

# A 35-Year Summary of Pancreas Club Program Content

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This brief historical summary of the annual Pancreas Club meetings illustrates development of medical understanding of pancreatic disease during the course of these meetings. It also attempts to document how various hypotheses have evolved or been disproved. Understandably, experimental techniques have expanded in their ability to delve more deeply into basic cellular function. Many talented people have dedicated their careers to advancement of this particular discipline. These pages document the scientific efforts of those who have wrestled with the afflictions of the pancreas.

The Pancreas Club, Inc., which has been in existence since 1966, has met annually for the past 35 years. Although the program now includes many high-tech scientific papers and has a large attendance representing nations around the globe, it had modest beginnings. The room was small and the chairs were hard when the first meeting took place at Northwestern University in Chicago under the leadership of Dr. Marion C. Anderson in 1966. Apparently this meeting was the result of intense interest in diseases of the pancreas by a small number of dedicated clinical surgeons and researchers studying diseases of the pancreas who felt the need to share information and insights. The first meeting was a daylong series of seminars and, although the exact identity of the original members is still somewhat uncertain, we are confident that the number totaled less than 10. This meeting was tape recorded by Dr. Anderson, but several subsequent efforts to locate this important tape were unsuccessful, and the ultimate disposition of the tape remains a mystery to this day. The first of four seminars was entitled "The Role of Proteolytic Enzymes in Acute Pancreatitis." The moderator was Dr. Fraser Gurd and panelists included Drs. Alan Thompson, Max Rittenbury, and Marion Anderson. The second seminar, entitled "Vascular Changes in Hemorrhagic Pancreatitis," was moderated by Dr. Anderson and notably contributed to by Drs. Larry Carey and Alan Thompson. In the afternoon the third seminar, entitled "Results of Experimental Therapeutic Efforts in Acute Pancreatitis," was moderated by Dr. Rittenbury. The final session of the day was entitled "Research Problems in Pancreatitis" and

was moderated by Dr. Carey. The meeting was followed by a cookout at Dr. Anderson's home in Evanston. The meeting was so well received and enthusiasm high enough that it was decided that another meeting would be held the following year at the same time, the Sunday before the annual meeting of The Society for Surgery of the Alimentary Tract (SSAT).

The second meeting of the Pancreas Club took place in Philadelphia in 1967, and the host was Dr. John Howard. This meeting also was constructed in seminar format. During the first seminar entitled "Experimental Models for Study of Acute Pancreatitis," moderated by Dr. Warren Nugent, there was considerable discussion concerning the retrograde pancreatic ductal injection model of pancreatitis, which is not used extensively today, because it is well known to produce serious physiologic and hemodynamic artifacts. The second session was related to the physiology of pancreatic secretion, moderated by Dr. David Dreiling. The third session was a summary of the current status of surgical therapy for chronic pancreatitis. The fourth session was devoted to therapy for acute pancreatitis. One of the interesting discussions at this particular session was whether or not the peritoneal fluid produced by acute pancreatitis was toxic to the patient and the nature of such toxicity.

Additional participants at the second meeting of the Pancreas Club included Drs. Dan Elliott, Warren Nugent, John Howard, William Schiller, and Robert Hermann.

The third meeting of the Pancreas Club, hosted by Dr. Leon Goldman, which was held in San Francisco had 14 members listed, although other guests were present. The program still adhered to the seminar style, although eight subjects (double the number compared to the two previous meetings) were presented at this meeting. There was a case presentation on multiple endocrine adenoma syndrome, a short seminar discussion on Zollinger-Ellison syndrome, and the remainder of the meeting focused primarily on inflammation of the pancreas. A further discussion on peritoneal fluid was presented along with some mention of inflammatory mediators and the role of enzymes in pancreatitis. At the end of the meeting, there was a discussion of what the future of the Pancreas Club should be, and it was decided that there

would, in fact, be further meetings because interest in the organization remained high.

*Dr. Frey and I were unable to locate programs for 1969 and 1970, and therefore we would like to solicit copies of these programs from anyone who has them. We are also missing programs from 1972 and 1983.*

The meeting in 1971 represented the sixth meeting of the Pancreas Club, which was held in Philadelphia and again hosted by Dr. John Howard. At this time the program had made a transformation from the almost pure seminar form to a solicited presentation format with a dedicated discussion period, each paper being allotted 20 minutes for presentation. The morning meeting of the Pancreas Club constituted a discussion primarily of acute pancreatitis, but some information about pancreatic physiology was also included. In the afternoon, a variety of subjects were presented including significance of serum methemalbumin by Dr. Tom Kelly, along with abnormalities observed in acute pancreatitis, pancreatic hormone-secreting tumors, and 95% resection of the pancreas for chronic pancreatitis. At the end of the formal presentations, there was a panel discussion regarding treatment of acute pancreatitis. This particular program represents the first time the agenda included a business meeting, which was followed by cocktails and dinner; a bus then took the members to Atlantic City for the SSAT meeting.

As mentioned previously, the program for 1972 is missing, but the 1973 meeting was held in New York City at Mount Sinai Hospital, with Dr. David Dreiling as the host. The morning session consisted of an unspecified program of presentations by the host institution. (*Anyone who knows the identity of these presentations could make a contribution to the history by providing them to either Dr. Frey or me.*) After lunch, the program consisted of rather random presentations that were not grouped by any particular subject matter but which continued the 20-minute presentation and discussion format. These presentations were still dominated by discussions of acute pancreatitis. There was, however, a paper presented concerning endoscopic retrograde cholangiopancreatography (ERCP). There was also a paper reporting on the diagnostic use of ultrasound imaging to manage pseudocysts. Also of note at the 1973 meeting and later at the 1975 meeting were papers that attempted to give early information regarding the surgical treatment of acute necrotizing pancreatitis. These papers summarized the Denver experience of Dr. Larry Norton, who advocated surgical removal of the necrotic pancreas in patients with severe disease as a method of improving survival.

As is well known in the history and legends of the Pancreas Club, there was no meeting in 1974; the reason for this remains rather vague and mysterious. Following this lapse, there was a discussion between Drs. Frey and Schiller regarding what could be done to revitalize and continue the function of the Pancreas Club. Subsequently it was decided to solicit papers for the 1975 Pancreas Club meeting, using the same format as the 20-minute presentation and the discussion style that had evolved earlier. The meeting was held in San Antonio and the host was Dr. Brad Aust. The program was divided into three main parts; the first included several papers and discussions regarding pancreatitis and its complications, along with some diagnostic techniques, including the use of isoenzymes, pancreatography, and ultrasonography. Also, there was further discussion on treatments for pancreatitis. The remainder of the program concerned various mutations of pancreas transplantation and several papers on pancreatic oncology. Dr. Isidore Cohn gave a luncheon presentation concerning the National Pancreatic Study Group, which was to be repeated in 1976. A business meeting was convened during which time it was debated whether to encourage multi-institutional studies of pancreatic diseases; some of the definitions and requirements for membership were discussed along with the program for the following year, and the potential for cooperative studies from multiple institutions of pancreatic diseases was mentioned. During the course of 1975, the Pancreas Club became incorporated under the laws of the state of Michigan.

The 1976 meeting was held in Miami Beach and was hosted by Dr. Robert Zeppa. The first morning session continued the tradition of problems related to acute pancreatitis and included a paper on peritoneal dialysis as treatment for pancreatitis, which was based on the theory that removal of toxic peritoneal fluid would improve outcome. The second session of the morning consisted of invited abstracts. The third session in the afternoon concerned pancreatic hormones, elastase in pancreatitis, and endocrine pancreatic tumors. Included in this session was a paper on computerized tomography as an aid to diagnosis of pancreatic disease. Other subjects in the third session included markers of pancreatic tumors and thin-needle biopsies of the pancreas. The fourth session included a panel discussion of complications of pseudocysts. This included rupture of pseudocysts, associated ascites, and pseudoaneurysm formation. The final presentation of the day regarded operations for chronic pancreatitis. At the end of the meeting, there was a preliminary meeting of those interested in defining "severe pancreatitis."

The 1977 meeting was held in Toronto with Dr. Roger Keith as the host. By now the revitalization of the Pancreas Club seemed stable and was under the firm leadership of Drs. Frey and Schiller. The first session of the meeting appears to have been devoted primarily to pancreatic trauma and its management. The second session was devoted to obscure causes of pancreatitis. Late in the day there was a 1-hour discussion on whether or not to perform biopsies of the pancreas. Discussions for and against this particular diagnostic maneuver were given, and complications of the biopsy technique were reviewed followed by a vigorous discussion of how this technique should evolve and be used in pancreatic disease. The final session of the day included a discussion of the use of ultrasonography and ERCP to plan operations on the pancreas.

The 1978 meeting, which was held in Las Vegas and hosted by Dr. Charles Frey, was the beginning of a new philosophy devised by Drs. Frey and Schiller. The old format of the meeting had consisted primarily of presentations solicited by the co-chairmen with dedicated discussion periods for each paper. A decision was made between the 1977 and 1978 meetings to formulate a more user-friendly technique of soliciting abstracts for the meeting as a means of constructing the program and filling in, as necessary, with invited participation. The 1978 meeting ultimately was constructed of approximately half invited discussions and half presentations chosen from solicited abstract submissions. The program went well, and subsequently the primary content of the meetings came from abstract submissions. The 1978 meeting program subdivisions included transplantation of the endocrine pancreas, several papers on carcinomas of the pancreas, anatomic causes of pancreatitis, and presentations of the submitted abstracts. Another panel discussion was presented on the role of peritoneal exudates and ascites in pancreatitis. A rather intense presentation was given on the subject of whether or not acute pancreatitis evolves to chronic pancreatitis or if chronic pancreatitis has a separate etiology, with acute inflammatory episodes superimposed on the chronic inflammatory process. The number of attendees had grown from the original handful to approximately 60, which was partially the result of the change in format.

The 1979 meeting, which was held in New Orleans and hosted by Dr. Isidore Cohn, was primarily constructed from the pool of submitted abstracts. In addition, all of the submitted abstracts were printed as part of the program syllabus. This made the Pancreas Club program more complete than it had been in the past and allowed the participants to see a summary of each paper presented. The meeting was arranged into

topical subsections with defined moderators, much as is done at present. This meeting was also the first that we can document where the program lists the now famous Pancreas Club dinner as a regular part of the program. In the 10 years of the Pancreas Club's growth, the role of the host also expanded. The host secured suitable meeting space, identified the location, and made arrangements for the Pancreas Club dinner.

The 1980 meeting was held in Salt Lake City and was hosted by Dr. Frank Moody; this meeting continued the topically grouped sessions of presentations of submitted abstracts with a designated moderator and discussion leader for each session. This particular meeting of the Pancreas Club marked the first discussion of H<sub>2</sub> blockers in pancreatic disease and also included another paper on ascitic fluid in pancreatitis.

The 1981 meeting in New York City, hosted by Dr. John Ranson, was dominated by studies of acute pancreatitis and included a paper on the use of aprotinin (Trasylo). There were also presentations concerning gallstone pancreatitis and the pathologic aspects of pancreatic disease. During that meeting, a paper was presented on the use of a new technique of pancreaticoduodenectomy, wherein the stomach and pylorus were preserved, assuming better nutritional function for survivors of the operation.

The 1982 meeting, hosted by Dr. A. R. Moosa, was held in Chicago; it marked the first time that the program of the Pancreas Club was distributed in a softbound program format similar to that seen today along with all of the abstract titles. The 1983 meeting program was not available for review.

Dr. Carter Nance hosted the 1984 meeting, which was held in New Orleans. This particular meeting contained the first mention of superoxide free radicals contributing to the pathology of acute pancreatitis. There also was a discussion of the pulmonary pathologic response to pancreatitis. A paper was presented concerning the production of tumor antigens by pancreatic cancers. This particular meeting also was the first to document the participation in the program by overseas guests. This aspect of Pancreas Club meetings is now well established and is a significant part of its strength as an organization.

The 1985 meeting was hosted by Dr. David Dreiling and was held in New York City. Various aspects of the program included a continuation of the discussion of oxygen free radicals as a source of cellular damage as a result of pancreatic inflammation. There was a discussion of necrotizing pancreatitis and the role of bacterial contamination of the retroperitoneal tissues as a determinant of outcome. It was documented that presence of infection in the inflamed

retroperitoneal tissues resulted in a higher mortality rate and longer hospital stay. There also was a paper concerning the use of somatostatin in Zollinger-Ellison syndrome and the effects of this particular drug on pancreatic secretion.

The 1986 meeting was held in San Francisco. The meeting was hosted by Dr. Carlos Pellegrini and featured a symposium dedicated to the subject of the pathologic role of oxygen free radicals in pancreatitis. Other subjects on the program included the role of intracellular calcium influx in the pathogenesis of pancreatitis, pancreatitis and duct obstruction, and vascular and parenchymal changes in pancreatitis. There was a paper on resuscitation that compared the use of colloids and crystalloids. A paper was presented concerning the pathogenesis of pancreatic fibrosis. There was session on pancreatic necrosis and abscess, a paper on pancreatic cell antigenicity, and a discussion of management of pancreatic malignancies. The meetings of the late 1980s began to feature papers that were increasingly complex, and discussed sophisticated technology that allowed for inquiries concerning basic physiology and pathophysiology of common pancreatic illness.

The 1987 meeting, which was held in Chicago and hosted by Dr. Philip Donahue, continued the exploration of tissue and serum antigens in pancreatic carcinoma, several papers on chronic pancreatitis and pancreatic fistulas, and use of beta-agonists in acute pancreatitis. The 1988 program held in New Orleans further explored the use of somatostatin, and there were also presentations on the use of cholecystokinin blockade in pancreatitis, which was partially protective, and the use of alpha-1 protease inhibitors, which did not prevent pancreatic edema. The treatment of pancreatic necrosis was discussed at some length, as was pancreatic transplantation. This particular program is of note because for the first time there is a listing in the program of formal poster presentations, complete with their specific abstracts. Attendance, now, was at a consistent 80 to 90 individuals annually. The 1988 meeting marked the first publication of the summarized Pancreas Club program in the *American Journal of Surgery*. This was the beginning of a tradition that would last nearly a decade and provided considerable information to readers interested in current thinking on pancreatic disease.

Several individuals including Drs. George Bulkley, Francis Milligan, and John Cameron hosted the 1989 meeting, in Washington, DC. Continued studies of inhibitors of pancreatic function, including use of somatostatin and a prostaglandin E analog inhibitor, were presented. There were more papers on toxic oxygen superoxide radicals and the role of infection in acute pancreatitis. A paper on the use of dynamic

computerized tomography to delineate the presence of pancreatic necrosis was presented at this meeting plus several papers on transplantation.

The 1990 meeting, hosted by Dr. Brad Aust, in San Antonio, included a study of free radical scavengers as a possible mechanism of ameliorating cell changes in acute pancreatitis, along with a paper on the use of cromolyn to block the function of peritoneal mast cells in experimental pancreatitis. The conclusion of the authors was that blockade of mast cells did not decrease pancreatic edema formation. A paper was presented which showed that cholecystokinin activates trypsin within cells and that acetaldehyde formation from alcohol may play a role in the formation of acute pancreatitis. Treatment of pseudocysts was presented, along with papers on basic pancreatic physiology, including the phenomenon of nesidioblastosis. Control of gastrinomas by means of octreotide was presented. The last session of the day included several papers on the management of necrotizing pancreatitis.

Drs. Elmo Cerise and J. Patrick O'Leary hosted the 1991 meeting, which was held in New Orleans. The programs of the 1990s were characterized by investigative techniques allowing for definition of the details of cell biology of pancreatic diseases. The program in 1991 also was the first to contain a printed acknowledgement of financial support from a pharmaceutical company. The first portion of the program was related to pancreatic transplantation and included such items as a description of transcystoscopic biopsy of pancreaticoduodenal transplants. There was a paper concerning the use of oxygen free radical scavengers to improve function of pancreatic transplants. A new model was described for the production of acute alcoholic pancreatitis, which included the production of oxygen superoxides by alcohol-derived acetaldehyde action on xanthine oxidase. There were several papers describing the characteristics of peripancreatic inflammatory processes, the sources and incidence of pathogens in pancreatic necrosis, and prognostic factors in sterile pancreatic necrosis. Production of pancreatic ischemia and pancreatitis following cardiogenic shock or cardiopulmonary bypass by means of intracellular calcium activation was included, as were papers on pancreatic cancer tumor markers.

The 1992 meeting hosted by Dr. Carlos Pellegrini was held in San Francisco and contained details concerning pancreatic necrosectomy and continued use of intraperitoneal lavage techniques. The relationship between cytokines and pancreatic inflammation, descriptions of intestinal permeability to macromolecules in pancreatitis, and studies of pancreatic

microcirculation in pancreatic inflammation were included. A further study of the capability of peritoneal fluid formed by pancreatitis to cause tachycardia was included. A paper on transplantation concluded that islets but not whole pancreatic transplants were more susceptible to recurrent autoimmune abnormalities.

The 1993 meeting in Boston hosted by Dr. Andrew Warshaw marked the 27th annual meeting and was heavy with studies of the role of mediators in pancreatic illness. Cytokines, colony-stimulating factors, nitric oxide, endothelin, various hormones, and endotoxin were studied. There were papers on pancreatic neoplasms, and results of the prospective randomized placebo-controlled trial of erythromycin administration to improve gastric emptying following pancreaticoduodenectomy was presented. Papers on the use of antibiotics in pancreatitis and further studies on the pancreatic necrosis of severe pancreatitis were presented. A paper concerning pancreatic cystic neoplasms described the use of tumor antigens in the aspirated cyst fluid to distinguish malignant from benign neoplasms. The luncheon speaker for this meeting was Ed Bradley, who summarized the symposium held in Atlanta on the classification of acute pancreatitis.

The 1994 meeting in New Orleans, again hosted by Drs. Elmo Cerise and Patrick O'Leary, was characterized by the first appearance of the large-sized program, which is still in use at present. This program included information about the program, the abstracts, and this particular meeting was the first time a printed map was included in the program, to aid attendees in attending not only the Pancreas Club but also other Digestive Disease Week activities. Once again the papers were quite complex in their approach to pancreatic disease. The papers were divided into four sessions throughout the course of the day. Descriptions of cytokines were presented and several papers on bacterial translocation were included. The second session of the day included two clinical papers concluding that nonoperative management of sterile pancreatic necrosis produces the best results as did late vs. early necrosectomy in a prospective, randomized study. The third session included a double-blind placebo-controlled multicenter study of the use of octreotide to decrease complications following pancreatic surgery. A paper concerning pancreatic transplantation added additional information regarding recurrence of autoimmune disease in islets as opposed to whole pancreatic grafts. The incidence of whole-graft failure was further diminished if donor spleen cells were transplanted into experimental animals to stimulate T-cell subpopulations, which appeared to be protective. Two papers concerning the relationship of cholecystokinin to tumor cell activity

were presented. In the fourth session a paper was given describing the use of preoperative chemoradiation prior to pancreaticoduodenectomy.

The 1995 meeting in San Diego was hosted by Dr. A.R. Moosa and marked the last of the Pancreas Club meetings organized by Drs. Frey and Schiller. Both the 1994 and 1995 meetings contained papers reporting on the use of genetically altered mice, which lacked the ability to form cytokines after acute pancreatitis. Cytokines and hormones were reported on at this meeting, as was the use of dextran vs. Hespan in protecting the pancreatic microcirculation during pancreatitis. Use of blocking medications to diminish the activity of inflammatory mediators such as platelet-activating factor was reported. A paper was presented discussing the successful use of imipenim as a means to prevent retroperitoneal infection in pancreatic necrosis. Descriptions of the effects of hormones on the growth of human pancreatic cancer cells and genetic modification of tumor lines were reported. A paper outlining the predictors of survival of 201 patients following pancreaticoduodenectomy indicated that important factors for survival were diploid tumor DNA, tumor size less than 3 cm, negative nodes, and negative resection margins. The fourth session of the day outlined various techniques for performing pancreaticoduodenectomy, and a paper was presented reporting increased survival from 8 to 17.8 months in patients who had adjuvant chemotherapy in association with pancreaticoduodenectomy. The incidence of pancreatic fistula following pancreaticoduodenectomy appeared to be equal in a study designed to define whether pancreaticojejunostomy or pancreaticogastrostomy was superior as a reconstruction technique. Pylorus-preserving pancreaticoduodenectomy may be superior in patients with chronic pancreatitis as a means of allowing an optimal nutrition response after the ablative procedure.

The 1996 meeting in San Francisco hosted by Sean Mulvihill was the first meeting to be held under the direction of the new Pancreas Club leadership, which included Drs. Richard Bell, William Nealon, and Michael Sarr. Also, the program was altered to include three paper sessions and a fourth session organized as a "How I Do It" symposium, where various opinions were presented and subjected to group discussion. Because of this change, the number of papers presented decreased from the average of approximately 22 in previous years to 18 in 1996. The first of these sessions was entitled "Various Techniques for Doing Pancreaticojejunostomy." The program was marked again by highly sophisticated and specifically targeted inquiries into pancreatic function. A paper that defined the spectrum of malignancy in cystic lesions of the pancreas was presented. Mucinous

ductal ectasia and intraductal papillary neoplasms constituted approximately one third of this group of cystic lesions. A description of pancreatic gene transfer in mice using adenoviral vectors was presented, as were studies concerning tumor angiogenesis and pancreatic edema formation by complement fragments. Platelet-activating factor antagonists were used to decrease neutrophil accumulation in the lung and pancreas in experimental rats. Genetic details of hereditary pancreatitis were explored and abnormalities on chromosome 7 were implicated. A paper on cost analysis of pancreatitis, pancreaticoduodenectomy, and treatment of common bile duct injuries was presented. Further inquiries into management of retroperitoneal peripancreatic necrosis also were presented.

The 1997 program, which was held in Bethesda and hosted by Dr. John Harmon, again changed the format to reflect the increasing technicality of pancreas research. The meeting sessions were arranged by topic, and the "How I Do It" segment of the program was continued. A dedicated presentation on acute pancreatitis, clinical aspects of pancreatic cancer, and the basic science of pancreatic cancer were among the topics presented. Studies of the effects of cytokine on pancreatic inflammation, use of gene therapy, and various cellular toxic mediators of pancreatic injury were explored. The "How I Do It" session featured information regarding staging of pancreatic cancer.

The 1998 meeting in New Orleans, hosted by Drs. Patrick O'Leary and Elmo Cerise, featured a luncheon/lecture by Dr. John Howard entitled "The Wirsung Story." The three sessions included papers on acute pancreatitis, necrotizing pancreatitis, chronic pancreatitis, and pancreatic neoplasia in the first and second sessions and clinical pancreatic cancer in the third. The "How I Do It" segment was devoted to pancreatic necrosis—definition and management. Adjuvant chemoradiation in stage I pancreatic cancer with micrometastasis was noted to produce improved median survival from 18.5 to 24.4 months when combined with pancreaticoduodenectomy. In another paper, 242 five-year survivors of periampullary adenocarcinoma were analyzed and four subgroups of

tumors with their own survivor characteristics were presented.

The 1999 meeting in Orlando, hosted by Drs. Michael Murr and James Norman, contained a "How I Do It" session, and the organizers also were able to include 23 papers for formal presentation. The sessions by subject included the following: pancreatic cancer, acute pancreatitis, chronic pancreatitis, and neoplasms. The "How I Do It" session presented information concerning extended lymphadenectomy during pancreaticoduodenectomy for carcinoma of the pancreas. In the course of the program, a paper was given regarding some of the physiologic properties of elastase in acute pancreatitis. The paper concluded by hypothesizing that elastase activity in pancreatic inflammation produced tumor necrosis factor and was responsible for the systemic nature of the illness. Several papers regarding pancreatic cystic lesions were presented.

The 2000 meeting in San Diego, hosted by Dr. A. R. Moosa, also featured three sessions and a "How I Do It" session entitled "Pancreatic Cancer and Adjuvant Therapy." Sessions featured basic studies of pancreatic cancer, including genetic and antigenic studies. The second session was devoted to studies of acute pancreatitis. The third session featured clinical studies of carcinoma of the pancreas and chronic pancreatitis.

Overall, in reviewing these programs encompassing 35 years, one is impressed by the profound increase in the ability to precisely define the effects of mediators, genes, hormones, and multiple bacterial products on pancreatic inflammation. Various factors influencing pancreatic neoplasms and attempts at pancreatic transplantation not only have yielded increasing insight into these problems but also have defined future pathways for ongoing research concerning these pathologic entities. More than 400 scientific papers plus special symposiums and reports have been presented by the membership, which by now includes almost 50 international institutions. Young careers have been inspired by the information presented and the friendships formed at the annual meeting.