical experts with expertise in basic research so that the latest knowledge derived from basic research data can be translated into clinical decision making.

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