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# History of the European Pancreatic Club: The First 40 Years 1965–2005

## The Scientific Profile of the European Pancreatic Club and What Stood the Test of Time

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**Abstract**

The invited lectures, the symposia and panels and the printed abstracts of the meetings are the basis for analysis of the development of pancreatic research over the 40 years from 1965 to 2005. 245 invited lectures and 59 symposia, panels and round tables presented and discussed the latest state of the art at the meetings of the European Pancreatic Club (EPC). We analyze in detail the contributions to physiology and biochemistry of the pancreas, the neurohormonal control of pancreatic secretion, cell biology, stimulus-secretion coupling, and cell receptors. The research on the endocrine-exocrine relationship, nutrition and the pancreas, experimental and clinical acute and chronic pancreatitis, function tests and imaging of the pancreas, pancreatic development and growth, experimental and clinical pancreatic carcinoma, genetics and inherited pancreatic diseases over the years are listed in special sections and discussed. At the center of the EPC meetings there are scientific sessions with either oral or poster presentations. From 1971 to 2004, 4,837 contributions were accepted and printed as abstracts. In the first 30 years papers on basic research usually amounted to around 30–40%, on pathophysiology also 20–40% and the rest were on clinical work. In the years since 1993 the basic contributions became less with 20% and even only 10% of all papers in the last years. Abstracts from pathophysiology and pathology increased in the 1990s, mainly with work on pancreatic carcinoma. Papers on clinical topics also rose to 40–50% of all in the years since 1998. The interest in clinical topics shifted over the years. Chronic pancreatitis was the main topic in the 1970s; in the 1980s until 2000, acute pancreatitis gained more interest, and pancreatic cancer is now an attractive field of study due to new methods of research with cancer cell lines and genetic models. Since 1993 a Young Researchers Corner with international experts is offered at the meetings of the EPC, the programs are analyzed. In the last section the question of 'what stood the test of time?' is asked as reflected in 40 years of meetings of the EPC. Topics are physiology, biochemistry and cell biology in relation to the pancreas, pathogenesis of acute and chronic pancreatitis, methods of diagnosis, treatment of pancreatitis and of carcinoma.



### The Scientific Profile of the European Pancreatic Club

The founders of the European Pancreatic Club (EPC) intended to create a forum, where European scientists with an interest in the pancreas could meet and discuss

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**Table 1.** Number of invited lectures at the meetings of the EPC from 1968 to 2004 and nationality of the lecturers

*Number of invited lectures*

| 1968 | 1969 | 1971 | 1973 | 1974 | 1975 | 1976 | 1977 | 1978 | 1979 | 1981 | 1982 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Prague | Göttingen | Brussels | Gothenburg | Dundee | Toulouse | Oslo | Dublin | Zürich | Copenhagen | Krakow | Essen |
| 12 | none | 3 | 7 | 1 | 3 | 2 | 2 | 2 | 2 | 3 | 2 |
| 1983 | 1984 | 1985 | 1986 | 1987 | 1988 | 1989 | 1990 | 1991 | 1992 | 1993 | 1994 |
| Verona | Cascais | Manchester | Nijmegen | Marseilles | Budapest | Glasgow | Basel | Lund | Ulm | Paris | Bologna |
| 2 | 9 | 12 | 2 | none | 11 | 9 | 9 | 3 | 11 | 3 | 10 |
| 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | | |
| Barcelona | Mannheim | London | Thessaloniki | Lüneburg | Kiel | Toulouse | Heidelberg | Liverpool | Padova | | |
| none | 23 | 18 | 12 | 26 | 15 | 14 | 6 | 4 | 7 | | |

*Nationality of invited lecturers*

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Germany | 67 | France | 25 | Belgium | 8 | Netherlands | 4 | Norway | 3 |
| UK | 50 | Italy | 11 | Switzerland | 5 | Spain | 4 | Israel, Poland, Austria, | |
| USA | 38 | Sweden | 10 | Denmark | 4 | Japan | 3 | Greece, Portugal, Hungary | 1 each |

Titles, lecturers and the symposia are listed in tables 2–13. We apologize for any omissions that might have occurred.

**Table 2.** Names of invited scientists to give lectures in their field of research

| | | |
|---|---|---|
| 1968 | Prague | Jorpes S, Mutt S, Morley UK, Anastasi I, Harper UK, Morris UK, Erspamer I, Howat UK, J.C. Sarles F, Smith UK, Edlund S, Arrigas E, Wagner D |
| 1969 | Göttingen | None |
| 1971 | Brussels | Jamieson USA, Schramm ISR, Malaisse B |
| 1973 | Gothenburg | Case UK, Christophe B, Creutzfeldt D, Worning DK, Howat UK, Schmidt D, H. Sarles F |
| 1974 | Dundee | Lagerlöf S |
| 1975 | Toulouse | Scratcherd UK, Meldolesi I, H. Sarles F |
| 1976 | Oslo | Petersen N, Creutzfeldt D |
| 1977 | Dublin | H. Sarles F, Konturek PL |
| 1978 | Zürich | Christophe B, Seifert D |
| 1979 | Copenhagen | Bloom UK, Wormsley UK |
| 1981 | Krakow | Schaffalitzky de Muckadell DK, Creutzfeldt D, Wormsley UK |
| 1982 | Essen | Kern D, Malaisse D |
| 1983 | Verona | Solcia I, DiMagno USA |
| 1984 | Cascais | Case UK, Bockmann USA, Creutzfeldt D, Go USA, H. Sarles F, Lees UK, Goebell D, Domschke D, Joyeux F |
| 1985 | Manchester | Scheele USA, Kern D, Bockmann USA, Foulis UK, Braganza UK, Noronha P, Vaysse F, Dormer UK, Lees UK, Williamson UK, Klapdor D, Singer D |
| 1986 | Nijmegen | McMaster UK, Geuze NL |
| 1987 | Marseilles | None |
| 1988 | Budapest | Ammann CH, Dreiling USA, Howat UK, H. Sarles F, Singer D, Vaysse F, Case UK, Goebell D, Gullo I, Imrie UK, Nagy HU |
| 1989 | Glasgow | Foulis UK, Freeney USA, Garber UK, Henriksen DK, Laugier F, Carter UK, Hermon-Taylor UK, Vaysse F, Adler D |
| 1990 | Basel | Rommens CAN, Dobelbower USA, Dagorn F, Adler D, Ensinck USA, Alberti UK, Gerzof USA, Rösch D, Wynick UK |
| 1991 | Lund | Ammann CH, Mitelman S, Braganza UK |
| 1992 | Ulm | Petersen UK, Creutzfeldt D, Case UK, Vaysse F, Korc CAN, Schmiegel D, Trede D, Klöppel D, Steer USA, Christophe B, Neoptolemos UK |
| 1993 | Paris | Lamberts NL, Williams USA, Halliwell UK |
| 1994 | Bologna | H. Sarles F, Mann UK, Frey USA, Jensen USA, Singer D, LaVecchia I, Sutherland USA, Erlansson S, Mastella I |
| 1995 | Barcelona | None |
| 1996 | Mannheim | Gyr CH, Schölmerich D, Wigmore UK, Laubenberger D, Chalmers UK, Reske D, Nagoya JAP, Weber USA, Solomon USA, Bockman USA, Ammann CH, Schmiegel D, Lemoine UK, Urrutia USA, McKay UK, Larssonn S, Pollak CAN, Moore CAN, Hoolingsworth USA, Bramhall UK, Fink D, Kimura JAP, Trede D |
| 1997 | London | Müller-Esterl D, Griesbacher A, Lerch D, Klöppel D, Gearing UK, Lemoine UK, Sies D, Vina E, Moncada UK, Eizirik B, Beglinger CH, Laugier F, Petersen UK, Ashcroft UK, Gray UK, Kanno JAP, Saklatvala UK, Goris NL |
| 1998 | Thessaloniki | Mann UK, Calvo I, Cremer B, Layer D, Fölsch D, Nousia-Arvanitakis GR, Whitcomb USA, Lankisch D, Dagorn F, Vaysse F, Erlansson S, Petersen UK |
| 1999 | Lüneburg | Williams USA, Muallem USA, Miller USA, Tsunoda USA, Buscail F, Lerch D, Saluja USA, Ullrich 2nd USA, Borgström S, McMahon UK, McKay UK, Rathmann D, Scolapio USA, Merkrod D, Singer D, Tiemann D, Mössner D, Adler D, Cohn USA, Creutzfeldt D, Gudjonsson N, Johnson UK, Kalthoff D, Gansauge D, Friess D, Löhr D |
| 2000 | Kiel | Rathmann D, Moreau USA, Lemoine UK, Riemann D, Weber D, Buscail F, Klöppel D, Schmid D, Real E, Scarpa I, Wagner D, Kalthoff D, Pinzani I, Wison A, Sjöholm S |
| 2001 | Toulouse | Gullo I, Löhr D, Buscail F, Chen F, Witt D, Hammel F, Neoptolemos UK, Urrutia USA, Serup DK, Glasbrenner D, Layer D, Jovanna F, Van Laethem B, Escourrou F |
| 2002 | Heidelberg | Argent UK, Schmid D, Vollmar D, DiMagno USA, Obertop NL, Schmidt D |
| 2003 | Liverpool | Urrutia USA, Whitcomb USA, Muallem USA, Büchler D |
| 2004 | Padova | Kalthoff D, Gaudernack N, Fernandez-Cruz E, Bachem D, Büchler D, Wyke UK, Friess D |

S = Sweden; UK = United Kingdom; I = Italy; F = France; E = Spain; D = Germany; B = Belgium; PL = Poland; USA = United States of America; ISR = Israel; P = Portugal; NL = The Netherlands; CH = Switzerland; HU = Hungary; CAN = Canada; JAP = Japan; A = Austria; GR = Greece; N = Norway.

their mutual problems and questions from different angles: anatomy, physiology, biochemistry, internal medicine and surgery. This goal was reflected by the professions of the 9 founders: 1 physiologist (A.A. Harper), 1 biochemist (J. Christophe), 2 surgeons (A. Delcourt, Y. Edlund) and 5 physicians (W. Creutzfeldt, O. Fitzgerald, K. Herfort, H.T. Howat, H. Sarles), specialized in gastroenterology. Acute pancreatitis, chronic pancreatitis and cancer of the pancreas are entities with many facets and interrelationships. The meetings have shown that clinicians learn from basic sciences by adopting their methods and applying them to the study of diseases experimentally and clinically. For clinicians the problems of conservative and surgical treatment are essential issues. The correct diagnosis leads the way to adequate treatment. Originally, the diagnosis was only based on clinical symptoms. Thereafter, biochemical and physiological methods have contributed much to a correct diagnosis, for instance by the function tests for the pancreas. Imaging of the pancreas gained increasing importance over the years, starting with angiography, scintigraphy, ultrasonography and endoscopic retrograde pancreatography (ERP) with imaging of the ducts. Now the progress lies in computerized tomography and magnetic resonance imaging, not only of the parenchyme but with contrast also of the ducts. Endoscopic ultrasound must also be mentioned.

We will follow these lines over the years as they are reflected in the meetings. We will use the invited and state-of-the-art lectures for analysis, because they demonstrate what was considered to be important at the time. The topics of symposia and panels give an additional view. We will also analyze the papers which were submitted over the years for presentation in the scientific sessions either orally or as posters.

A short study of the European pancreatic research in the EPC was presented by Andren-Sandberg and Johnson [1] at the 30th EPC meeting in 1998.

## Invited Lectures and Symposia

It is a privilege of the President of an EPC meeting to invite scientists for lectures. A total of 245 of those lectures were given at the meetings from 1968 to 2004 (tables 1 and 2).

These lectures presented as state-of-the-art or key note lectures should outline the frontier in a certain field of research. In the years from 1971 to 1983, only 2–3 key lectures were given at each meeting. In 1984 for the first time more scientists were invited (n = 9). This tendency increased in the following years with an average of 10 invited lecturers. From 1996 on, it increased even further: in 1996 n = 23, in 1997 n = 18, in 1998 n = 12, in 1999 n = 26, in 2000 n = 15, and in 2001 n = 14. The reason for this inflation of invited lectures is possibly the opening of the EPC meetings to more attendants, also from outside of Europe, especially the joint meetings of the EPC with the IAP in Mannheim 1996 and in Heidelberg 2002. From 2002 on, the number of additional lectures came down again to 4–7.

The symposia, panel discussions and round tables were another instrument to keep the attendants up to date. Table 3 summarizes these events together with the respective chairmen. A total of 59 were organized between 1968 and 2004, on average 1 or 2 at each meeting. From 2002 on, a certain inflation can be observed. So in Heidelberg in 2002, eight symposia took place, in Liverpool five plus a whole day on basic science and in Padua 2004 it still was four. The analysis of the symposia and the lectures are integrated in the following sections.

*Physiology and Biochemistry of the Pancreas* (tables 4 and 5)

In the first meetings the structure and functional aspects of the gastrointestinal hormones were of outstanding interest. In Prague in 1968, the pioneers in the field presented their data on secretin (J.E. Jorpes), cholecystokinin-pancreozymin (V. Mutt, A.A. Harper), gastrin (J.S. Morley), and cerulein (A. Anastasi). The function of the hormones in the regulation of pancreatic secretion from there on has been a constant topic over the years, especially the fascinating interplay with the nerval regulation.

In 1975, a whole working session with K.G. Wormsley and 9 speakers dealt with 'Regulation and Adaptation of Pancreatic Secretion', and another symposium under the moderation of S.J. Konturek and 8 speakers with 'Gastrointestinal Hormones and Related Peptides'.

'Intestinal Hormones and the Exocrine Pancreas' was the title of a summarizing lecture by O. Schaffalitzky de Muckadell in 1981. Lectures on the neurohormonal regulation of secretion were given in 1977 by S.J. Konturek and 11 years later by M.V. Singer (1988) signaling progress in this field.

Parallel to the constant interest in the regulation was the study of the biochemistry and secretion of the pancreatic enzymes and their synthesis. At most meetings there were sessions with papers on these topics. In 1983, a large symposium was held in Verona with the title 'Pancreatic Proteases and Antiproteases in Physiological and Patho-

**Table 3.** Symposia, round tables, working sessions, panel discussions and their chairmen at the meetings of the EPC

| | | | |
|---|---|---|---|
| 1968 | Prague | Panel Discussion: Surgical treatment of pancreatitis | W. Hess |
| 1969 | Göttingen | Panel Discussion: Standardization of pancreatic function tests | W. Creutzfeldt |
| 1975 | Toulouse | Pathophysiology and treatment of experimental and human acute pancreatitis | T.T. White |
| | | Gastrointestinal hormones and related peptides | S.J. Konturek |
| | | Regulation and adaptation of pancreatic secretion | K.G. Wormsley |
| | | Endoscopic retrograde catheterism of the papilla | P.B. Cotton |
| 1977 | Dublin | Panel: Current problems in pancreatic inflammatory disease | |
| | | Excitation-contraction coupling in the pancreas | J. Scott |
| | | Experimental pancreatitis | D.J. Hingerty |
| | | Experimental studies using alcohol and its metabolites on the pancreas | J.M. Fitzpatrick |
| 1982 | Essen | Controversies in medicine: The treatment of acute pancreatitis | R. Ammann |
| 1983 | Verona | Pancreatic proteases and antiproteases in phys. and path. conditions | A. Ribet |
| | | Controversies in medicine: Pancreatic cancer, diagnostics and therapeutics | K.G. Wormsley |
| 1984 | Cascais | Pancreatic secretion | J. Christophe |
| | | Pathogenesis of chronic alcoholic pancreatitis | J.C. Bode |
| 1987 | Marseilles | Acute pancreatitis – pseudocysts | H.G. Beger |
| 1988 | Budapest | Pain in chronic pancreatitis – causes and management | H. Goebell |
| 1989 | Glasgow | The role of interventional radiology and other imaging modalities in pancreatic disease | C.W. Imrie |
| | | Pancreatic disease of the Atlantic salmon | A.K. Foulis |
| 1991 | Lund | Report on diagnosis of exocrine pancreatic disease | I. Ihse |
| 1992 | Ulm | The role of somatostatin and octreotide in pancreatic disease | R. Arnold |
| | | The role of enzyme treatment in pancreatic disease | H.G. Beger |
| 1993 | Paris | Chloride channels in normal and pathological pancreas | O.H. Petersen |
| | | Cystic tumors of the pancreas | A.L. Warshaw |
| 1994 | Bologna | New therapeutic approaches in chronic pancreatitis | H. Worning |
| 1995 | Barcelona | Pancreatic cancer | C.D. Johnson |
| | | Acinar islet cell interaction | J.B. Jansen |
| | | Laparoscopy as a new tool of diagnosis and treatment of pancreatic disease | H.G. Beger |
| 1996 | Mannheim | New treatment of pancreatic cancer | E. DiMagno |
| | | Islet transplantation – dream or reality? | U.R. Fölsch |
| | | Cytokines in pancreatic diseases | H. Goebell |
| 1997 | London | Reactive oxygen radicals | L. Fernandez-Cruz |
| 1998 | Thessaloniki | Imaging methods in pancreatic disease | J.B. Jansen |
| 1999 | Lüneburg | Molecular biology in pancreatic cancer | N. Lemoine |
| | | Satellite Meeting: Pancreatic enzyme therapy following surgical procedures in the gastrointestinal tract; half day | P.G. Lankisch |
| | | Basic Science Satellite Symposium: Frontiers in pancreatic physiology; 1 day (Advisory Board: G. Adler, A. Fink, L. Miller, S. Muallem, J.Williams) | M. Case and P.G. Lankisch |
| 2000 | Kiel | Prophylactic antibiotics and early nutrition in acute pancreatitis | C. Beglinger |
| | | Cytokines and acute pancreatitis | A. Andren-Sandberg |
| 2001 | Toulouse | Future prospects for the medical management of adenocarcinoma of the exocrine pancreas | P. Rusziewski |
| | | Role of pancreatic surgery | H.G. Beger |
| 2002 | Heidelberg | Pancreas development and tumor cell biology | B. Greenhalf |
| | | Clinical controversies in acute pancreatitis | M.W. Büchler |
| | | Clinical controversies in chronic pancreatitis | H.G. Beger |
| | | What's new in imaging and endoscopic treatment? | J.E. Cunha |
| | | Pancreas cell physiology and pancreatitis cell biology | G. Adler |
| | | Pancreatic surgery – how it's done | I. Ihse |
| | | Clinical controversies in pancreatic cancer | M. Brennan |
| | | Acute pancreatitis – indications for surgery | J.P. Neoptolemos |
| 2003 | Liverpool | Clinical advances in pancreatic cancer | N. Lemoine |
| | | Clinical controversies in acute pancreatitis | R. Charnley |
| | | Pathophysiology of acute pancreatitis | M. Bhatia |
| | | Basic science | O.H. Petersen |
| | | Clinical chronic pancreatitis | R. Malfertheiner |
| | | International Pancreas Basic Science Workshop; 1 day | O.H. Petersen |
| 2004 | Padova | Diabetes in pancreatic diseases | J. Permert |
| | | Endocrine pancreatic tumors | K. Öberg |
| | | Pancreatic cancer | C. Johnson |
| | | Signal transduction in pancreatic islet cells | T. Pozzan |

On average, 4–8 researchers were involved. We apologize for any omissions that might have occurred. Symposium is used as a synonym for panel, round table and symposium.

**Table 4.** Invited lectures (L) and symposia (S) dealing with hormones, nerves and regulation of pancreatic secretion

| | | | |
|---|---|---|---|
| Structure and function of hormones (secretin, pancreozymin, gastrin, cerulein) | L | J.E. Jorpes, V. Mutt, J.S. Morley, A. Anastasi, A.A. Harper | 1968 |
| New aspects of hydrelatic secretion of the exocrine pancreas | L | T. Scratcherd | 1975 |
| New aspects of enzyme secretion | L | J. Meldolesi | 1975 |
| Regulation and adaptation of pancreatic secretion | S | Toulouse | 1975 |
| Gastrointestinal hormones and related peptides | S | Toulouse | 1977 |
| Secretin: Physiological and clinical implications | L | K.G. Wormsley | 1979 |
| Intestinal hormones and exocrine pancreas | L | O. Schaffalitzky de Muckadell | 1981 |
| Pancreatic proteases and antiproteases in physiological and pathological conditions | S | Verona | 1983 |
| Pancreatic secretion | S | Cascais | 1984 |
| Ion channels and pumps in pancreatic acinar cells | L | O.H. Petersen | 1987 |
| Pharmacology of the pancreas | L | H. Goebell | 1988 |
| Pancreatic basic research and clinical sciences | L | L. Gullo | 1988 |
| New aspects in the neural regulation of pancreatic function | L | M.V. Singer | 1988 |
| Evidence of hormonal status of somatostatin 28 | L | J.W. Ensick | 1990 |
| Gene regulation of pancreatic enzymes in pancreatitis | L | J.C. Dagorn | 1990 |
| The role of somatostatin and octreotide in pancreatic disease | S | Ulm | 1992 |
| Pancreatic colipase: Structural and physiological aspects | L | G. Erlanson-Albertsson | 1994 |
| Neurohormonal control of pancreatic secretion | L | T. Solomon | 1996 |
| Neural changes in pancreatic disease | L | D. Bockman | 1996 |
| Nitric oxide and pancreatic secretion | L | J.J. Calvo | 1998 |
| Regulation of pancreatic secretion | L | P. Layer | 1998 |
| Protein kinase signaling cascades induced by pancreatic secretagogues | L | U.R. Fölsch | 1998 |
| Control of pancreatic duct cell secretion | L | B. Argent | 2002 |

logical Condition'; 'The Amino Acid Transport in the Pancreas' was a lecture by G. Mann in 1994, on colipase by G. Erlansson-Albertsson in 1994 and J.C. Dagorn reported first on the gene regulation of pancreatic enzymes in 1990. The secretion of water and electrolytes from the ducts was also of special interest in some lectures (T. Scratcherd, 1975 and B. Argent, 2002).

The role of the newly discovered hormone somatostatin in the pancreas was discussed in a working session under the moderation of S. Bloom with 4 speakers in Toulouse in 1975 and later at a symposium in Ulm in 1992, covering also aspects of possible use in the treatment of pancreatic inflammation via the inhibitory effect on pancreatic secretion.

*Cell Biology of the Pancreas* (table 5)

The development of new methods for the study of intracellular events in the 1970s and 1980s opened the field of cell biology also to the pancreas (receptors, calcium signaling, patch-clamp technique, cell culture). The interest of basic scientists was raised by the fact that the pancreatic acinar cell and the duct cell system offer models for the study of fundamental biological processes. This was reflected also in the meetings of the EPC over many years (see table 5) until today.

The events of stimulus-secretion coupling (M. Case, 1988), the study of ion channels and pumps (O.H. Petersen, 1987; symposium in Paris, 1993; workshop in Liverpool, 2003), the role of calcium in these processes (O.H. Petersen, 1992; M. Case, 1992; workshop, 2003) were the main topics.

In the 1970s, the analysis of receptors on the acinar and duct cells started. Major contributions to lectures and symposia came from J. Christophe (1978), H.J. Geuze (1986), W. Creutzfeldt (1992), J.A. Williams (1993), J. Jensen (1994) and others. In 1992, Creutzfeldt analyzed our knowledge on CCK-receptor antagonists.

At the 31st meeting in Lüneburg a whole day was dedicated to basic science ('Frontiers in Pancreatic Physiology') organized by Maynard Case and Paul Lankisch with the help of G. Adler, A. Fink, L. Miller, S. Muallem and J. Williams. The topics were regulation, signaling, acinar secretory pathway, duct cell secretion and gene expression.

The ongoing interest in the field of cell biology was documented only recently at the meeting in Liverpool in 2003. A symposium on 'Basic Science' gave information on the progress in this field with J.A. Williams (new insights in the working of the acinar cell), Y. Maryama (G-binding proteins), B. Argent (secretion by pancreatic duct cells)

**Table 5.** Invited lectures (L) and symposia (S) dealing with special topics in basic science

| | | | |
|---|---|---|---|
| *Intracellular events* | | | |
| Excitation-contraction coupling | S | Dublin | 1977 |
| *Stimulus-secretion coupling, calcium signaling* | | | |
| Ion channels and pumps in pancreatic acinar cells | L | O.H. Petersen | 1987 |
| Development of secretory polarity in the pancreatic acinar cell | L | J.D. Jamieson | 1987 |
| Critical evaluation of results obtained in the field of stimulus-secretion coupling | L | M. Case | 1988 |
| Molecular aspects of calcium signaling | L | O.H. Petersen | 1992 |
| Secretory polarity | L | M. Case | 1992 |
| Chloride channels and transporters in normal and pathological cells (Petersen, Argent, Schulz, deJonge) | S | Paris, 4 speakers | 1993 |
| The role of calcium in pancreatic secretion | L | O.H. Petersen | 1998 |
| Intracellular signaling in pancreatic acinar cells | L | S. Muallem | 1999 |
| Tyrosine phosphorylation and dephosphorylation in pancreatic signal transduction | L | L. Buscail | 1999 |
| Regulation of pancreatic protein synthesis | L | J.A Williams | 1999 |
| Nitric oxide and pancreatic function | S | London | 1997 |
| Basic science: Acinar cell, G-binding proteins, duct cells, calcium (Williams, Maruyama, Argent, Tepikin) | S | Liverpool, 4 speakers | 2003 |
| Intern. Basic Science Workshop: Secretion, calcium, etc. | S | Liverpool, 13 speakers | 2003 |
| *Receptors* | | | |
| Hormone responsiveness of the plasma membrane of pancreatic cells | L | J. Christophe | 1978 |
| Molecular and structural aspects of pancreatic adaptation | L | H. Kern | 1982 |
| Sorting of membrane receptors in the secretory and endocytotic pathway | L | H.J. Geuze | 1986 |
| From receptors of VIP-and CCK families to G protein in acinar cell line | L | J. Christophe | 1992 |
| CCK receptor antagonists | L | W. Creutzfeldt | 1992 |
| Cytokine-growth factor receptor interaction | L | W. Schmiegel | 1992 |
| New developments in the control mechanisms of pancreatic acinar cells | L | J.A. Williams | 1993 |
| Molecular biology of pancreatic receptors | L | J. Jensen | 1994 |
| Gene regulation of pancreatic cell receptors | L | H.C. Weber | 1996 |
| $CCK_A$ receptors coupled to multiple signal transduction systems in pancreatic acini | L | Y. Tsunoda | 1999 |
| Molecular basis of cholecystokinin receptor binding | L | J. Miller | 1999 |
| *Applied cell biology* | | | |
| Cell biology of acute pancreatitis | L | M.L. Steer | 1992 |
| Pancreas cell biology and pancreatitis (Adrian, Iovanna, Graf, Saluja, Petersen, Göke) | S | Heidelberg, 6 speakers | 2002 |

and A. Tepikin (calcium signaling in the acinar cell). At the same meeting over a whole day the 'International Pancreas Basic Science Workshop – Beyond Frontiers' with 17 speakers showed the unbroken interest in these fields.

Methods of cell biology were also applied to the pathogenesis of acute pancreatitis (M. Steer, 1992) and this was, furthermore, the topic of a symposium in 2002 (regulation of protein synthesis, pancreatic cell response to stress, pancreatic stress proteins, intracellular colocalization, calcium signaling and acute pancreatitis). Cytokine studies started in the 1990s, especially the relation to growth factor receptor (W. Schmiegel, 1992), in pancreatic cancer and in acute pancreatitis (panel on cytokines and acute pancreatitis, 2000, see table 8).

*Endocrine-Exocrine Relationship* (table 6)

The role of the endocrine pancreas was highlighted in 1979 for the first time at an EPC meeting in a lecture by S. Bloom. The endocrine pancreas attracted attention itself, in relation to the exocrine pancreas and clinically with endocrine tumors (E. Solcia, 1983; D. Winick, 1990; S.W. Lamberts, 1993; P. Serup, 2001). The interaction between the islet cells and exocrine tissue (W.J. Malaisse, 1982; V.L. Go, 1984; a panel on 'Acinar-Islet Cell Interaction', Barcelona, 1995) but also the enteroinsular axis (W. Creutzfeldt, 1981) were issues of lectures.

Total pancreatectomy and its pathophysiological consequences attained attraction (W. Creutzfeldt, 1981) as well as pancreas transplantation (D. Sutherland, 1994).

**Table 6.** Invited lectures (L) and symposia (S) dealing with the endocrine pancreas and relations to the exocrine pancreas

| | | | |
|---|---|---|---|
| The endocrine pancreas | L | S. Bloom | 1979 |
| Entero-insular axis, physiological and clinical aspects | L | W. Creutzfeldt | 1981 |
| Total pancreatectomy, indications and pathophysiological consequences | L | W. Creutzfeldt | 1981 |
| Cellular heterogeneity and interrelationship in pancreatic islet and acinar tissue | L | W.J. Malaisse | 1982 |
| The endocrine tumors of the pancreas | L | E. Solcia | 1983 |
| Pancreas endo-exocrine interaction | L | V.L. Go | 1984 |
| Endocrine tumors of the pancreas, clinics, diagnosis and treatment | L | D. Wynick | 1990 |
| Evidence of the hormonal status of S-28 on endo- and exocrine pancreatic functions in man | L | J.W. Ensinck | 1990 |
| Nutritional (tropical) diabetes and pancreatitis | L | K.G. Alberti | 1990 |
| Recent advances in the imaging of pancreatic endocrine tumors | L | S.W. Lamberts | 1993 |
| Pancreas transplantation – present and future | L | D. Sutherland | 1994 |
| Acinar-islet cell interaction (Jensen, v. Schoenfeld, Figarella) | S | Barcelona, 3 speakers | 1995 |
| Islet transplantation – dream or reality | S | Mannheim, 7 speakers | 1996 |
| Pancreatic beta cell proliferation | L | A. Sjöholm | 2000 |
| Control of pancreatic endocrine lineage determination | L | P. Serup | 2001 |
| Epidemiology of pancreatic exocrine insufficiency and diabetes mellitus | L | W. Rathmann | 2002 |
| Signal transduction in pancreatic islet cells | S | Padova, 4 speakers | 2004 |
| Endocrine pancreatic tumors | S | Padova, 5 speakers | 2004 |
| Diabetes in pancreatic diseases | S | Padova, 6 speakers | 2004 |

**Table 7.** Invited lectures (L) dealing with nutrition and the pancreas

| | | | |
|---|---|---|---|
| The gastrointestinal handling of different meals in man | L | H.O. Lagerlöf | 1974 |
| Geographical pancreatitis | L | H. Sarles | 1977 |
| Molecular and structural aspects of exocrine pancreatic adaptation to changing functional demands | L | H. Kern | 1982 |
| Pathophysiology and treatment of pancreatic maldigestion and meal absorption | L | E. DiMagno | 1983 |
| Nutritional factors and pancreatic cancer | L | H. Worning | 1988 |
| Nutritional (tropical) diabetes and pancreatitis | L | K.G. Alberti | 1990 |
| Nutrition in pancreatitis – the role in pathophysiology and treatment | L | J.S. Scolapio | 1999 |
| Pancreatic enzymes and digestion | L | C. Erlanson-Albertsson | 1998 |

*Nutrition and the Pancreas* (table 7)

Nutritional factors are important in the etiology of chronic pancreatitis. H. Sarles reported in a lecture on geographical pancreatitis in Africa and India, mainly Kerala, as did K.G. Alberti in 1990. A combination of certain foodstuffs (cassava) and protein malnutrition at that time seemed to be decisive factors for a clinical picture like chronic pancreatitis with calcification but without alcohol intake.

In the meantime, the detection that 50% of the patients with tropical pancreatitis carry SPINK 1 mutations also classifies this disease entity as an inherited disease.

The pancreas also has the potential to adapt to different food. This finding of possible adaptation in the 1980s stimulated many experimental studies (H. Kern, 1982 on molecular and structural aspects of exocrine pancreatic adaptation). H. Worning summarized the knowledge about nutritional factors in pancreatic cancer (1988). Maldigestion due to pancreatic insufficiency was an important issue in lectures by H.O. Lagerlöf (1974), E. DiMagno (1983) and J.S. Scolapio (1999).

*Acute Pancreatitis* (table 8)

At all EPC meetings the issue of the etiology, pathogenesis, pathology, diagnosis and treatment of acute pancreatitis were important topics in experimental work and clinical presentations (symposia in Prague, 1968; Toulouse, 1975; Dublin, 1977). In 1982, a panel discussion took place in Essen on the treatment of acute pancreatitis and controversial views (conservative against surgical). A similar discussion was held at a symposium in 2002 in Heidelberg, showing that the problem was still unsolved. In 1988, C. Imrie gave a lecture on terminology, pathogenesis and therapy of acute pancreatitis and laid ground for future work and systematic analysis.

**Table 8.** Invited lectures (L) and symposia (S) dealing with experimental and clinical acute pancreatitis

| | | | |
|---|---|---|---|
| Panel: Surgical treatment of pancreatitis | S | Prague | 1968 |
| Pathophysiology and treatment of experimental and human pancreatitis | S | Toulouse | 1975 |
| Current problems in pancreatic inflammatory disease | S | Dublin | 1977 |
| Controversies in medicine: The treatment of acute pancreatitis | S | Essen, 4 speakers | 1982 |
| Pancreatitis: Terminology, pathogenesis, therapy | L | C. Imrie | 1988 |
| Acute pancreatitis and pseudocysts (Beger, Büchler, Engelholm, Henriksen, Imrie, Malfertheimer, Sahel, Sarles) | S | Marseilles, 8 participants | 1987 |
| Cell regeneration in acute pancreatitis | L | G. Adler | 1990 |
| Interventional therapeutic approaches for complications of pancreatic abscess | L | S. Gerzof | 1990 |
| Cell biology of acute pancreatitis | L | M.L. Steer | 1992 |
| Biliary pancreatitis – Facts and fashion | L | J.P. Neoptolemos | 1992 |
| Free radicals and tissue damage | L | B. Haliwell | 1993 |
| The acute pancreatitis patient with extended necrosis | L | C. Frey | 1994 |
| Cytokines in pancreatic disease | S | Mannheim | 1996 |
| Nitric oxide and pancreatic function | S | London | 1997 |
| Bradykinin and pancreatic dysfunction | S | London | 1997 |
| Intracellular events in acute pancreatitis | L | G. Mann | 1998 |
| Management of acute pancreatitis | L | P.G. Lankisch | 1998 |
| Activation peptides of pancreatic proteases | L | A. Borgström | 1999 |
| Premature pancreatic protease activation – mechanisms | L | M. Lerch | 1999 |
| Cytokines and chemokines – multiple players and a single goal | L | A. Saluja | 1999 |
| The role of the gut in acute pancreatitis | L | M. McMahon | 1999 |
| Laparoscopic interventions for pancreatitis | L | C. McKay | 1999 |
| Early nutrition in acute pancreatitis and prophylactic antibiotics | S | Kiel, 5 participants | 2000 |
| Cytokines and pancreatitis | S | Kiel, 3 participants | 2000 |
| TGF beta – impact on acute and chronic pancreatitis | L | J. van Laethem | 2000 |
| Gene expression of cytokines in acute pancreatitis | L | J.C. Dagorn | 2000 |
| Acute pancreatitis and cytokines | L | J.L. van Laethen | 2001 |
| Evaluation of trypsinogen activation peptide as a prognostic marker in the assessment of acute pancreatitis | L | J.P. Neoptolemos | 2001 |
| Molecular pathology of trypsinogen in acute pancreatitis | L | J.M. Chen | 2001 |
| Attack or defense in acute pancreatitis | L | M. Lerch | 2002 |
| Do we need prognostic scores or markers? | L | J. Schmidt | 2002 |
| Acute pancreatitis: Indications for surgery – IAP guidelines development | S | Heidelberg, 11 participants | 2002 (together with the IAP) |
| Microcirculatory dysfunction in acute pancreatitis | L | B. Vollmar | 2002 |
| Clinical controversies in acute pancreatitis (contrast-enhanced CT, prophylactic antibiotics, enteral feeding yes or no) | S | Heidelberg, 9 participants | 2002 |
| Pancreas cell physiology and pancreatitis | S | Heidelberg, 9 participants | 2002 |
| Clinical controversies in acute pancreatitis (early mortality, prophylactic antibiotics, minimally invasive necrosectomy, interventional radiology) | S | Liverpool, 11 participants | 2003 |
| Bile acids cause death of pancreatic acinar cells | L | S. Muallem | 2003 |

In the 1990s, studies on the cell biology of acute pancreatitis gave new ideas for experimental research. The role of lysosomes was investigated by M. Steer (1992), free radicals and tissue damage by B. Haliwell (1993) and the role of cytokines in the disease process was looked at in a symposium in 2000 and in a lecture by J.L. van Laethen in 2001. It is important to say that the discovery of trypsinogen mutations by D. Whitcomb as a genetic basis in hereditary pancreatitis also led to a better understanding of the pathogenesis of acute pancreatitis. D. Whitcomb gave state-of-the-art lectures on this topic in 1998 and 2003 (see table 14). Molecular pathology of trypsinogen in pancreatitis was also reported by J.M. Chen in 2001, and microcirculatory dysfunction in acute pancreatitis was discussed in a lecture by B. Vollmar in 2002. Important issues of pancreatic cell physiology in acute pancreatitis were summarized only recently at a symposium in Heidelberg in 2002.

Items of clinical care in acute pancreatitis turned up from time to time in lectures, i.e. on 'Biliary Pancreati-

**Table 9.** Invited lectures (L) and symposia (S) dealing with experimental and clinical chronic pancreatitis

| | | | |
|---|---|---|---|
| Physiopathology of alcoholic chronic pancreatitis | L | H. Sarles | 1975 |
| Pathogenesis of chronic alcoholic pancreatitis | S | Cascais, 8 participants | 1984 |
| Pancreatic structure – a broad view | L | D.E. Bockman | 1984 |
| Pancreatic lithiasis | L | H. Sarles | 1988 |
| Pain in chronic pancreatitis – cause and management | S | Budapest, 12 participants | 1988 |
| Gene regulation of pancreatic enzymes in pancreatitis | L | J.C. Dagorn | 1990 |
| Staging of chronic pancreatitis to optimize therapy and prognosis | L | R. Ammann | 1991 |
| The role of enzyme treatment in pancreatic disease | S | Ulm, 8 participants | 1992 |
| Inhibition of calcium salt crystallization and lithiasis in the digestive tract and the kidney | L | H. Sarles | 1993 |
| Does acute alcoholic pancreatitis occur in the absence of chronic pancreatic lesions? | L | M.V. Singer | 1994 |
| New therapeutic approaches in chronic pancreatitis | S | Bologna | 1994 |
| Pancreatic enzyme therapy following surgical procedures in the gastrointestinal tract | S | Lüneburg, 11 participants | 1999 |
| Pancreatic exocrine insufficiency and diabetes mellitus | L | W. Rathmann | 1999 |
| DBTC – pancreatitis: A new experimental model for chronic pancreatitis? | L | J. Merkord | 1999 |
| Alcohol-induced acute pancreatitis – does it exist? | L | M.V. Singer | 1999 |
| Autoimmune chronic pancreatitis – a relevant entity? | L | M. Tiemann | 1999 |
| Pancreatic enzyme substitution – does particle size make a difference? | L | J. Mössner | 1999 |
| Pancreatic stellate cells – new players in pancreatic fibrosis? | L | G. Adler | 1999 |
| TGF beta – an autocrine loop for stellate cells? | L | M.L. Kruse | 1999 |
| 100 years of pancreatic enzyme substitution – present state and future developments | L | J. Moreau | 2000 |
| Pancreatic stellate cells in human and experimental pancreatic fibrosis | L | J.S. Wilson | 2000 |
| Porcine, bovine, fungal or bacterial lipase – benefits and deficits | L | P. Layer | 2001 |
| SPINK 1 mutations in chronic pancreatitis | L | H. Witt | 2001 |
| Molecular pathology of trypsinogen in pancreatitis | L | J.M. Chen | 2001 |
| Problem of pain in chronic pancreatitis | L | E. DiMagno | 2001 |
| Clinical controversies in chronic pancreatitis | S | Heidelberg, 11 participants | 2002 |
| What can genetics tell us about the pathophysiology of chronic pancreatitis | L | H. Witt | 2003 |
| Clinical chronic pancreatitis | S | Liverpool, 8 participants | 2003 |
| The problem of advanced chronic pancreatitis | L | M.W. Büchler | 2003 |
| Molecular pathology of chronic pancreatitis | L | H. Friess | 2004 |
| On the role of stellate cells in fibrogenesis | L | M.G. Bachem | 2004 |
| Role of surgery in chronic pancreatitis | L | M.W. Büchler | 2004 |

tis – Facts and Fashions' (J. Neoptolemos, 1992) and on 'Early Nutrition and Prophylactic Antibiotics' (a panel in Heidelberg, 2002). Clinicians have always been very interested in prognostic scores and markers in acute pancreatitis. They have been absolutely essential in prospective trials since the work of Ranson in the 1970s and have been the topic of a summarizing lecture in 2002 (J. Schmidt).

*Chronic Pancreatitis* (table 9)

Several approaches have been made to develop an internationally accepted classification of pancreatitis, first of the chronic variety, but also of the different stages of acute inflammation. On the initiative of Henri Sarles a first classification was defined in Marseilles in 1963. Another approach was undertaken in 1984 in Marseilles again to develop the principles further. These classifications were based on pathology, on pancreatic function and on etiology. Chronic calcifying pancreatitis played an important role in relation to alcohol intake.

Another classification of chronic pancreatitis was formulated on the initiative of M. Sarner and P.B. Cotton in Cambridge in 1983. It was based on the alterations of the pancreatic ducts which are visualized by ERP. These classifications, incomplete as they were, have contributed greatly to the understanding of pancreatitis. In 1991, R. Ammann gave a lecture on 'Staging of Chronic Pancreatitis to Optimize Therapy and Prognosis'.

The main poison for the pancreas seems to be alcohol. In 1975, Henri Sarles presented 'The Physiopathology of Alcoholic Pancreatitis' in a lecture. He developed the hypothesis that a defect in the secretion of a calcium-binding protein (pancreatic stone protein, PSP) is responsible for the precipitation of calcium salts in the ducts, which in turn lead to chronic pancreatitis. The discussions on the existence and possible role of PSP have been ongoing

**Table 10.** Invited lectures (L) and symposia (S) dealing with function tests and imaging of the pancreas

| | | | | |
|---|---|---|---|---|
| Function tests | Standardization of pancreatic function tests | S | Göttingen | 1969 |
| | The gastrointestinal handling of different meals in man | L | H.O. Lagerlöf | 1974 |
| | Are function tests still useful as diagnostic tools in diseases of the exocrine pancreas? | L | R. Ammann | 1988 |
| | Why and how to search for pancreatic insufficiency | L | B. Glasbrenner | 2001 |
| Endoscopy and imaging | New aspects of endoscopy in pancreatology | L | G.S. Nagy, L. Safrany | 1988 |
| | Endosopic sonography for the pancreas – does it help in the diagnosis and management of pancreatic disease? | L | T. Rösch | 1990 |
| | Interventional therapeutic approaches for complications of pancreatic abscess | L | S. Gerzof | 1990 |
| | The role of interventional radiology and other imaging modalities in pancreatic disease | S | Glasgow | 1989 |
| | Imaging methods in pancreatic disease | S | Thessaloniki | 1998 |
| | Magnetic resonance pancreatography (MRP) | L | J.F. Riemann | 2000 |
| | Positron emission tomography (PET) | L | W. Weber | 2000 |
| | Endosonography | L | L. Buscail | 2000 |
| | Laparoscopy as a new tool for diagnosis and treatment of pancreatic disease | S | Heidelberg | 2002 |
| | What's new in imaging and endoscopic treatment | S | Heidelberg | 2002 |
| | Laparoscopic surgery in pancreatic diseases | L | L. Fernandez-Cruz | 2004 |

at the EPC meetings for many years. In 1984, a symposium in Cascais on the pathogenesis of chronic alcoholic pancreatitis tried to further elucidate the problem. Direct toxic damage to the pancreatic tissue by alcohol without involvement of altered secretion of PSP was a point of discussion. The question of whether acute alcoholic pancreatitis can occur in the absence of chronic pancreatic lesions was discussed by M.V. Singer in a lecture (1994). The question could not be finally answered. The problem of PSP was finally settled, by stating that it is not the ultimate explanation for the development of chronic calcifying pancreatitis. Obviously PSP does not exist in the proposed molecular form.

More practical problems of chronic pancreatitis, like pain management (symposium in Budapest, 1988; lecture by E. DiMagno, 2001) and the enzyme treatment of maldigestion (symposium in Ulm, 1992; also in Bologna, 1994, and in Lüneburg, 1999, and state-of-the-art lectures by J. Moreau, 2000 and by P. Layer, 2001) demonstrated the widespread interest in these questions at the EPC meetings over the years. In Heidelberg in 2002 and in Liverpool in 2003, symposia took place on clinical controversies in chronic pancreatitis (conservative and surgical treatment).

*Function Tests and Imaging of the Pancreas* (table 10)

Over the 40 years, from 1965 until now, some progress has been made concerning the diagnostic tools as regards diseases of the pancreas. The evaluation of enzyme levels in the serum (amylase, lipase) and the measurement of pancreatic exocrine function remained the basic principles.

Great efforts were made to develop standardized tests for the function of the exocrine pancreas. Special tubes (Lagerlöf tube, double lumen, double balloon tube) and the application of test meals (Lundh test) or of intravenous standardized doses of secretin and pancreozymin/cerulein allowed the controlled suction of duodenal juice. The analysis of bicarbonate and enzymes in the basic and stimulated duodenal (pancreatic) juice made it possible to define normal secretion and different grades of impairment as pancreatic exocrine insufficiency in chronic pancreatitis (symposium on 'Standardization of Pancreatic Function Tests', Göttingen, 1969). Also the concentration of chymotrypsin in stool (and later of elastase) was used as a parameter for the function of the exocrine pancreas. In 1988, R. Ammann asked in a lecture: 'Are Function Tests Useful as Diagnostic Tools in Diseases of the Exocrine Pancreas?' L.B. Glasbrenner discussed the same question in 2001 in a lecture. The answer is: yes, they are.

Scintigraphy of the pancreas using $^{75}$Se-methionine started being used in the 1970s but was soon obsolete, because ultrasonography, computerized tomography and endoscopic retrograde cholangiopancreaticography with contrast medium (ERCP) offered better methods of imaging. ERCP became a leading tool, also for interventional treatment (stenting, stone extraction). All these methods were frequent topics at the EPC meetings in Free Paper Sessions, but also in lectures (L. Safrany, 1988; S. Gerzof, 1990; symposium, 2002). The development of endoscopic ultrasound imaging (T. Rösch, 1990; L. Buscail, 2000), of magnetic resonance imaging/magnetic resonance chol-

**Table 11.** Invited lectures (L) and symposia (S) dealing with pancreatic development and cell growth

| | | | |
|---|---|---|---|
| Interrelation of secretory and trophic responses in the exocrine pancreas | L | N. Vaysse | 1988 |
| Cytokine growth factor receptor interaction | L | W. Schmiegel | 1992 |
| Growth factor receptors and growth of pancreatic cancer | L | M. Korc | 1992 |
| Pancreatic cell growth – facts and fashion | L | N. Vaysse | 1992 |
| New developments in the control mechanisms of pancreatic acinar cells | L | J.A. Williams | 1993 |
| TGF beta and regulated transcription factors in pancreatic development and cancer | L | R. Urrutia | 2001 |
| Pancreatic development and tumor cell biology (Bockman, Mayerle, Tosh, Wagner, Fries) | S | Heidelberg, 5 speakers | 2002 |
| Apoptosis in pancreatic pathology | L | J.J. Dagorn | 1998 |
| Pancreatic development | L | L.M. Wagner | 2000 |
| Complex in vitro systems | L | H. Kalthoff | 2000 |

angiopancreatography (MRCP; J. Riemann, 2000) and also of positron emission tomography (PET; W. Weber, 2000) were critically discussed as a new way to diagnosis at the EPC meetings.

*Pancreatic Development and Cell Growth* (table 11)

The trophic behavior of the pancreas gained great interest with respect to the development of cancer. In 1988, a lecture by Nicole Vaysse dealt with the 'Interrelationship of Secretory and Trophic Responses in the Exocrine Pancreas'. In 1992, she was invited to give another lecture on this topic ('Pancreatic Cell Growth – Facts and Fashions'). W. Schmiegel (1992) investigated cytokine-growth factor receptor interactions and M. Korc (1992) growth factor receptors and the growth of pancreatic cancer. Also transcription factors in pancreatic development and cancer were investigated (lecture by R. Urrutia, 2001). In 2002, at Heidelberg a symposium on 'Pancreas Development and Tumor Cell Biology' with 5 speakers tried to summarize the knowledge.

*Pancreatic Cancer: Experimental Work* (table 12)

Although much experimental work on pancreatic cancer was presented over the last 40 years at the EPC meetings, there were only real new results with new methods of molecular biology and genetic research. Two state-of-the-art lectures were held in the early 1990s (F. Mitelman, 1991; G. Klöppel, 1992) and then again in 2000. Transgenic models for pancreatic cancer were developed (R. Schmid, 2000 and 2002), TGF-β and cancer were investigated (R. Urrutia, 2001), and the molecular genetics of pancreatic cancer (N. Lemoine, 2000) and the functional and structural characteristics of cultured pancreatic cancer cells (G. Klöppel, 2000) were addressed in lectures. A whole symposium was dedicated to pancreas development and tumor cell biology in Heidelberg in 2002. Gene therapy of pancreatic cancer was discussed by M. Löhr and by L. Buscail in 2001 in lectures.

*Pancreatic Cancer: Clinical Work* (table 13)

In the EPC meetings there were regular Free Paper Sessions on the clinical problems of cancer, diagnostic and therapeutic aspects. Lectures and panel rounds were invited to summarize our knowledge. The first extended report was given in 1981 by K.G. Wormsley ('Experimental and Clinical Problems of Pancreatic Carcinogenesis'), diagnostic and therapeutic problems were the topic of a symposium in Verona in 1983 and again in Barcelona in 1995. Members of another panel gave a talk in Heidelberg in 2002 and in Liverpool in 2003. This intensification of discussion rounds on cancer in comparison to former years shows that in recent years there has been considerable hope for better diagnosis and treatment.

In lectures the topics of nutritional aspects (H. Worning, 1988), of epidemiology (C. LaVecchia, 1994), of radiotherapy (R. Dobelbower, 1990), of early clinical signs for diagnosis (L. Gullo, 2002) and of chemotherapeutic agents for the treatment (E. van Cutsem, 2000) have been presented by invited speakers. A special symposium was organized on the question of familial pancreatic cancer in Toulouse 2001 (3 speakers). In this context it is interesting that in the frame of the EPC since 1995 a European study group for pancreatic cancer has been founded, which runs several trials (ESPAC) and has had sessions at all EPC meetings since then.

*Genetic Studies and the Pancreas* (table 14)

Hereditary pancreatitis has been known for a long time in families with acute and chronic disease. Also, the sporadic occurrence of chronic calcifying pancreatitis in very young people without alcohol intake points in this direction (Ammann). Hereditary pancreatitis was the topic of

**Table 12.** Invited lectures (L) and symposia (S) dealing with experimental pancreatic cancer

| | | | |
|---|---|---|---|
| Potential value of chromosome investigation in pancreatic cancer | L | F. Mitelman | 1991 |
| Pancreatic cancer: What makes it so different from other GI carcinomas | L | G. Klöppel | 1992 |
| Molecular biology of pancreatic tumors (genetics, nucleic acid fingerprinting, etc.) | S | Mannheim | 1996 |
| Pathology and treatment of pancreatic cancer | S | London | 1997 |
| Antimitogenic signaling via somatostatin A receptors | L | N. Vaysse | 1998 |
| Resistance to apoptosis | L | H. Kalthoff | 1999 |
| Functional and structural characteristics of cultured pancreatic cancer cells | L | G. Klöppel | 2000 |
| Transgenic models for pancreatic cancer | L | R. Schmid | 2000 |
| Xenotransplantation model of pancreatic cancer | L | F.X. Real | 2000 |
| Molecular genetics of pancreatic cancer | L | N. Lemoine | 2000 |
| Complex in vitro systems | L | H. Kalthoff | 2000 |
| Gene therapy for pancreatic cancer – intratumoral targeted chemotherapy | L | M. Löhr | 2001 |
| Gene therapy for pancreatic cancer – gene correction by Ssst? | L | L. Buscail | 2001 |
| TGF beta and regulated transcription factors in pancreatic development and cancer | L | R. Urrutia | 2001 |
| Pathogenesis of early pancreatic cancer | L | R. Schmid | 2002 |
| Pancreas development and tumor cell biology (development, cell contact regulation, transdifferentiation, murine tumor model, adaptation) | S | Heidelberg, 5 speakers | 2002 |
| Apoptosis signaling in pancreatic cancer cells: Suitable targets for therapy | L | H. Kalthoff | 2004 |
| Targeting K-ras mutations and telomerase in pancreatic cancer by therapeutic vaccines | L | G. Gaudernack | 2004 |

**Table 13.** Invited lectures (L) and symposia (S) dealing with clinical pancreatic cancer

| | | | |
|---|---|---|---|
| Experimental and clinical problems of pancreatic carcinogenesis | L | K.G. Wormsley | 1981 |
| Pancreatic cancer: Diagnostic and therapeutic problems | S | Verona, 6 participants | 1983 |
| Treatment of pancreatic cancer | L | H. Joyeux | 1984 |
| Nutritional factors and pancreatic cancer | L | H. Worning | 1988 |
| Radiotherapy of pancreatic cancer | L | R.R. Dobelbower | 1990 |
| Progress in diagnosis and treatment pancreatic carcinoma | L | M. Trede | 1992 |
| Epidemiology of pancreatic cancer | L | C. La Vecchia | 1994 |
| Pancreatic cancer (endoscopic ultrasonography, laparoscopy, resection, second look) | S | Barcelona, 4 speakers | 1995 |
| New treatment of pancreatic cancer (somatostatin, gemcitabine, vaccines, chemotherapy, surgery) | S | Mannheim | 1996 |
| Intraductal papillary mucinous tumors | L | M. Cremer | 1998 |
| Prodrug activation – a new treatment for pancreatic cancer? | L | M. Löhr | 1999 |
| Immunological changes in pancreatic carcinoma – basis for novel strategies | L | F. Gansauge | 1999 |
| Metastasis formation in pancreatic cancer | L | H. Friess | 1999 |
| Novel chemotherapeutic agents for the treatment of pancreatic cancer | L | E. van Cutsem | 2000 |
| Familial pancreatic cancer, EUROPAC | S | Toulouse, 3 speakers | 2001 |
| Future prospects for the medical management of adenocarcinoma of the exocrine pancreas (CT, MRI, endoscopic ultrasonography, surgery, radiotherapy, chemotherapy) | S | Toulouse, 4 speakers | 2001 |
| Are there early clinical signs for pancreatic carcinoma? | L | L. Gullo | 2001 |
| Clinical controversies in pancreatic cancer (stents vs. surgery, resection head of p. pylorus preserving vs. standard Whipple resection, Pap, Reber, Kawarada, Gouma, Permert, Warshaw) | S | Heidelberg, 6 speakers | 2002 |
| Pathogenesis of early pancreatic cancer | L | R. Schmid | 2002 |
| The role of case load and experience in pancreas cancer surgery | L | H. Obertop | 2002 |
| Dominant signaling pathways in pancreatic cancer progression | L | R. Urrutia | 2003 |
| Clinical advances in pancreatic cancer (gene therapy, improved survival, adjuvant therapy) | S | Liverpool, 3 speakers | 2003 |
| Physiopathology of cachexia in pancreatic cancer | L | S. Wyke | 2004 |
| Pancreatic cancer (gene therapy, chemotherapy, radiotherapy, Vaysse, Löhr, Uomo, Heinemann, Alessio) | S | Padova, 5 speakers | 2004 |

**Table 14.** Invited lectures (L) and symposia (S) dealing with genetics and the pancreas and with cystic fibrosis

| | | | |
|---|---|---|---|
| Gene regulation of pancreatic enzymes in pancreatitis | L | J.C. Dagorn | 1990 |
| Potential value of chromosome investigation in pancreatic cancer | L | F. Mitelman | 1991 |
| Hereditary pancreatitis | L | D. Whitcomb | 1998 |
| Transgenic mouse models of hereditary pancreatitis – pathophysiology | L | C.D. Ullrich 2nd | 1999 |
| Transgenic models | L | J. Jänne | 2000 |
| Gene targeting | L | J. Brüning | 2000 |
| Transgenic models for studying endocrine tumors of the pancreas | L | G. Rindi | 2000 |
| Molecular genetics of pancreatic cancer | L | N. Lemoine | 2000 |
| SPINK 1 mutations in chronic pancreatitis | L | H. Witt | 2001 |
| Gene therapy for pancreatic cancer – gene correction by sst 2 | L | L. Buscail | 2001 |
| Gene therapy for pancreatic cancer – intratumoral targeted chemotherapy | L | M. Löhr | 2001 |
| Familial pancreatic cancer, hereditary pancreatitis | S | Toulouse, EUROPAC | 2001 |
| What can genetics tell us about the pathophysiology of chronic pancreatitis? | L | D. Whitcomb | 2003 |
| New genetic aspects of cystic fibrosis | L | J.M. Rommens | 1990 |
| The adult cystic fibrosis patient: Problems and therapeutic advances | L | G. Mastella | 1994 |
| Cystic fibrosis and the pancreas | L | S. Nousia-Arvanitakis | 1998 |
| Is idiopathic chronic pancreatitis cystic fibrosis? | L | J.A. Cohn | 1999 |

two lectures by D. Whitcomb, one of the pioneers in the field, in 1998 and 2003. Cystic fibrosis is another example of genetically determined pancreatic involvement. Molecular analysis of genes in pancreatic diseases began in the 1990s. In three lectures (J. Rommens, 1990; G. Mastella, 1994; J. Cohn, 1999) the genetic background of cystic fibrosis was discussed, and also whether idiopathic chronic pancreatitis might have a link to cystic fibrosis (J. Cohn, 1999). SPINK 1 mutations were described in chronic pancreatitis (H. Witt, 2001). J.C. Dagorn investigated the gene regulation of pancreatic enzymes in pancreatitis (1990).

The genetics of pancreatic cancer are of special interest. Already in 1991, F. Mitelman reported on the potential value of chromosome investigations in pancreatic cancer. Our present knowledge concerning the molecular genetics of pancreatic cancer was presented by N. Lemoine in Kiel (2000). As regards possible gene therapy for pancreatic cancer, L. Buscail reported in 2001 on gene correction by sst 2 and M. Löhr (2001) on gene therapy via intratumoral targeted chemotherapy.

The EUROPAC collects data on the hereditary background of pancreatitis and pancreatic cancer in Europe in the frame of the EPC. The increasing importance of this field of genetic studies for the EPC is documented by a 1-day symposium in connection with the 37th meeting of the EPC in Graz (5th International Symposium on Inherited Diseases of the Pancreas, 9 July, 2005).

## The Scientific Sessions of the EPC

The central part of the meetings without any doubt are the scientific sessions with either oral or poster presentation of new results by the members of the EPC. From 1971 to 2004, 4,837 abstracts were accepted and printed. They were presented in oral sessions (usually 25 per meeting) and also since 1977 in poster sessions (the majority). In table 15, there is a summary beginning in 1971 (the year in which the EPC meetings became uniform) until 2004. We have tried to classify the papers into three categories.

(1) Basic: Work on the physiology, biochemistry and structure of the normal pancreas, i.e. enzymes, electrolytes, hormones, secretion, neurohormonal control, enzyme synthesis, cell biology with receptors, intracellular events, stimulus-secretion coupling, and calcium signaling.

(2) Pathophysiological: Studies which are concerned with the diseased pancreas using the methods of basic research: morphology and pathophysiology of acute and chronic pancreatitis and pancreatic cancer, pathological structures, etiological agents like alcohol and their action, experimental pancreatitis, work with cancer cell lines, and function of the diseased pancreas in humans.

(3) Clinical: Clinical picture of acute and chronic pancreatitis, pancreatic carcinoma, natural history of these diseases, diagnostics, epidemiology, conservative and surgical approaches.

**Table 15.** The number of scientific presentations at the meetings of the EPC from 1971 to 2004

| | 1971 Brussels | 1973 Gothenburg | 1974 Dundee | 1975 Toulouse | 1976 Oslo | 1977 Dublin | 1978 Zürich | 1979 Copenhagen |
|---|---|---|---|---|---|---|---|---|
| Basic | 22 | 40 | 25 | 46 | 36 | 37 | 42 | 49 |
| Pathophysiological | 26 | 30 | 20 | 28 | 24 | 49 | 32 | 42 |
| Clinical | 16 | 20 | 24 | 31 | 23 | 55 | 24 | 48 |
| Total | 64 | 90 | 69 | 105 | 83 | 141 | 98 | 139 |
| Basic, % | 34 | 44 | 36 | 43 | 43 | 26 | 42 | 34 |
| Basic + pathophysiological, % | 75 | 77 | 62 | 70 | 72 | 60 | 75 | 64 |
| | 1981 Krakow | 1982 Essen | 1983 Verona | 1984 Cascais | 1985 Manchester | 1986 Nijmegen | 1987 Marseilles | 1988 Budapest |
| Basic | 36 | 51 | 54 | 41 | 67 | 47 | 51 | 48 |
| Pathophysiological | 51 | 48 | 33 | 33 | 46 | 58 | 55 | 51 |
| Clinical | 35 | 50 | 44 | 49 | 37 | 46 | 45 | 51 |
| Total | 122 | 149 | 131 | 123 | 150 | 151 | 151 | 150 |
| Basic, % | 29 | 34 | 41 | 33 | 44 | 31 | 33 | 32 |
| Basic + pathophysiological, % | 71 | 66 | 66 | 61 | 75 | 69 | 70 | 66 |
| | 1989 Glasgow | 1990 Basel | 1991 Lund | 1992 Ulm | 1993 Paris | 1994 Bologna | 1995 Barcelona | 1996 Mannheim |
| Basic | 43 | 55 | 45 | 31 | 35 | 35 | 30 | 33 |
| Pathophysiological | 66 | 55 | 49 | 62 | 68 | 67 | 58 | 90 |
| Clinical | 67 | 57 | 56 | 63 | 44 | 78 | 72 | 54 |
| Total | 176 | 167 | 150 | 156 | 147 | 180 | 160 | 177 |
| Basic, % | 25 | 32 | 30 | 21 | 23 | 19 | 18 | 18 |
| Basic + pathophysiological, % | 62 | 65 | 62 | | 70 | 56 | 55 | 69 |
| | 1997 London | 1998 Thessaloniki | 1999 Lüneburg | 2000 Kiel | 2001 Toulouse | 2002 Heidelberg | 2003 Liverpool | 2004 Padova |
| Basic | 38 | 21 | 24 | 16 | 22 | 22 | 13 | 20 |
| Pathophysiological | 94 | 62 | 73 | 72 | 73 | 140 | 61 | 80 |
| Clinical | 93 | 91 | 53 | 64 | 64 | 167 | 96 | 98 |
| Total | 225 | 174 | 150 | 152 | 159 | 331 | 170 | 198 |
| Basic, % | 16 | 12 | 16 | 10 | 13 | 6 | 7 | 10 |
| Basic + pathophysiological, % | 58 | 47 | 64 | 58 | 59 | 49 | 43 | 49 |

It was the rule of the EPC that about 60% of the papers should deal with basic science and pathophysiology and around 40% with clinical work. Table 14 demonstrates that this was the case over many years. On average, in the years until 1985 the percentage of papers dedicated to pure basic research was around 30–40% and from 1986 to 1993 around 25–30%; slowly this percentage declined to around 15–20%. Since 2000 basic topics are found only in 6–10%. Concomitantly the number of sessions, which were dedicated to basic topics such as enzymes, stimulus-secretion coupling, neurohormonal control of secretion, and receptors shrunk from as many as 5 or more in the early years to only 1 or 2 from the middle of the 1990s on. On the other hand, the papers with topics on pathology and pathophysiology were always about 25–35%. They increased in number from the 1990s and partly compensated for the decline in papers on basic science. Looking at the content, a specific increase in papers concerned with problems of carcinogenesis can be observed since the mid 1990s.

The percentage of clinical papers was low in the early years with 25–30%. Over time they slowly increased in number, in the last years since 1998 they have been approaching 40–50%.

In table 16, we show the absolute figures of abstracts dealing with basic science, pathophysiology or pure clinical work. We must look at these figures in conjunction with those in table 14. Basic science contributions had been in the range of 40–60 per meeting over many years until 1991; then the number declined to 30–40 per meeting till 1997, after that it went down to only 13–22 per meeting. At the same time the number of pure clinical papers increased to around 90 per meeting. In 2002, the figures were especially high (167) due to the joint meeting of EPC and IAP in Heidelberg.

Abstracts dealing with the pathophysiology of pancreatic diseases are very important in the sense that they reflect the applied effect of basic science on the clinical laboratories. This is one of the goals of the EPC. The number of abstracts in this category was stable around 30–50 per meeting until 1985, then it rose slowly to 60–70 and since 1995 up to 90. As shown in table 17, this increase is mainly due to work with carcinoma cell lines and not with 'classical' pathophysiology. The profile of interest in the diseases of the pancreas has changed over time (table 17).

Since 1981, acute pancreatitis was the issue of an increasing number of papers, whereas interest in chronic pancreatitis has decreased. This disease was a main topic of clinical research in the 1970s. One reason for the preference for acute pancreatitis might be the easier research with experimental models, which are still lacking in chronic pancreatitis. This also holds true in the field of pancreatic carcinoma. The work with cancer cell lines has increased greatly from the beginning of the 1980s. From 1981 to 1985, there were only 19 papers on experimental carcinoma, while from 1996 to 2000 there were 96.

*On the Problem of Declining Contributions to Basic Science*

Without doubt the phenomenon of decreasing contributions from basic scientists is a very severe problem. It is the contrary of the ideas of the founding era to bring basic scientists and clinicians together to create mutual stimulation of the work, and also to encourage friendship which grows in the familiar atmosphere of a relatively small scientific society (compared to others). Obviously this held true in the first 30 years of the Club, but now it seems to be changing.

What could be the reasons for this development? We would like to list a few ideas.

**Table 16.** Absolute number of abstracts dealing with basic science, pathophysiology or pure clinical work

| | 1971–1975 | 1976–1979 (4 years) | 1981–1985 | 1986–1990 | 1991–1995 | 1996–2000 | 2001–2004 (4 years) |
|---|---|---|---|---|---|---|---|
| Basic | 133 | 164 | 249 | 244 | 176 | 132 | 77 |
| Pathophysiology | 104 | 147 | 211 | 283 | 304 | 391 | 354 |
| Clinical | 91 | 150 | 215 | 303 | 313 | 355 | 425 |

**Table 17.** Number of abstracts on acute and chronic pancreatitis and carcinoma cell lines

| | 1981–1985 | 1986–1990 | 1991–1995 | 1996–2000 | 2001–2004 |
|---|---|---|---|---|---|
| Acute pancreatitis | 52 | 155 | 218 | 283 | 158 |
| Chronic pancreatitis | 112 | 55 | 87 | 139 | 129 |
| Carcinoma | 59 | 92 | 189 | 202 | 179 |

(1) In the last years a number of laboratories, also clinical-experimental ones, with pancreatic research, no longer participated because of retirement or waning interest in the EPC of that particular group. Examples are the groups of Jean Christophe in Brussels, of Henri Sarles in Marseilles, J.J. de Pont in Nijmegen, Irene Schulz in Homburg, Werner Creutzfeldt in Göttingen and Harald Goebell in Essen. Their activities have only partially been replaced by followers. New young working groups in particular should, therefore, be invited and encouraged to attend the meetings. (2) The officers of the Club are mostly clinicians. In the 40 years of the Club we had only 9 basic scientists as Presidents (J. Christophe in 1971, S.J. Konturek in 1981, M. Case in 1985, J.J. de Pont in 1986, C. Rozé in 1993, G.E. Mann in 1997, N. Vaysse in 2001, O.H. Petersen in 2003 and T. Grieshaber in 2005). This was one of the reasons why the new statutes mandate a basic scientist President for every other year. (3) The structure of the meetings does not attract basic scientists. Maybe some parallel sessions with basic papers would give more space to them for discussions with colleagues. To have in 2.5 days only one session with these topics is not attractive. In the first 20–30 years we had at least 4–6 sessions dedicated to basic contributions. (4) Big meetings like the joint ones of EPC and IAP are dominated by clinicians, mainly also surgeons, and are not attractive for basic scientists. The presidents of those meetings must be especially careful to counteract the trend of too many clinical sessions with the character of postgraduate train-

**Table 18.** Lectures given at the Young Researchers Corner

| | | |
|---|---|---|
| 1993 | Paris | Cultured cell, receptors, cell pathing, calcium signaling (Clemente, Estival, Williams, Petersen) |
| 1994 | Bologna | Methodology for the study of pancreatic receptors (de Weerth, Fourmy, Jensen, Buscail, Susini) |
| 1995 | Barcelona | Methodology for the study of genetic alterations in pancreatic cancer (Löhr, Fernandez, Lemoine, Peinado) |
| 1996 | Mannheim | Methodology in pancreatic physiology (Schmidt, Holst, Teyssen, Niebergall-Roth, Gullo) |
| 1997 | London | Signal transduction in islet and exocrine cells: Overview of methodology (Pedley, Elliott, Willems, Dunne, Persaud) |
| 1998 | Thessaloniki | Models of experimental pancreatitis and relevance to human disease (Lerch, Mössner, Vollmar, Ward, Beglinger) |
| 1999 | Lüneburg | Clinical epidemiology and biostatistics for the pancreatologists (Lowenfels, Bueno-de Mesquita) |
| 2000 | Kiel | Researchers think tank: Pancreatic cancer cells, genetics of cancer, pancreatic stellate cells (Klöppel, Schmid, Real, Lemoine, Wagner, Kalthoff, Pinzani, Wilson, Sjöholm) |
| 2001 | Toulouse | Genomic and post-genomic developments in biomedical sciences (Gress, Ferec, Prats, Pramanik) |
| 2002 | Heidelberg | Genetics, microdissection, proteomics, cell culture, transcriptomics (Hoheisel, Kleef, Scarpa, Costello, Siech, Löhr) |
| 2003 | Liverpool | Real time imaging of the pancreas: Confocal and 2-photon microscopy, electrophysiology, uncaging techniques (Tepikin, Maruyama, Ashby, Lerch) |
| 2004 | Padova | New biotechnologies in the diagnostic and therapeutic approach to pancreatic diseases: Use of microarrays, gene therapy (Lanfranchi, Gress, Sangro, Maruyama) |

ing. (5) The sponsoring by pharmaceutical companies might be an additional push towards too many clinical topics and should be observed. (6) The social side of the meetings must be of special interest to the organizers because in such a small society this can create the contacts and friendship which are also needed for research cooperation.

The authors think that one of the positive results of their work on the history of the EPC is to draw attention to these problems. They suggest that a small working group of representative EPC experts should be created for further analysis of the problem and for planning counteractions.

One of the strategies to reverse these trends has already been introduced, the Young Researchers Corner.

*The Young Researchers Corner*

In 1993, Claude Rozé started a new program: the Young Researchers Corner. The idea was to attract young people interested in learning methods of basic research in the field of the pancreas. Since then this small program has run successfully at all meetings. Top experts in their field were invited to give lectures (table 18).

## What Stood the Test of Time?

One of us (Werner Creutzfeldt), being one the 9 founding members in 1965, had been asked to give a lecture at the 32nd EPC meeting in Lüneburg in 1999 with this title. Based on the material concerning the scientific profile of the meetings of the Club we would like to answer this question. The EPC meetings summarized our knowledge at the time in a great number of state-of-the-art and invited lectures and symposia of experts. The meetings were also accepted as platforms for the presentation of current research and of new results with an immense number of published abstracts. All topics have been investigated. So it is justified to put the question of what remains.

*Physiology, Biochemistry, Cell Biology* (table 19)

The pancreas obviously attracted the interest of a significant number of excellent basic researchers and the EPC can be glad that they regarded this Club as a panel to present their data.

The pancreatic acinar cell with its ability to synthesize large amounts of proteins, the sorting and package of these proteins and transport in zymogen granules to the membrane seems to be ideal to study these basic biological processes. Already in the 1950s, George E. Palade and his group analyzed the morphological steps in this process (Nobel Prize in 1974). The analysis of gastrointestinal hormones (secretin, cholecystokinin-pancreozymin, gastrin, and others like bombesin or vasointestinal peptide), the studies of their receptors, and the interplay with the neural system resulted in fascinating results. The neurohormonal control of secretion, therefore, was a big issue at many EPC meetings. The intracellular events which follow this stimulation in the acinar and in the ductal cells (stimulus-secretion coupling, intracellular signaling, es-

**Table 19.** Physiology, biochemistry, cell biology of the pancreas: What stood the test of time?

| | |
|---|---|
| Gastrointestinal hormones and pancreas | yes |
| Nerves and pancreatic stimulation | yes |
| Neurohormonal control of secretion | yes |
| Receptors and second messengers | yes |
| Protein synthesis, transport, secretion | yes |
| Intracellular signaling, stimulus-secretion coupling, role of calcium | yes |
| Islet cell-acinar interrelationship | yes |
| Entero-insular axis (incretins) | yes |
| Genetic basis of inherited pancreatic disorders | yes |

**Table 20.** Experimental work on pancreatic disease: What stood the test of time?

| | |
|---|---|
| Pathogenesis of pancreatitis and cancer | |
| Enzyme activation (proteases, lipases) | yes |
| Explanation of the mechanisms | no |
| Analysis of pathophysiology of acute pancreatitis | yes |
| Infected necrosis as major risk factor for mortality | yes |
| Feedback control of pancreatic secretion by intraduodenal trypsin in man | no |
| Pancreatic stone protein | no |
| Molecular and cell biology of pancreatic cancer | yes |
| Miscellaneous | |
| Attempts to attract diabetologists (the pancreas: one organ or two?) | no |
| The informality of the EPC | ? |
| To promote the exchange of ideas and the friendship between basic and clinical scientists in Europe | yes |

pecially the role of calcium) are even today a matter of research with model character. Also, the studies of interactions between the gut and the islet cells (enteroinsular axis) and of islet cells and the acinar cells have yielded many insights. All these results stood the test of time. Many of the classical studies on hormonal and nerval regulation of pancreatic secretion both in animals and in humans have been carried out by clinical investigators in clinical laboratories oriented to basic research.

*Pathogenesis of Pancreatitis and of Pancreatic Cancer* (table 20)

The studies on activation of enzymes in the pancreas have shown that these processes, especially the activation of trypsinogen and other proenzymes, play a decisive role in the pathogenesis of acute pancreatitis. Also, the place of lysosomes in this context is interesting. But we have no stringent explanation yet despite extensive experimental work of what mechanism really sets off the starting process of acute pancreatitis.

Good progress has been made with the explanation of the pathophysiology of pancreatic inflammation and its consequences for the whole organism. The key role of infection of the pancreas in the course of acute pancreatitis with respect to morbidity and mortality has been better defined. This knowledge has contributed significantly to a better and consistent treatment of the patients and a better survival chance. We have no explanation yet of which steps lead to the evolution of chronic pancreatitis with its variations (noncalcifying, calcifying). The role of alcohol intake and action is still unclear. The possible existence of a calcium binding PSP and its diminished secretion in chronic pancreatitis could not be proved and did not stand the test of time. The finding that the concentration of trypsin in the duodenum inhibits the secretion of CCK (feedback control) in animals gave hope for a therapeutic effect of pancreatic enzymes in humans with severe pancreatic pain in chronic pancreatitis. However, this could not been confirmed in patients. Finally, the studies of molecular and cell biology and the corresponding gene defects of pancreatic cancer obviously open new therapeutic perspectives. But this field has only just been opened.

*Methods for Diagnosis of Pancreatic Diseases* (table 21)

Since the 1950s, it has been one of the aims to develop tests for the function of the exocrine pancreas. Knowledge increased that in chronic pancreatitis as consequence of the destruction of the tissue a progressive diminution of the function occurs. The secretion of enzymes and of bicarbonate decreases, leading eventually to maldigestion of all nutrients. Test meals with an estimation of the enzyme concentration in duodenal juice (Lundh test) were not reliable enough and also the idea that the stimulation of the pancreas results in a different elevation of amylase/lipase in the blood according to the remaining functional tissue leads to erratic results (evocative tests). The development of a functional test was accomplished by the use of secretin (fluid and bicarbonate) and pancreozymin-cholecystokinin/cerulein (enzymes) and analysis of the duodenal/pancreatic juice. The members of the EPC cooperated closely in the standardization of this test, which was time-consuming, but sensitive and reproducible, the gold standard in scientific studies. For practical purposes, Ammann developed a method for the estimation of chymotrypsin in feces (nowadays replaced by elastase) as a

**Table 21.** Methods for diagnosis of pancreatic diseases: What stood the test of time?

| | |
|---|---|
| Pancreatic function tests | |
| Evocative tests | no |
| Test meal | no |
| Secretin-CCK (cerulein) test | yes |
| Enzymes in feces | yes |
| Tubeless absorption tests (PABA and pancreolauryl tests) | yes |
| Amino acid consumption test | no |
| Imaging methods | |
| Angiography | no |
| Tomography and pneumoperitoneum | no |
| $^{75}$Se scintigraphy | no |
| Endoscopic retrograde pancreatography (ERP) | yes |
| Computer tomography (CT) | yes |
| Ultrasonography | yes |
| Endoscopic ultrasonography | yes |
| Magnetic resonance imaging (MR) | yes |
| MR cholangiopancreatography (MRCP) | yes |
| Positron emission tomography (PET) | yes |
| Somatostatin receptor scintigraphy for endocrine tumor localization | yes |

**Table 22.** Treatment of acute pancreatitis: What stood the test of time?

| | | |
|---|---|---|
| 1 | Enzyme inhibitors | |
| | Aprotinin (Trasylol) 1960–1978 | no |
| | Gabexate mesilate (Foy) 1980–1990 | no |
| 2 | Inhibitors of enzyme secretion | |
| | Calcitonin | no |
| | Glucagon | no |
| | Somatostatin | no |
| | Octreotide | no |
| 3 | Inhibition of inflammatory mediators | |
| | Lexipafant (PAF antagonist), 1997 | no |
| | Antioxidant, sodium selenite, 1997 | no |
| 4 | Intensive care | |
| | Systematic basic and problem-oriented therapy | yes |
| | Prognostic scores | yes |
| | Visualization of necrotic areas in the pancreas (contrast-enhanced dynamic CT) | yes |
| 5 | Surgical intervention | |
| | Total pancreatectomy | no |
| | Early operation | no |
| | Early ERCP and papillotomy without obstructive jaundice | no |
| | Necrosectomy, drainage | yes |

simple clinical test, ideal for the follow-up of patients; it is, however, less sensitive and quantitative than the secretin-CCK test. Tubeless absorption tests with the splitting of orally applied nonabsorbable esters (PABA = N-benzoyl-*L*-tyrosyl-para-aminobenzoic acid) by trypsin and of pancreolauryl-fluorescein by pseudocholesterolesterase (pankreolauryl test) and the respective increase of the digestion products in blood in correlation to the normal or diminished amount of trypsin or esterases in the duodenum are elegant, but have not found broad distribution. Finally, the use of the consumption of amino acids in the pancreas as a marker test for the synthetic capacity of the gland did not prove to be reproducible.

Imaging of the pancreas has shown great progress since the 1980s. Evolving from the classical radiology, angiography was developed for the detection of pancreatic cancer, and also scintigraphy of the pancreas with $^{75}$Se-tagged methionine. They were soon abandoned when the ERP set standards for the imaging of the duct system. The external ultrasound investigation and the newer endoscopic endosonography opened new possibilities for the daily practice. Computer tomography, also with the dynamic contrast-enhanced technique for the detection of necrotic areas in the inflamed pancreas, magnetic resonance and MRCP set absolute new fascinating possibilities for the imaging of the pancreas and its ducts. Nevertheless, the early diagnosis of pancreatic carcinoma is still difficult. In some cases the PET may detect early small tumors especially when combined with CT investigation (PET-CT). A very elegant method for the detection of hormone-producing endocrine tumors of the pancreas and the duodenum was found through the use of tagged somatostatin (octreotide) which binds to the somatostatin receptors on the hormone-producing tumors and their metastases.

*Treatment of Acute Pancreatitis* (table 22)

To increase the chances of survival in patients with acute pancreatitis has been the goal for gastroenterologists and surgeons over the last century. The theories changed from being absolutely conservative ('don't touch the inflamed gland') to very aggressive approaches like total pancreatectomy. It is now generally accepted that the conservative treatment should be first in line. Results have much improved with the introduction of intensive care and systematic basic treatment, fluid, pain treatment and close supervision, in order to identify complications early and to start additional problem-oriented treatment. The development of prognostic scores sharpened the vigilance. In contrast, the search so far for specific means to

**Table 23.** Treatment of chronic pancreatitis and cancer: What stood the test of time?

| | |
|---|---|
| Treatment of chronic pancreatitis | |
| Pancreatic oral enzyme preparation in maldigestion | yes |
| Oral enzymes against pain | no |
| Endoscopic papillotomy plus lithotripsy, stenting | yes |
| Drainage procedures | yes |
| Partial pancreatic resection | yes |
| Duodenum-preserving resection of pancreatic head | yes |
| Treatment of pancreatic carcinoma | |
| Early surgery | yes |
| Chemotherapy | no |
| Radiotherapy | no |

positively influence the course of the disease has failed (enzyme inhibitors, inhibitors of pancreatic secretion such as glucagon, calcitonin, somatostatin). Multicenter trials (also within the framework of the EPC) laid the ground for these experiences. Surgical intervention was also critically evaluated. Total pancreatectomy was abandoned as well as early intervention. Drainage procedures, especially of the infected necrosis, together with necrosectomy and antibiotics in well-planned time frames have found their place and have increased the chances of the patients. ERCP is not indicated in idiopathic acute pancreatitis. In gallstone pancreatitis the performance of ERCP has increased the diagnostic certainty. However, early ERCP with papillotomy in biliary pancreatitis cases without obstructive jaundice is not justified. In three prospective studies (Fan, Neoptolemos, Fölsch) there was no benefit regarding the mortality and in two studies also regarding the complications of biliary pancreatitis.

*Treatment of Chronic Pancreatitis and Carcinoma* (table 23)

Maldigestion is one of the leading symptoms of advanced chronic pancreatitis due to the lack of pancreatic enzymes in the gut, thus leading to steatorrhea and weight loss. The enzyme deficiency can be compensated for by oral replacement of enzymes. Enzymes easing the pancreatic pain, based on the idea of a feedback inhibition of CCK-stimulated pancreatic secretion by intraluminal proteases, have failed. The endoscopic interventional methods with stenting and lithotripsy have given at least temporary relief. Surgical drainage procedures and partial pancreatectomy have proved to be beneficial. New methods of resection of the pancreatic head with preservation of the duodenum (Beger resection) have brought progress in comparison with the classical Whipple procedure.

The new imaging methods have increased the chances for earlier detection of the developing tumor. So early surgery has better chances than before. Trials with chemotherapy and radiation on the other hand have ultimately not yet found a beneficial outcome.

## Conclusion

Looking back on 40 years of the EPC and of pancreatic research we are proud that the result is positive. When the 9 founders met in 1965, they had the vision that the existence of a forum of investigators with a common interest in the pancreas would promote both, basic and clinical research.

The founders of the Club relied upon the interacting forces of friendship in informal surroundings. This turned out to be true. Numerous contacts developed. Many young researchers went to other laboratories, got new ideas with the help of the EPC and multicenter studies were encouraged. Especially the idea that basic research (physiology, biochemistry, molecular biology, genetics) has much to contribute beyond the mere interest in biological mechanisms for the benefit of a better life for patients with diseases of the pancreas proved to be positive. On the other hand, the analysis of the scientific sessions of the EPC revealed that in the last 10 years the number of contributions from basic scientists has markedly decreased. This is a phenomenon which is in contrast to the ideas of the founders and must be seriously counteracted by the officers of the EPC who are responsible for the future of the EPC.

At the end of our work about the history of the EPC we would like to say that in 40 years this scientific society has stood the test of time and will also stand it in the future.

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## Reference

1 Andren-Sandberg A, Johnson C: A quantitative analysis of European pancreatic research as reflected by abstracts from the annual European Pancreatic Club meetings 1982–1997 (abstract 167). Digestion 1998;59:262.