

The early development of cardiology in Zurich – a personal account¹

Part I

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*“L’avenir est un présent
que nous fait le passé”*

(André Malraux, 1901–1976)

Summary

Thanks to the outstanding surgical talent and competence of Åke Senning, since 1961 head of cardiovascular and visceral surgery at the University Hospital of Zurich, the indications for operative corrections were gradually extended to most congenital and acquired heart diseases. His influence considerably stimulated and challenged all those working in the field of heart disease in the Medical Clinic (Paul Lichtlen) and in the Polyclinic (Ernst Lüthy) and led ultimately to the development of an official Cardiology Division (Wilhelm Rutishauser) in 1970. Children and adults with acquired and congenital diseases of the heart underwent catheterisation and angiography for a more accurate and quantitative diagnosis. Echocardiographic and Doppler methods only came later.

Pressure measurements with fluid-filled and catheter-tip manometers allowed for a precise evaluation of gradients at stenosed valves and dye-dilution and thermodilution permitted flow measurements necessary for the calculation of valve areas. The dye-dilution method allowed for the measurement of right to left and left to right shunts on all levels of the circulation and was superior to the estimation of shunts by oxygen saturation of blood samples. The upstream sampling by dye and thermodilution made the assessment of the severity of valvular regurgitations more accurate before echocardiographic and nuclear methods became available. The characterisation of ventricular function by measurement of dP/dt with tip-manometers during pacing, handgrip and ergometric exercise allowed the study of the performance of the heart. Of considerable

interest was the alteration of ventricular function during ischaemia induced with the above-mentioned

stress tests in the catheterisation laboratory. A big step forward was the use of angiography in a quantitative way. Densitometry made possible the appreciation of stenoses in vessels more precisely than the measurement of diameter reduction. Cine- and videodensitometry allowed the measurement of blood flow by angiography in individual vessels in conscious men, which was impossible before without the introduction of these devices.

The perspective that utilisation of catheters would one day lead to therapeutic interventions on vessels and the heart – reserved until then for surgery – was fascinating and a major impetus. Initiating dilatation of narrowed coronary arteries needed vision and courage. Grüntzig’s previous successes with percutaneous treatment of iliac and femoral stenoses gave us confidence. After careful experiments in dogs with artificial coronary stenoses and intraoperative dilatation Andreas Grüntzig performed the first successful coronary angioplasty on 16 September 1977 on a 36-year-old patient, who is still alive today. Bernhard Meier, responsible for the medical ward of this patient, carefully described the circumstances, later followed Grüntzig to Atlanta and has devoted his life to interventional cardiology.

Key words: dye-dilution; thermodilution; roentgen-densitometry; circulation times; mean transit time; catheter-tip manometers; first coronary angioplasty

Introduction

Why this flashback to a limited timeframe? Firstly, an editor-in-chief brought up the idea. Secondly, Goethe said: *“Eine Chronik schreibt nur derjenige, dem die Gegenwart wichtig ist.”* This second argument emphasises continuity of evolution and tradition. Tradition is

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not the admiration of the ashes but may serve to pass on the glowing fire and ensure continuity. Imagination, diligence and perseverance lead further.

Robert Hegglin's initiative

Robert Hegglin (fig. 1B) was appointed full professor of Internal Medicine and chief of the Medical Policlinic of the University of Zurich in 1958. At that time the Medical Policlinic and the Medical Clinic were two largely independent entities without departmental affiliation. Being interested in cardiology and appreciating the academic potential of Max Holzmann, Hegglin convinced the Zurich Medical Faculty to promote Holzmann as lecturer and titular professor at the same time. Holzmann (fig. 1A) had been held back by his superior in the Medical Clinic, even though he was author of the well-known textbook "Klinische Elektrokardiographie" [1] and co-founder of the Swiss Society of Cardiology in 1948 [2].

In the year of his appointment Robert Hegglin hired Ernst Lüthy, a previous co-worker of Richard Bing in St. Louis, Missouri, as "Oberarzt" in cardiology and Wilhelm Rutishauser, with a pharmacologic background, as scientific assistant.

At that time the therapeutic arsenal for the treatment of cardiovascular patients was extremely limited. Nitroglycerine was used to alleviate angina pectoris, digitalis, mercurial diuretics and the new drug hydrochlorothiazide to treat congestive heart failure.

Hegglin asked Rutishauser to establish a laboratory for research in cardiovascular circulation. A cardiovascular unit or division, envisioned by Lüthy, came into being bit by bit.

In the Medical Clinic, directed by Prof. Paul Rosier, Frank Schaub was especially interested in electrocardiography and endocarditis but unfortunately died early of a malignant disease. Albert Bühlmann, in charge of the Pulmonary Function Laboratory, analysed venous and arterial blood gases and practised catheterisation of the right heart, assisted by Harry Gattiker and Anastasios Tsakiris. Frank Nager was interested in phonocardiography and hypertension. He became titular professor and chief of Internal Medicine at the Cantonal Hospital in Lucerne. Later Paul Lichtlen joined the team of the Medical Clinic, so that a dynamic competition between the Medical Clinic and Policlinic arose.

Surgeons as pioneers

At the Children's Hospital of the University of Zurich, surgeon Max Grob ligated, in 1947, for the first time in Switzerland, a patent Ductus Arteriosus Botalli. But the pioneers of open heart surgery were in the French part of Switzerland. Andreas Naef in Lausanne performed the first mitral commissurotomy in 1951, three years after Charles Bailey in Philadelphia. Jean-Louis Rivier was the cardiologist and Michel Dolivo had constructed the heart-lung machine. Charles Hahn took

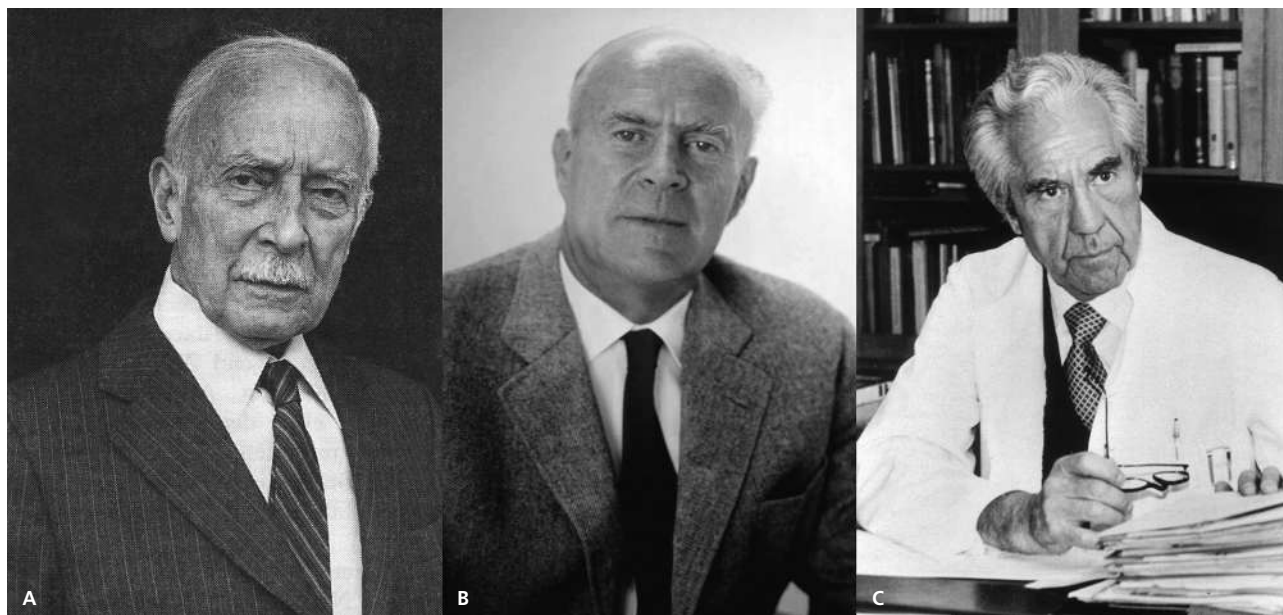


Figure 1

- A Max Holzmann, 1899–1994, famous cardiologist in Zurich mainly by his book "Klinische Elektrokardiographie".
 B Robert Hegglin, 1907–1969, Professor of Internal Medicine at the University of Zurich, known by his book "Differentialdiagnose Innerer Krankheiten".
 C Åke Senning, 1915–2000, born in Sweden, from 1961 to 1985 Professor of Surgery at the University of Zurich, famous for several new operating techniques to improve heart disease.

the lead in Lausanne in open heart surgery as private lecturer.

He became full professor in Geneva in 1967. As founder and chief of the newly built private clinic in Genolier, Charles Hahn could enormously increase his activities later, sometimes operating on as many coronary patients, mostly coming from foreign countries, as all five Swiss university clinics of surgery together.

In 1959, in Zurich we searched through the archives of the Medical Policlinic for patients with right bundle branch block in the ECG and an enlarged heart on the 5 × 5 cm chest X-ray. We found more than 70 patients of all ages and asked them to come for a dye-dilution curve. In the presence of a large left to right shunt and often a small right to left shunt, a diagnosis of atrial septal defect was made. If a short transient arterial desaturation occurred at the end of a Valsalva manoeuvre, the diagnosis was absolutely certain. Lüthy or Rutishauser travelled with two symptomatic patients each fortnight by train from Zurich to Berne, where Tyge Søndergaard, a guest cardiac surgeon from Aarhus, Denmark, sutured the defect with a curved needle and thread (circumclusion technique) in hypotension and hypothermia by surface cooling. As a late complication, suture failure occurred very rarely, which we could demonstrate by a dye-dilution test.

In 1957, Max Grob was promoted to associate professor of Pediatric Surgery at the Children's Hospital in Zurich. He has operated on many children with congenital heart disease with hypothermia and later with the heart–lung machine.

At the beginning of 1960 Kaufmann and Rutishauser diagnosed by history, auscultation and quantitative phonocardiography a bilateral atrial myxoma in a 30-year-old woman who was previously hospitalised in a sanatorium because of vanishing shadows in the lung. Echocardiography did not exist at that time. Hegglin ruled out an operation in Zurich since at that time adult cardiac surgery at the University Hospital had a mortality rate of up to 50%.

We referred the patient to the famous Thoracic Clinic of Clarence Crafoord at the Karolinska Hospital in Stockholm. In June 1960, the patient was successfully operated on in extracorporeal circulation by Åke Senning, then lecturer at the Crafoord's Clinic. Hegglin presented this lady to his staff, to the students and the medical faculty as a wonderful example of successful heart surgery. A distinguished delegation of the Zurich Medical Faculty consisting of the pathologist Erwin Uehlinger and the neurosurgeon Hugo Krayenbühl went to see Senning at the Karolinska Hospital. They were impressed by his accomplishments, namely the development of the Crafoord-Senning's heart–lung machine and several methods for the correction of congenital cardiac malformations, the first permanent pacemaker implantation in a patient in 1958, and a new therapy to widen coronary stenoses by patch grafts. The delegation con-

vinced the Zurich Medical Faculty, which appointed Senning full professor of cardiovascular and visceral surgery in April 1961. The government also assured him of the construction of a new cardiovascular research building.

Before Åke Senning started in Zurich he looked for the most talented anaesthetist Ruth Gattiker from Zurich to train with him in Stockholm. Despite initial skepticism Ms Gattiker became a highly esteemed collaborator of Åke Senning, who always listened to her suggestions and advice in the long years of their fruitful collaboration.

Ruth Gattiker, head of cardiovascular anaesthesia at the University Hospital of Zurich, recalls that between 1961 and 1968 they performed, with Senning, 350 operations in hypothermia by surface cooling to a rectal temperature of 28–30°C and circulatory standstill up to maximal 7 minutes. These concerned mainly different forms of atrial septal defects with or without aberrant lung-veins, pulmonary stenoses, Fallot's trilogy and coarctations. No mortality and only very few complications occurred in all those patients because the anaesthetists controlled and corrected the circulatory alterations, changes in metabolism, blood gases and effects of drugs under those low temperatures. If, under extracorporeal circulation and gas exchange, the mortality in the year 1961 in Zurich was still high – but similar as in the best European centres – it went down in 1968 to 15%, which was excellent in consideration of the many severely affected patients.

Robert Hegglin was the moving force behind the organisation of the first continuing education course in cardiology held in Zurich from 9 to 11 October 1961. Cardiologists from the French-speaking part of Switzerland criticised the Zurich Faculty for giving the course only in German and trying to monopolise the continuing education in cardiology by promoting mainly the Zurich heart surgery under Senning. Therefore Pierre Duchosal in Geneva, together with Holzmann and Mahaim – the founders of the Swiss Society of Cardiology – and Jean-Louis Rivier, who had supported the heart surgery development in Lausanne, dissociated themselves from the course in Zurich and organised on 11 November 1961 a course of continuing cardiology education in French, with the placet of the Swiss Society of Internal Medicine. In order to prevent a splitting of Swiss cardiology, the committee of the Swiss Society of Internal Medicine as the mother society of cardiology and other subspecialities participated in corpora at the French course in Geneva [2].

Åke Senning (see fig. 1C) dominated heart surgery in Zurich for 25 years (1961–1985). He developed new operative techniques. In 1964, he performed the first renal transplantation in Switzerland and in 1969, two years after Christiaan Barnard in Cape Town, the first heart transplantation on the continent. Senning's optimistic personality, his profound understanding of cardiovascular physiopathology, his innovative approach

and his technical skills made him a widely recognised pioneer in cardiac surgery. He made important contributions to the surgical treatment of congenital and acquired heart diseases and thereby helped to shape the “golden era” of heart surgery. In Zurich Senning trained a whole generation of excellent cardiovascular surgeons, who all obtained leading positions in Switzerland and abroad. Marko Turina was elected as successor of Senning in 1985.

Towards quantification of circulation

Pressure, volume and specially flow are the main parameters defining circulation. Shear stress depending on flow velocity is a most important factor determining vascular growth but also local atherosclerosis. Lord Kelvin has stated: “When you can measure what you are speaking about, and express it in numbers, you know something about it; when you cannot express it in numbers your knowledge is of a meagre and unsatisfactory kind ...” It may sound pretentious, but accurate measurements were always our goal.

The dye-dilution method

In the circulation laboratory Rutishauser practised peripheral injection and registration of dyes and mechanocardiography, including registration of carotid, apical and venous pulses. With the dye-dilution method we measured the arm-ear appearance time after rapid injection into a brachial vein and recording at the hypaemic external ear. The lung-ξear time was meas-

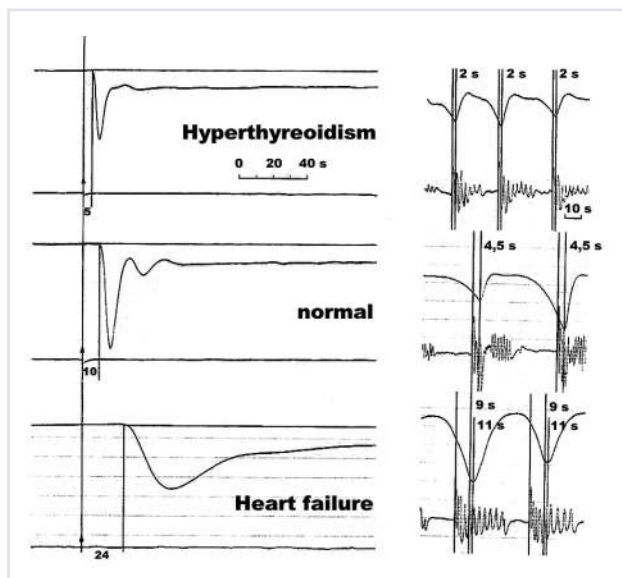


Figure 2
Left Measurement of arm-ear appearance times by dye dilution.
Right Measurement of lung-ear appearance times by oxygen saturation after apnoea in the same three conditions. Circulation times as quotient of volume and flow are very sensitive parameters of the right and left ventricular function.

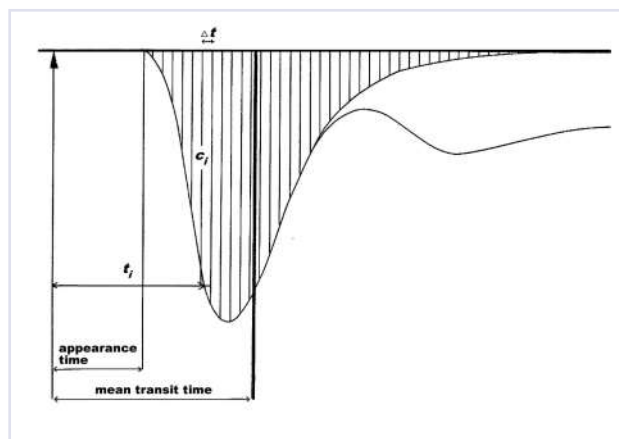


Figure 3

The mean transit time \bar{t} is the average time the indicator particles travel from the point of injection (start) to the recording area (goal) at the primary passage. This first passage has to be extrapolated semi-logarithmically from the recirculating particles. The mean transit time is the vertical line of gravity of the primary passage. This time also corresponds to the blood volume between injection and detection site divided by the flow and is therefore an important measurement which we used in roentgendensitometry.

ured as the reappearance of oxygenated blood after apnoea (fig. 2) [3]. The latter is representative of left ventricular function. In left ventricular failure it is prolonged (>5 seconds) due to increased blood volume in the pulmonary veins as well as in the left heart and low cardiac output. In combined systolic left and right heart failure the arm-ear time is very much prolonged (>12 seconds) due to the markedly increased blood volume in the venous system of the body and the decreased cardiac output. The circulation times, measured peripherally as the quotient of blood volume and output, are very sensitive parameters of the degree of decompensation of the heart. This is often forgotten today in the era of echocardiography.

With the dye-dilution method we measured the cardiac output (Q), a most important parameter of circulation, according to the Stewart-Hamilton principle. It is the quotient of mass of the injected dye (I) divided by the area of the primary concentration-time curve ($\int c(t)dt$). $Q = I/\int c(t)dt$. The mean transit time of the first passage of the dye (\bar{t}) corresponds to the line of gravity $\bar{t} = \int c(t) \cdot t dt / \int c(t) dt$ (fig. 3) which is equal to the quotient of the blood volume (V) between the injection point and the detection site, divided by the cardiac output $\bar{t} = V/Q$ [4].

The contour of the dye-dilution curve is specifically changed by shunts and valvular regurgitation, which can be accurately measured, more precisely than by several other methods. Therefore, one parameter, namely the arterial dye concentration after venous bolus injection, allows a multitude of quantitative measurements. Based on these results Hegglin and Rutishauser, with the collaboration of Georg Kaufmann, Ernst Lüthy and Heiner Scheu, have written the book



Figure 4

A photograph of our fluoroscopy catheterisation room in 1963 after exercise test on a 19-year-old patient. The scrubbed cardiologist (W.R.) to the right is helped by two assistants. The charming girl is recording the ECG with pressures and derived parameters.

“*Kreislaufdiagnostik mit der Farbstoffmethode*” [5]. Running over more than 300 pages it deals with circulation times, cardiac output, valvular regurgitations and shunts.

However, Hegglin’s greatest accomplishment was the publication since 1952, as sole author, of the book “*Differentialdiagnose Innerer Krankheiten*” [6], which was edited 11 times and translated into 10 languages. After Hegglin’s death his successor Walter Siegenthaler, followed by Edouard Battegay, edited the book with the collaboration of multiple authors.

Invasive cardiology

Starting in 1961 Lüthy and Rutishauser developed catheterisation of the right and left heart at the Medical Policlinic. Lüthy introduced the thermodilution method for measurement of the volume of the right ventricle and based his postdoctoral thesis on this topic [7]. A 12F catheter with multiple side perforations was introduced into an axillary vein and advanced into the right heart. By a nearly instantaneous injection of cold saline solution into the right ventricle and the registration of the temperature with a fast responding thermistor behind the pulmonary valve the right ventricular volume and ejection fraction were estimated from the temperature steps.

At that time there were no left heart catheters commercially available and we did not like left ventricular puncture as practised by Senning. To gain access to the left ventricle by an arterial approach according to the Seldinger technique, Rutishauser shaped catheters from rolls of thin red and thick black Ödman tubes in hot water. At one end a hook of more than 270° was formed with a diameter corresponding to the width of the ascending aorta of the patient to be catheterised next day. The tip was tapered by stretching it over the Seldinger wire. The other end was equipped with a stop cock. These catheters were cold sterilised in ethylene gas. The advantage was that they could be introduced over the wire into an artery and advanced into the left ventricle without radioscopy. As soon as extrasystoles appeared, we knew that the tip of the catheter had

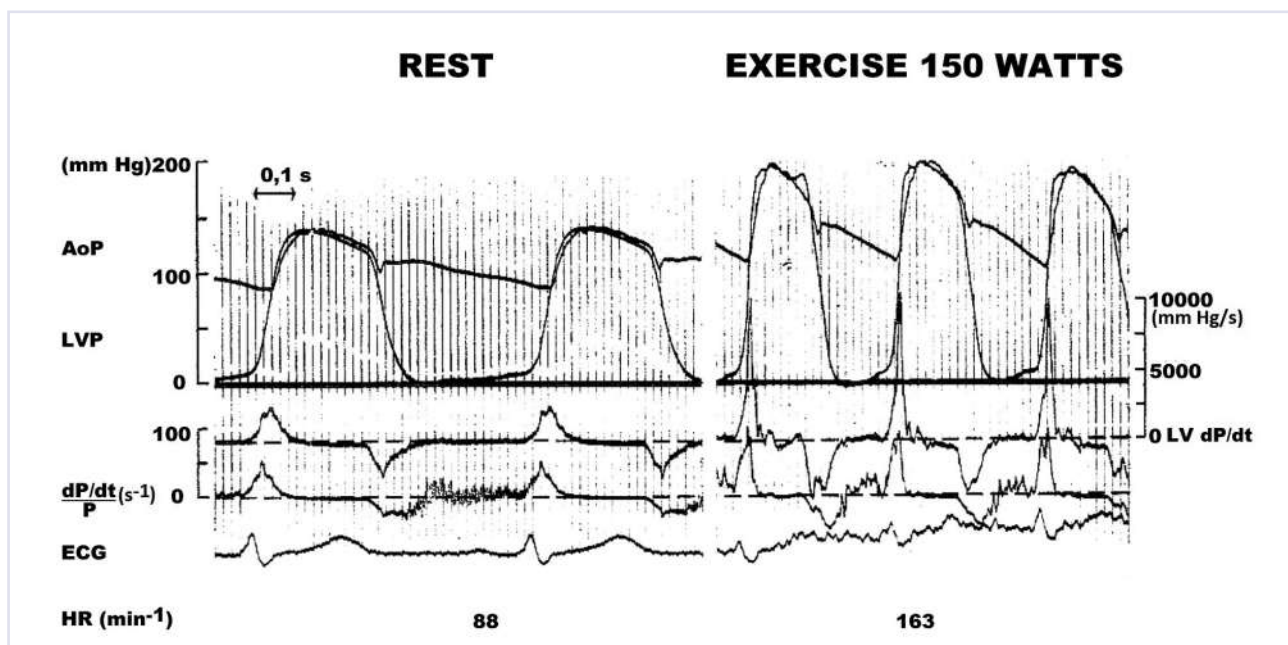


Figure 5

Left ventricular (LVP) and ascending aortic (AoP) pressures measured by catheter-tip manometers in the young patient from figure 4 at rest (left) and during exercise of 150 watts (right). Below the pressure tracings are the instantaneous left ventricular derivative and the quotient $dP/dt/P$ corresponding, in the absence of asynchrony, to the contractile function of the LV myocardium. During exercise in this normally functioning ventricle the max. dP/dt quadruples and the $dP/dt/P$ doubles as expression of the sympathetic drive to the myocardium, while enddiastolic pressure is practically unchanged from rest.

reached the left ventricle (fig. 4). After repositioning the tip left ventricular pressure could be recorded without extrasystoles. From 1963 on we also used the trans-septal approach to the left atrium and ventricle, using the newly available Brockenbrough needle and preformed catheter.

Left heart catheterisation was also introduced in the Medical Clinic by Harry Gattiker and Anastasios Tsakiris. Both went later to the Mayo Clinic in Rochester, Minnesota, first Tsakiris for cardiovascular research and, in 1969, Gattiker for further training in clinical cardiology. In 1970 and 1971, respectively, they were appointed professors at the University of Sherbrooke, Québec, in Canada and Gattiker became the chief of Cardiology thereafter Tsakiris died prematurely of a malignant brain disease.

The evolution of invasive cardiology by right and left heart catheterisation in the sixties was significant and fascinating. We measured pressures at rest and during exercise in the cavities of the heart (fig. 5) and major veins and arteries, injected dye [8] or cold saline solution at various sites, also into coronary arteries recording with fiber optic in the coronary sinus [9], localising and quantitating shunts and valvular regurgitations by the upstream technique [10]. This led to a better under-

standing of the haemodynamics of the whole cardiovascular system and the resistances of the vascular trees under exercise, pacing and beta-blockade [11].

Lüthy resigned from the catheterisation laboratory after his postdoctoral thesis. He was replaced by Heiner Scheu, later by Martin Rothlin from the Medical Clinic, and finally by Hanspeter Krayenbühl as “Oberärzte”. We often used tip-manometers to assess left ventricular performance. The tip-manometers allowed for the recording of the maximal rate of increase in ventricular pressure (max. dP/dt) as a measure of contractility and min. dP/dt as a measure of relaxation velocity. Under simplified conditions the quotient $(dP/dt)/P$ provided, according to Sonnenblick, a measure of the velocity of the contractile elements during contraction [12] and relaxation in synchronous working hearts. We showed in coronary patients that in the course of ischaemia left ventricular relaxation becomes altered before contractile function [13]. This leads to an upward shift of left ventricular diastolic pressure–volume relationship due to incomplete or asynchronous relaxation [14]. We also studied the time relation between apex cardiogram and left ventricular events using simultaneous high-fidelity tracings.

These measurements increased our understanding

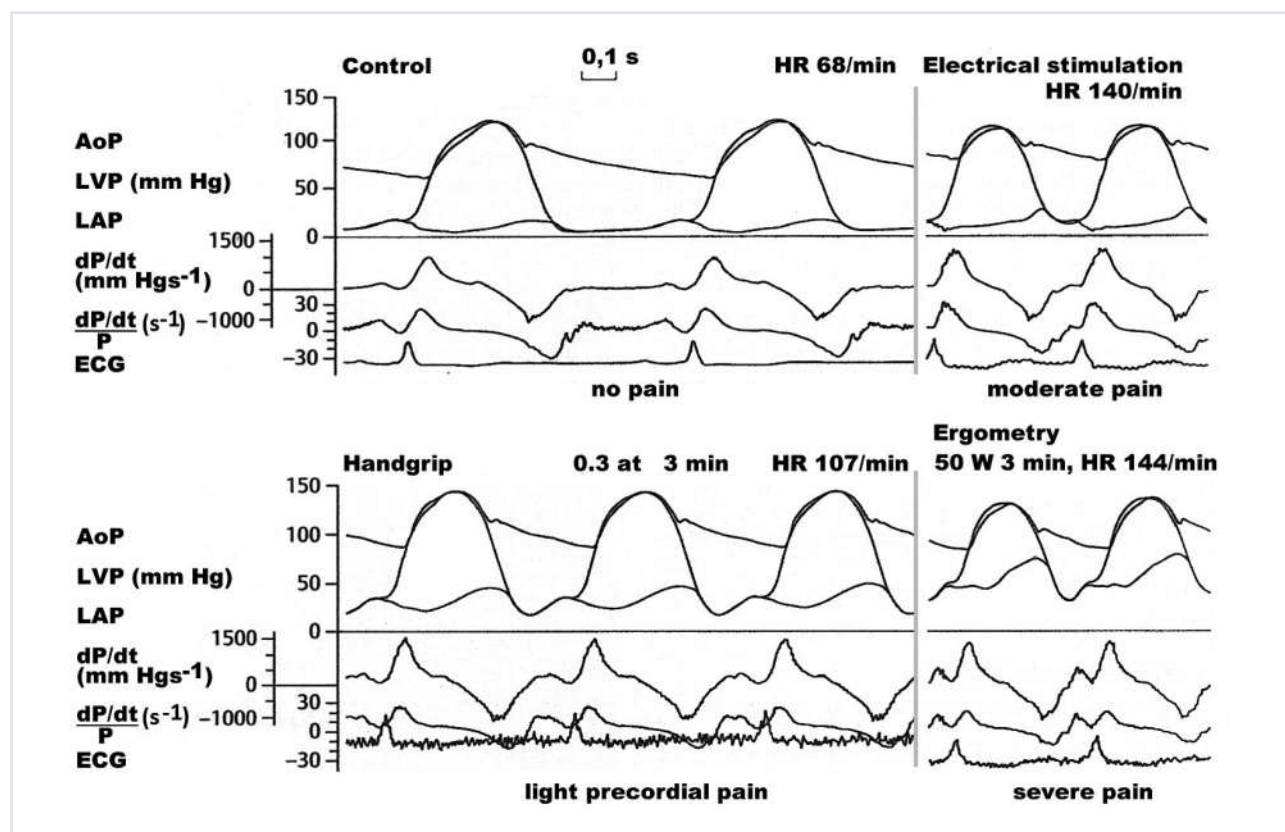


Figure 6

Aortic (AoP), left ventricular (LVP) and left atrial (LAP) tip-manometer pressures in a 45-year-old patient with advanced 3-vessel disease at rest (control), after 3 minutes of handgrip, during atrial electrical stimulation at a rate similar as that attained during 3 minutes of ergometry with 50 watts. The enddiastolic and mean atrial pressures, slightly elevated at rest, increase considerably during handgrip and specially during the 3-minute low level exercise, together with increasing precordial pain and dyspnoea, while the dP/dt and the $dP/dt/P$ barely increase because of severely disturbed left ventricular contraction and relaxation of this ischaemic ventricle.

of the complex adaptations of the cardiovascular system in the healthy heart and in ischaemic heart disease e.g., during pacing, handgrip and exercise (sympathetic stimulation) compared with at rest (fig. 6) [15] and under beta-blockade [11].

Angiography

Senning as a surgeon was naturally very interested in a precise morphological preoperative diagnosis. Our catheterisation room and the one in the Medical Clinic were, by instruction of Josef Wellauer, director of the Radiology Department, equipped only with an X-ray tube and a fluoroscopic screen, certainly not suited for angiography (fig. 4). We had to transport our patients in bed from our catheterisation laboratory to the angiography room and often had to wait until the room was available, while the catheters, lying in the heart and vessels, had to be flushed very carefully in order to avoid thrombosis. Ventriculographies without extrasystoles were used to measure ventricular volumes and ejection fractions [15].

In addition children and babies with congenital diseases, selected to be operated on by Senning in the Kantonsspital were brought by Franz Real and Ingrid Oberhänsli-Weiss from the Children's Hospital into the same angiography room, and naturally had priority. Paul Lichtlen and his assistants Yvonne Scholer, Helmut Lydtin and Tiziano Moccetti with their patients of

the Medical Clinic often had to wait as well, even though the distance from their catheterisation laboratory to the angiography room was shorter. Moccetti later became titular professor and chief of Cardiology at the Cardiocentro Ticino in Lugano.

Coronarography

In 1962, we performed the first good visualisation of the coronary arteries in Zurich with Swedish help in the angiography room of the Radiology Institute: It consisted of a massive bolus of contrast material deposited into the root of the aorta ascendens, while the heart had been stopped 6 to 12 worrisome seconds by an intravenous injection of acetylcholine. Obviously this procedure showed both coronary arteries simultaneously (fig. 7).

In the early years of selective imaging of the coronary arteries – not free from complications – a controversy arose: Mason Sones, in Cleveland, Ohio, was the first to accidentally accomplish a selective coronary angiography in 1958. But his method required a direct exposure of the brachial artery for introduction of a tapered catheter with an end hole and 4 small side holes. Melvin Judkins in Portland, Oregon, on the other hand, used a percutaneous approach from the femoral artery with catheters having preformed tips different for the right or the left coronary artery. After comparing the complication rate in large series it became clear that more experience with either method was essential to reduce complications. It also became evident that only cardiologists with a good knowledge of arrhythmias, ischaemia and infarction should be responsible for coronary angiography.

Paul Lichtlen returned to Zurich in 1965, after his training at Johns Hopkins University in Baltimore, Maryland, as a convinced supporter of the Sones method. He defended it everywhere and also used it for his perfusion measurements by the Xenon-method. Rutishauser was never in favour of performing a cut-down on arteries when they could be reached percutaneously by puncture, which also allowed catheters to be changed over a wire by the Seldinger technique without blood loss.

Only in 1971 when the new research building granted to Senning, with its modern X-ray equipment, was ready, did it become possible to obtain optimal quality coronary angiographies. The cardiologists were solely in charge and our team and Lichtlen with his collaborators had free access to this new building with our patients and for experimental work.

The development of angiology

Alfred Bollinger was also an assistant in the cardiovascular division of Ernst Lüthy, where he mainly worked with patients having arterial and venous diseases. He later became chief of the division of angiology at the University Hospital of Zurich. In 1965, Hegglin sug-



Figure 7

First nonselective coronary angiography in Zurich on a 57-year-old patient with moderate chest discomfort at rest and during exercise. While the heart was stopped for 6–12 seconds by means of intravenous injection of acetylcholine, a massive bolus of contrast medium was deposited into the ascending aorta by a retrogradely introduced black Oedman catheter. Both coronary arteries were filled simultaneously and there is no significant coronary disease visible. The aortic valves during cardiac arrest allowed some contrast backflow into the left ventricle.

gested to Bollinger that he set up an angiology unit. Bollinger introduced the plethysmographic flow measurement of extremities by vein closure. He quantitated peripheral artery disease of the lower extremity by measurement of the reactive hyperaemic response after arterial occlusion. Thereafter Bollinger introduced, together with the Institute of Biomedical Techniques, Doppler ultrasound flow measurements in arteries and veins and also the microscopic evaluation of nailfold capillaries. After having had angiography in the Radiology Department, the patients with severe claudication were transferred to Hans Schwarz and Willy Meier in the Surgical Clinic A or to Bruno Vogt and Urs Brunner in the Surgical Clinic B. The treatment consisted either in endarterectomy or bypass grafting.

Felix Mahler who had a complete education in cardiology with us, was then resident with John Ross, but was also very much interested in peripheral circulation. He became later professor and chief of angiology at the University of Berne where he realised, among other important projects, the first dilatation of a renal artery stenosis.

Important early collaborators

Martin Rothlin became, along with anaesthetist Ruth Gattiker, also a person of confidence and trust for Åke Senning. Rothlin had obtained his medical and cardiological training in Geneva and with Robert Bing, then in Detroit, Michigan. He specialised in postoperative diagnostics and intensive care. By following all the patients Senning had operated on, he was “a sort of con-

science” for the cardiovascular surgeon. As private lecturer he was active in the catheterisation laboratory of the Medical Clinic as well as in our laboratory. After Senning retired, Martin Rothlin, who had become titular professor, founded together with other colleagues the HerzZentrum Hirslanden in Zurich.

Istvan Babotai also became an essential collaborator of Senning. As an electro-engineer, recently graduated from the Swiss Federal Institute of Technology, he controlled, during operations in hypothermia, the temperature in different organs of the patients and also improved Senning’s heart–lung machine. His main interest was, however, in the electrical stimulation of the heart. He helped to improve the pacemakers’ electrodes and influenced manufacturing firms to produce better and smaller pacemakers. After Senning’s retirement he became responsible for all pacemaker patients of the Zurich Hirslanden Clinic.

Paul Lichtlen had become a very successful cardiologist at the Zurich Medical Clinic. In 1973, he was appointed professor and chief of the Cardiology Division in the Medical Clinic of the University of Hannover. He stayed in good contact with Switzerland, mainly by organising since 1975 every second year the postgraduate course on “*Myocardial Infarction and Angina Pectoris*” in Davos, which later became under Thomas Lüscher the well-known “*Cardiology Update*” congress. Walter Steinbrunn replaced Paul Lichtlen as head of the catheterisation laboratory of the Medical Clinic.

Martin Gander trained on our team and later in San Diego, California, and with Melvin Judkins in Portland, Oregon. In 1965, he became an assistant at



Figure 8

- A Earl H. Wood, 1913–2009, eminent researcher in cardiovascular physiology who recorded after contrast injection the first densitograms from films and videotapes at the Mayo Clinic in Rochester.
 B Peter Osypka, born 1934, electro-engineer, fellow of Wood and Heintzen, later founder of Osypka AG, Rheinfelden, Germany.
 C Paul Heintzen, 1925–2009, famous paediatric cardiologist in Kiel. He created with his group the first digital subtraction angiogram.

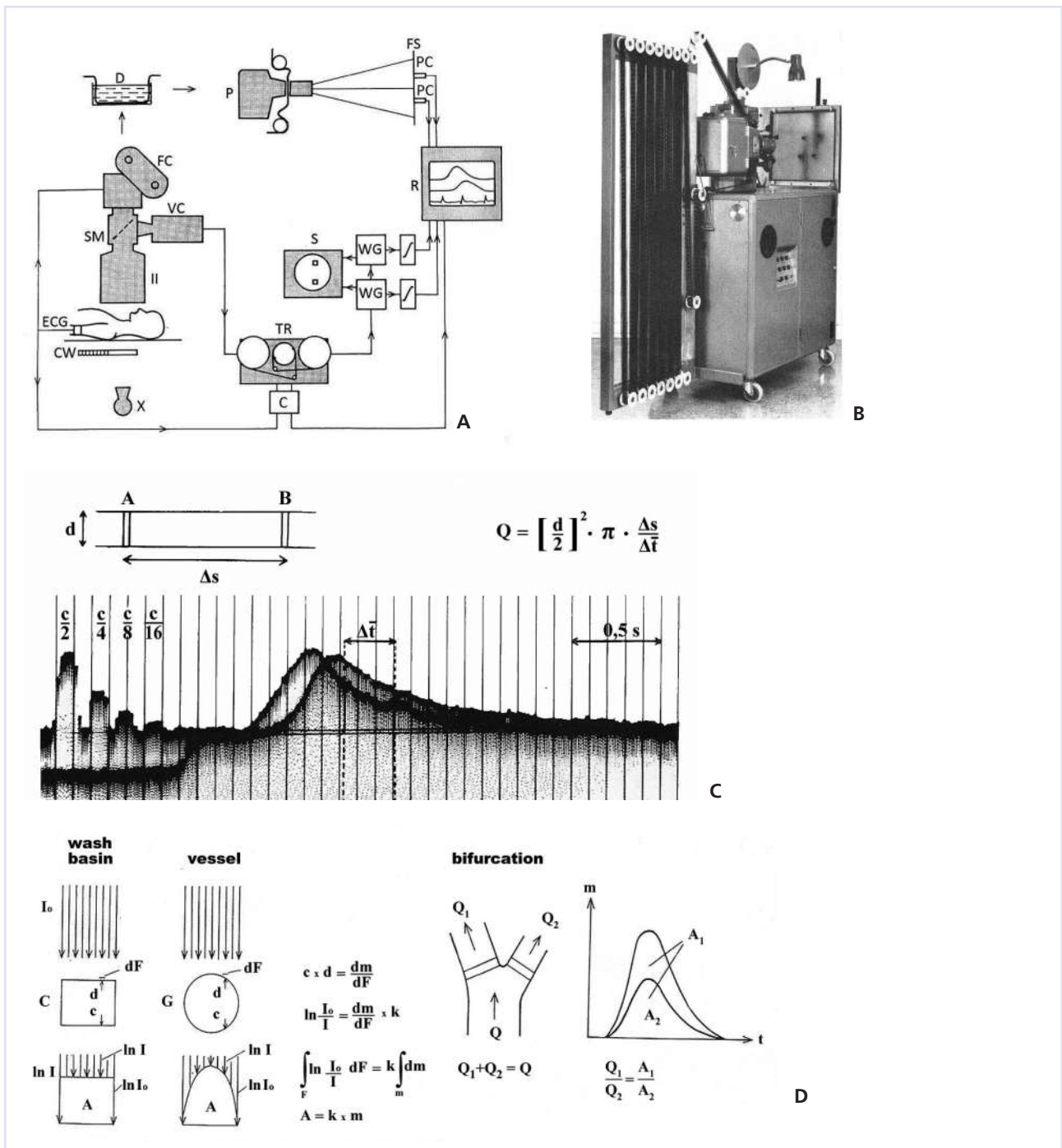


Figure 9

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- A Schematic diagram of roentgen cine- and videodensitometry. Set up to measure flow through the neck vessels in a patient. The X-rays of the source (X) pass through the water basin of the contrast "wedge" (CW) with different contrast concentrations, which for calibration was drawn over the field of interest. The light of the image intensifier (II) is split by the semipermeable mirror (SM) 90% to the film camera (FC), 10% to the video camera (VC). In cinedensitometry the film is developed (D) and projected (P) onto the focusing screen (FS) where photocells (PC) record the density changes (R). In videodensitometry the output of a video camera is recorded on a tape recorder (TR) or a videodisc. The signal in the window generators (WG) is integrated and recorded (R). The ECG signal is converted (C) on tape or disc and recorded with the density curves.
- B View of the projector for cinedensitometric measurements. Four photo cells are localised on the focusing screen on which the film is projected by a direct current lamp. In order to avoid backplay for optimally positioning the photo elements and to regulate amplification, the film is glued as an endless loop.
- C Flow measurement by cinedensitometry. At the top two photoelectric cells A and B are positioned at a distance Δs over a circular vessel of diameter d . Below left is the linear cinedensitometric recording (proved by deflections due to the different contrast concentrations) and the curves during the passage of the contrast medium injected upstream over A and B. The flow is calculated as the volume between A and B divided by the difference between the two mean transit times.
- D Videodensitometric measurement of mass (m) in a wash basin (C) and a cylindrical vessel (G) of unit length. The incoming beam I_0 is attenuated by the contrast medium at each point by the product $c \cdot d$ so that $\ln I$ exits. The area (A) under the curve $(\ln I_0 - \ln I)$ per unit length is proportional to the mass of contrast m per unit length. This is also correct for the mass and flow distribution at bifurcations (right part of the figure).

the Zurich Radiology Institute and established with us the Judkins method as the standard for coronary arteriography. In the early seventies Gander returned to Loma Linda, California, and became the right hand of Melvin Judkins. Later he introduced coronary angiography in Luzern and in Sion. Unfortunately he died early of a malignant disease.

In 1963, Rutishauser joined the brilliant Earl Wood (fig. 8A) at the Mayo Clinic in Rochester, Minnesota. He was a pioneer in Aeronautic Medicine, who designed the first anti-G-suit. Wood was also a pioneer in instrumentation for cardiac catheterisation and was the first to record densitograms during the passage of X-ray contrast. Later Wood designed the “dynamic spatial reconstructor”. Back in Zurich in 1965, Rutishauser focused his research on roentgendensitometry. He first used density curves based on 35 mm film with photocells [16], later based on videotape or disc with electronic windows (fig. 9A). He included cine- and videodensitometry for his postdoctoral thesis [17]. By replaying the film (fig. 9B) or video image of contrast-perfused vessels and measuring the density of an unbranched vessel at two cross-sections by photocells or electronic windows the flow could be measured on the basis of the volume of the vessel between the recording sections and the difference in mean transit time (fig. 9C). Rutishauser applied this method in models and in variety of vessels of the body (carotid and vertebral arteries, venae cavae, venous bypass grafts, the right coronary arteries [17, 18]).

The densitometric method was also used to measure the mass of contrast in the window provided the mass–space relation was correctly obtained by using contrast steps and leaving a water-filled cuvette over the area of measurement (fig. 9 A, C and D). Peter Osypka (fig. 8B), a German engineer, was fellow in Earl Wood’s team in Rochester together with Rutishauser. He advised and built the window generators necessary for video densitometry for us in Zurich.

Paul Heintzen (fig. 8C), paediatric cardiologist in Kiel, was visiting Earl Wood’s laboratories during our time in Rochester. With the aid of Peter Osypka he set up an institute of biomedical technics in Kiel. After Rutishauser had used multiple smaller windows for background compensation and visited the engineer Otto Schott and others several times at the Siemens Company in Erlangen, these industry partners devel-

oped the principle of digital imaging, changing from storage phosphors and video technics to high-resolution (512^2 – 1024^2 pixels) digital flat panels. Finally every pixel is a densitometer! But Heintzen’s group was the first to show that the heart chambers can be visualised by very small amounts of X-ray contrast medium using digital imaging with correct phasic subtraction [19]. Densitometry has become the standard for today’s digital radiology.

Other important members of our cardiology team at the Policlinic Zurich during these early years were Hanspeter Krayenbühl, Otto Hess and Felix Mahler. Krayenbühl did his doctorate under Hegglin in St. Gallen and started to work there in internal medicine. After a period in psychiatry he trained in 1965 and 1966 in physiology and cardiology under Robert Schlant at Emory University in Atlanta, Georgia. In 1967, he joined our cardiology group, studied specially aortic valve disease and obtained his postdoctoral thesis by work on contractility measurements of the left ventricle. After Rutishauser had been called director of Cardiology at the University of Geneva in 1976, Krayenbühl became chief of the Cardiology Division, was later elected treasurer of the European Society of Cardiology and president from 1988 to 1990. Sadly he also died in his best years.

Otto Hess was hired as an assistant by Rutishauser in 1973, right at his final medical exam. He showed an early talent for clinical research. Specially interested in the diastolic function of the heart, he worked in ventricular hypertrophy and cardiomyopathies. After his residency with John Ross in San Diego, California, he was promoted to private lecturer at the Zurich Faculty and thereafter, due to a large spectrum of excellent papers, to professor. Later he went to the University of Berne, where he became co-director of cardiology. Unfortunately he also died prematurely in 2011.

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References

All references: see end of Part II.