

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 patho-

physiology 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.

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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

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

<i>Number of invited lectures</i>													
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				
<i>Nationality of invited lecturers</i>													
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, DiMugno 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, Freaney 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, Ensinnck 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, Larsson 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, DiMugno 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 neural 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
2003	Liverpool	Acute pancreatitis – indications for surgery	J.P. Neoptolemos
		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
2004	Padova	International Pancreas Basic Science Workshop; 1 day	O.H. Petersen
		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, pancreaticozym, 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. Erlanson-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

<i>Intracellular events</i>			
Excitation-contraction coupling	S	Dublin	1977
<i>Stimulus-secretion coupling, calcium signaling</i>			
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
<i>Receptors</i>			
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
<i>Applied cell biology</i>			
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. Ensink	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 Laethem	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 Laethem 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. Whit-

comb 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
	Endoscopic 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/erulein 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 ⁷⁵Se-methionine started being used in the 1970s but was soon obsolete, because ultrasonography, computerized tomography and endoscopic retrograde cholangiopancreatography 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. Löhre 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, Warsaw)	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	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, Teysen, 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

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 neural 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

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

a therapeutic effect of pancreatic enzymes in humans with severe pancreatic pain in chronic pancreatitis. However, this could not be 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

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 ⁷⁵Se-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

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

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.

Acknowledgments

We thank Mrs. Rita Shinkle for checking the linguistic quality of the manuscript and Professor Maynard Case and Professor Markus Lerch for their critical comments, which helped to make the manuscript more precise and readable.

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