Meet the Champions

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# 'Mentoring Is about Inspiring Interest and Excitement in Others'

**An Interview with Charles Frey, MD, Professor Emeritus, University of California, Davis, Calif., USA**

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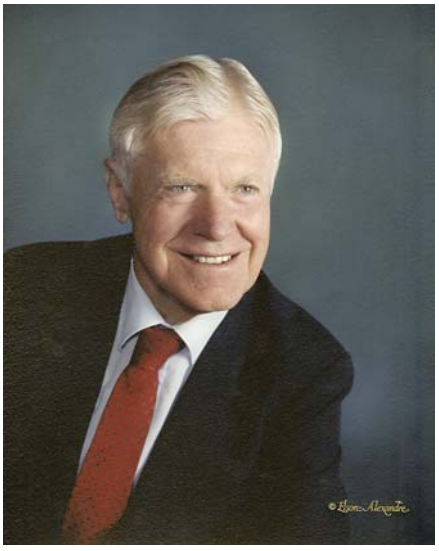
**Abstract**

Prof. Charles Frey led the way in the field of therapeutic approaches in pancreatic diseases by developing one of the most frequently used surgical operation: the Frey procedure for chronic pancreatitis. In this interview for *Pancreatology*, Prof. Frey shares his life experiences as a pancreatologist and provides advice to young pancreatic researchers.





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*Prof. Charles Frey*

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

**C.F.:** This was a process that evolved over 9 years. In 1954, while a 3rd-year medical student assigned to the Surgical Service at Cornell Medical School, a 41-year-old man was admitted to the surgical service early in the morning with severe acute pancreatitis. The night before he had had a heavy meal accompanied by alcohol. Over the ensuing days he showed classical signs of shock with tachycardia, cold clammy skin and onset of oliguric renal failure. He died about 2 weeks later. None of the professors seemed to know much about pancreatitis. I was curious to learn more about this mysterious and sometimes deadly disease. Later, as a surgical resident at the New York Hospital (Cornell's teaching hospital) and after a 2-year stint in the Air Force between 1957–1959, I began to focus my reading on the pancreas. I read everything I could on the subject. Then I looked through over 500 charts to learn about the natural history of the disease. As a result of this review I noted the frequency of renal failure in 490 patients hospitalized with acute pancreatitis. Of 111 patients with elevated blood urea nitrogen levels 92 died. Only 6.6% of the 111 patients had preexisting evidence of renal disease [Frey CF: American Journal of Surgery, 1965]. A number of national presentations and additional publications on childhood pancreatitis, post-

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operative pancreatitis and biliary pancreatitis resulted from this review. The review also provided me with a focus for my research year after completion of my clinical training, i.e. to understand better the relationship between severe acute pancreatitis and its initiation of renal failure. Soon surgical attendings were asking me to consult on their patients. This was heady stuff for a surgical resident. Study of the pancreas as a career choice was a perfect fit for me as I found doing something needed provided me with the most satisfaction. There were not many fields more neglected than that of the exocrine pancreas. In the context of the times, almost all NIH research funds were directed at research in portal hypertension or peptic ulcer disease and most surgeons going into academic surgery were not stupid. Like Willie Sutton they 'followed the money'. I had nothing per se against 'following the money', but I wanted to do something where I was needed. That was not the case in peptic ulcer and portal hypertension research. There was no shortage of capable young surgeons (or mentors for them) wanting to work on peptic ulcer disease and portal hypertension. In contrast, there were few young surgeons (or knowledgeable mentors available for them) wanting to work on the pancreas. I went into a field which had been neglected in part because at the time the pancreas could not be imaged or easily studied and there was virtually no NIH funding. Surely, I was taking the path less traveled, but the need to improve our understanding of pancreatic disease was great and few were taking up the challenge. Here was an area where I might do something useful and make a contribution.

**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?

**C.F.:** I've gotten tremendous satisfaction from my work and collaborations with others working to increase our understanding of pancreatic disease. Two projects stand out. (1) It has now been 20 years since Jeff Smith and I described the operation 'the local resection of the head of the pancreas combined with longitudinal pancreaticojejunostomy' (LR-LPJ) [Frey CF: Description and rational of a new operation for chronic pancreatitis. Pancreas 1987;2:701–707]. Over the years, it has become one of the three frequently used procedures in the management of pain and some of the complications of chronic pancreatitis. The LR-LPJ is simpler to perform than pancreaticoduodenectomy, yet it is equally effective in the relief of pain and results in a better nutrition and quality of life. The duodenal preserving head resection of Beger is also a better operation than pancreaticoduodenectomy for patients with chronic pancreatitis. Strata's randomized controlled study with an 8.5-year follow-up reported in the *Annals of Surgery* in 2005 compared the LR-LPJ operation to the duodenal preserving head resection of Beger. In this large study with a very long follow-up, Strata and Izbicki found no differences in pain relief or quality of life between the two operations. The only difference between the two operations: LR-LPJ is easier to perform. (2) To prove there is a life after retirement, 3 years ago and 6 years after my retirement, as a result of discussions and a challenge by Clem Imrie and John Neoptolemos, I became interested in population-based studies of acute pancreatitis. To date two publications have resulted derived from a database of 84,000 patients hospitalized in California with their first attack of pancreatitis between 1991–2001. These are the first population-based studies on acute pancreatitis published in the United States in over 40 years. Without abundant help from my good and very generous friend Richard White, Professor and Chief of the Section of Internal Medicine at UC Davis, these publications would not have been possible. Richard possesses grant support, computer programming, statistical skills and experience with population-based studies and databases, all areas in which I am deficient. So in my dotage I am back to being mentored and I have a very good one!

**M.F.-Z.:** Based on your experience as mentee and mentor, are you able to comment on the value of mentorship for the development of new investigators?

**C.F.:** There was no one in the New York Hospital's Department of Surgery who was involved in pancreatic surgery or research at the time, so I had no direct mentoring, but I did have a lot of encouragement regarding my pancreatic interests and confidence building from John Beal who was in charge of the Surgical Research Unit, my chairman Frank Glenn and George Wantz, a vascular and portal hypertension surgeon. As a young faculty member at the University of Michigan I was provided laboratory research funding and clinical direction from Gardner Child, Chairman of Surgery. Taking the road less traveled is not, however, without risks and bumps. Gardner Child had arranged for me to spend a year in the Department of Physiology, which I had requested in pursuit of my pancreatic interests. Apparently, the communication had not been very specific about my duties. When I presented myself to the Chair of Physiology I was told I was to spend the year under his direction doing test tube experiments related to gastric physiology. Alternatively, I asked if he would help me instead with pancreatic physiology. It was made clear this was not an option.

I continued to decline to do gastric physiology. I guess the Chairman of Physiology took my refusal as a sign of my stupidity and poor judgment or a personal insult and terminated my year in physiology. It was a demoralizing experience as a new arrival to the Department of Surgery to have to report to Gardner Child my research year in physiology was over soon after it began. However, Gardner stood by me and funded my research in the surgical research laboratory. During that year I studied the effects of acute pancreatitis on renal function in dogs, developed various models of acute and chronic pancreatitis and received an NIH grant for a germ-free pig model of acute pancreatitis. In dogs with untreated severe acute pancreatitis, I found renal function as measured by blood urea nitrogen, creatinine and para-aminohippuric acid clearances to be impaired and that this was associated with increased renal vascular resistance. I further found that renal failure, but not a fatal outcome, could be prevented by fluid administration; that antibiotics improved survival, but did not prevent renal failure [Frey CF, Brody GL: Archives of Surgery, 1996]. Dealing with adversity I believe builds character and I had been given an unexpected and unwanted dose of it. I found it ironic when many years later it turned out that the multimillions of dollars the NIH had spent on funding peptic ulcer research, which had been the path most traveled for young surgical investigators, was off target. Sometimes the seemingly risk-free path most often taken is the road to nowhere, mediocrity or like the lemmings takes you off a cliff. Don't be afraid to innovate, or be deterred from your goals by others' advice whose motives may be obscure or in their own self-interest.

My greatest inspiration in my early professional years came from a small group of surgeons and gastroenterologists (10) from disparate locations in the United States and Canada who formed the Pancreas Club. The first meeting of the Pancreas Club was organized by Marion Anderson at Northwestern University Medical School in Chicago. Marion was at the time an Associated Professor of Surgery. Nine individuals were at the first meeting. Two were from Canada, Francis Gurd and Alan Thompson from Montreal General Hospital; Max Rittenbury from Charleston, South Carolina, and Larry Carey from Ohio State in Columbus, Ohio. These individuals were known to have been present from a surviving agenda of the first meeting which listed the presenters and their topics, but no record of the other attendees survived. When attempts were made in the mid 1990s to determine the other 4 participants, it was not possible. Those known to have been at the meeting could not agree on who was there, and some of those who were thought to have been there denied that they were. And those who insisted they had been present, their presence was denied by those known to have been present. (I understand now why history is difficult to reconstruct accurately!) Topics of the first meeting were the role of proteolytic enzymes in acute hemorrhagic pancreatitis, and vascular changes in hemorrhagic pancreatitis. The second meeting of the Pancreas Club was in Philadelphia hosted by John Howard. The third meeting was in San Francisco hosted by the Chairman of Surgery Leon Blum (father of US Senator Dianne Feinstein). This was the first meeting I attended along with the 5 original presenters plus Tom White from Seattle, John Howard from Philadelphia, Bill Schiller from Northwestern, Robert Herrman from the Cleveland Clinic, George Nardi from Massachusetts General Hospital, Dan Elliott from Pittsburg, George Jordan from University of Texas Houston, Warren Nugent from the Lahey Clinic, Alan Thal from University of Kansas, David Dreiling from Mount Sinai Hospital New York, Morton Grossman and Bernard Haverback from the Veterans Hospital UCLA. The members were committed to unraveling the mysteries of pancreatic disease. At our annual meeting, we looked forward to sharing and critiquing each others' ideas. We became a band of brothers, as we felt isolated and lonely at our individual universities in the absence of having anyone there to share our pancreatic interests. I later co-chaired this club with Bill Schiller for 20 years as it blossomed into an international forum with more than 300 members. As our official club T-shirt says, 'I love the pancreas'. The complete history of the Pancreas Club Inc. up to the year 2004 is available in the February 2004 supplementary issue of the *Journal of Gastrointestinal Surgery*. This history of the Pancreas Club also includes vignettes on about 100 pancreatologists who describe how they became interested in the study of pancreatic disease, as well as information about other pancreatic clubs and associations from around the world. At the present time, the Pancreas Club Inc. has about 300 members from around the world. The club hosts an annual scientific meeting held on Sunday, the day before the start of the DDW at a university facility in the same city as the DDW. Information about the meeting and a shortened version of the history can be obtained on the Pancreas Club Inc. website (www.pancreasclub.com). The club is informal and anyone who has an interest in the pancreas can join by paying the dues. The Pancreas Club is famous for not only having annually an outstanding scientific program, but an annual dinner of culinary excellence. The Club has outstanding leadership in Bill Tra-

verso of the Virginia Mason Clinic, Bill Nealon of the University of Texas, Galveston, and Douglas Evans of the University of Texas MD Anderson Cancer Center, Houston, Texas.

Mentoring to me is not giving younger colleagues advice, unless requested, but inspiring interest and excitement in others about the pancreas through your own enthusiasm and knowledge of the subject. Assisting in the development of skills essential to success, providing access to leaders and opinion makers and those who could help further their careers, providing encouragement and financial support to allow them to explore their ideas is important in mentoring.

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

**C.F.:** The best advice I ever received was from my father, a PhD Biochemist and Director of Research for Standard Brands (later taken over by Nabisco and then by R.J. Reynolds). He often told me stories which illustrated the importance of pursuing a career path that you found interesting and challenging and for which you had some talent. He assured me that in the long run such a course would bring me more happiness than making career choices based on financial rewards or what might seem expedient at the moment. Conversely, don't pick a career in pancreatic research because you are trying to please some one other than yourself. If you do make this mistake, happiness is elusive and it's hard to maintain the intensity of effort and necessary focus essential for success. He also emphasized the importance of setting goals. The need to have a flexible plan to reach those goals, as events not under one's control may require changes in strategy and tactics. If you hit a brick wall in your research, don't keep pounding your head against it, but seek a way around it. To be successful it is necessary to keep learning after your formal education has been completed, to keep acquiring new skills, to keep focused to prevent getting deflected by distractions from one's goals, to recognize the need for persistence and hard work, to solve a problem when needed by collecting the pertinent facts and analyzing them, to communicate clearly and accurately, and, most important of all, to be honest and fair to others. The origin of this advice was not limited to my father, but was reinforced by many of my professors and peers. You would be justified in asking: are not these the musings of a workaholic? Yes, balancing family and career is difficult, and choices must be made, but don't work out solutions on your own; involve your family before making commitments that will effect them.

If asked for advice, read extensively in your field of interest, so you can acquire an understanding of what is known and what are the important unanswered questions. Acquire the skills and tools needed in your research whether it is molecular genetics, computer programming, statistics, etc. Focus on one or two of the yet unanswered questions, which you think are both important and achievable. Develop a hypothesis which can be examined with the tools and resources currently available. Do not be afraid to challenge conventional wisdom, when your own reading and data convince you it is incorrect. Do not be afraid to take the path less traveled. Be inspired by all those start-ups in Silicon Valley which keep coming up with new ideas. Those start-ups that are successful usually succeed, because they came up with a simpler, better way of doing things. Don't forget to communicate the results of your findings for better or worse. If positive it will improve knowledge of pancreatic disease, if negative it will prevent others from wasting time and resources.

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

**C.F.:** Acute pancreatitis: there is a need to identify and treat those most at risk of death on the day of hospitalization with acute pancreatitis, as 40–50% of all deaths from acute pancreatitis occur within the first 7–14 days of hospitalization. Most university hospitals are largely unaware of these early deaths. Most patients who are referred to tertiary care centers have already been selected out having survived for 7–14 days. Therefore, university hospitals have largely focused on those patients with septic complications who have survived the fluid loss phase of severe pancreatitis. While there was a marked reduction in mortality associated with acute pancreatitis in the 1970s and 80s when the need for massive fluid replacement became widely recognized, there has been no measurable reduction in the 1990s. The failure to reduce mortality in the 1990s is not surprising in light of the fact that no new therapy has been developed to manage patients in the fluid loss phase of the disease, or identify those at risk the day of admission.

Chronic pancreatitis: five randomized controlled trials including one with 8.5 years of follow-up have clearly identified 3 operations which are effective in relieving pain and the complications of chronic pancreatitis and improve quality of life. However, no one knows why some patients with chronic pancreatitis get pain and others do not, nor why only a small percentage of alcoholic patients get pancreatitis, or how alcohol causes pancreatitis in susceptible patients, or why some patients have both

chronic pancreatitis and liver cirrhosis. There is as yet no medical therapy to slow the progress of chronic pancreatitis or relieve pain (except narcotics).

Pancreatic cancer: early detection of this exceedingly aggressive malignancy remains an unfulfilled dream. Surgical and adjunctive therapies have had an insignificant impact in improving overall survival.

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

**C.F.:** Select quality reports that speak to the needs of your audience. Most of the societies and pancreatic clubs for which *Pancreatology* is the official journal have as members a mixture of surgeons, gastroenterologists, and basic scientists whose work is focused on the pancreas. Therefore, it would seem appropriate for *Pancreatology* to publish reports which address the concerns of these three constituencies, e.g. reports of clinical and basic research which advance our understanding of pancreatic function, disease, and therapy. The journal should be inclusive and include reports ranging from the molecular and genetic level to epidemiology, and the natural history of pancreatic disease and how therapy alters the natural history of the disease.