ONE CENTURY OF URORADIOLOGY IN EUROPE: 1896 – 1996

Section 2: THE PARENTS (1950-1980)

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After the devastation of the Second World War, medicine progressed rapidly in the Western world, led by the Americans. The development of new surgical procedures was facilitated by progress in anaesthesiology and in postoperative intensive care and pharmaceutical research led to effective new medical treatments such as antibiotics, vasoactive drugs and hormones. More precise anatomical and physiological data were necessary to improve the early accurate diagnosis of disease and to follow up the effects of treatment. As the understanding of disease processes increased and new treatments were developed, medicine became sub-specialised, with nephrology emerging as a medical discipline separate from urology. Serendipity lost its prominence in major technical innovation, some of which came from military technology which was adapted for civilian use, for example nuclear medicine and ultrasonography [1,2].

HOSPITALS WITH UROLOGY AND NEPHROLOGY DEPARTMENTS.

Uroradiology became a credible radiological subspecialty when an increasing number of radiologists in the 1960s spent most of their time evaluating the urinary tract in centers with both urology and nephrology departments [3,4,5,6]. Renal transplantation became symbolic of the new approach to kidney disease after the first trials in 1952 at the Hôpital Necker, Paris and in 1959 at the Brigham & Women's Hospital, Boston, USA. The work of the Brigham urologist Joseph Murray [7] was recognised in 1990 with a Nobel Prize (although the nephrologist John P Merrill was not included in the award). The outstanding uroradiological work started by these prestigious centres spread quickly around the world and benefited the whole of uroradiology. Radiology teaching programs began to be divided by organ

subspecialty following the American model [8], as for example in France in 1968 [9], and national and international uroradiological special interest groups grew up.

NEW IODINATED CONTRAST MEDIA.

The development of uroradiology and angiography in the 1950s was facilitated by the synthesis of a new generation of triiodinated contrast medium molecules excreted by glomerular filtration, and no longer hampered by the tubular excretory threshold of the diiodinated agents [10,11,12,13]. Acetrizoic acid (Urokon[©], Mallinckrodt Chemical Company, St.-Louis, Missouri) became available in 1950 followed by iothalamic acid (Conray®, Mallinckrodt; Contrix[®], Guerbet), both developed in the USA. The Europeans followed with the German diatrizoate (Radioselectan®, Hypaque®, Schering) then the Norwegian metrizoate (Isopaque®, Winthrop), the Italian iodamide (Uromiro®, Bracco), and the French ioxithalamate (Télébrix®, Guerbet). Pollack [5] noted the importance of the angiocardiographers who injected large doses of contrast medium to the careful study of the nephrographic stage of the IVU. The author remembers a cardiologist who stated in 1971 he did not want to request a "dangerous IVU" in a hypertensive patient who was being referred for angiocardiography! Nonradiologists often did not appreciate that the same contrast medium was used from top to toe with identical toxicity regardless of the organ or anatomical volume being examined.

1960-1980: WHO WAS WHO IN EUROPEAN URORADIOLOGY?

Alan Davidson wrote a statement that could have been expressed by all European characters evoked furthermore, in a personal communication emailed on December 10th, 2009: *"I am very pleased that*

you acknowledge the role that the Swedes played in the late 1950's and throughout the 1960's in the development of renal angiography, capitalizing on Seldinger's breakthrough percutaneous technique their due recognition [...] in section 1 of your history. I consider Olle Olsson, Erik Boijsen, and Tord Olin pioneers in this effort. As a byproduct of their work, radiologists (at least in America) were able to seize the diagnostic initiative from urologists, who did not have the necessary skills, perspective or equipment to exploit this new approach to the kidneys, especially in the investigation and characterization of renal masses."

The "parents" of uroradiology all practised "conventional radiology" including IVU and urethrocystography [3,4,5,6]. Unlike most of their American colleagues, the majority of the early European uroradiologists undertook both



JOSHUA BECKER, HOWARD POLLACK ALAN DAVIDSON, (http://www.uroradiology.org/about/history.html) Lee Talner.





Fig. 1. The Society of Uroradiology Europeans' Godfathers.



uroradiology angiography conventional and themselves. In Scandinavian and Latin Europe, unlike Germany and Spain, the urologists no longer had their own X-ray rooms beside the operating theatre, and retrograde ureteropyelography (RUP) decreased because there was no longer urological self-referral [5]. Only Phillips[©] produced a table dedicated to urology called the UroDiagnost® [14]. Robert Leroy, who had been in charge of the Contremoulins' laboratory at the Hôpital Necker (which was destroyed in 1968) was the last French uroradiographer under the control of a urologist. After this time, all examinations were performed and interpreted by professional uroradiologists with the technical assistance of a radiographer.

At this time Europe could be divided into four main areas according to the languages used for international scientific publications.

English-Speaking Europe

Of course the British used English in their British Journal of Radiology and Clinical Radiology. The Scandinavians soon opened their regional journal Acta Radiologica to publications written in the English. The faculty of the teaching programs of the Davos courses which started in the 1970s were fluent English speakers from both Europe and the USA. One of the Davos courses was dedicated to uroradiology. In the USA, in 1962, Joshua Becker [15] at the Downstate Medical Center, Brooklyn, NY, and the former urologist Howard Pollack [5,16] (1928-2000) at the University of Pennsylvania, Philadelphia, founded the «wee-wee club» which became the «Society of Uroradiology» (SUR) in 1974 with about three dozen academic members practising mainly conventional uroradiology.

The SUR board soon invited the few English speaking European uroradiologists to join as corresponding members. In 1981, at the SUR meeting held in San Diego under Lee Talner's presidency, seven out of eight non-American members were Northern Europeans: three British (Ian Kelsey Fry, Hugh Saxton, Thomas Sherwood), two Danish (Sven Dorph and Victor Hegedus from Copenhagen), one Dutch (Paul van Waes from Utrecht), and one French (Jean-François Moreau from Paris). Many Europeans were members of the editorial board of the new "Urologic Radiology" journal edited by Joshua Becker and published by Springer Verlag from 1979; they will be major actors in the promotion of the English-speaking Europeans during the 1980ies (section 3).





Thomas Sherwwod** (left) and Hugh Saxton** (top)

Sven Dorph***, Ian Kelsey Fry**, Jean-François Moreau*, Paul vanWaes** (bottom from left to right)



Latin Europe

In 1965 France took the leadership in Latin Europe. Three academic radiologists - Guy Lemaître (1921-1985) of Lille, Jean-René Michel of Paris, and Jean Tavernier of Bordeaux, editors of the first comprehensive textbook of uroradiology [19] written by radiologists only - decided to meet every three months at the Hôpital Necker in Paris. The first French professor of nephrology, Jean Hamburger [20,21] (1909-2002) who founded the «Société de Néphrologie» in 1960, and the professor of urology, Roger Couvelaire [22] (1903-1986), designed a huge U-shaped building dedicated to the urinary tract at the Hôpital Necker. The so-called «Palais du rein» opened in 1968 with an 8 room department of uroradiology which included an angiography unit, and an ultrasound unit was opened in 1978.





The department was chaired by Jean-René Michel, assisted by Jean-François Moreau and three assistant professors (chefs de clinique). The uroradiology book published in 1970 was successful and a second edition was produced in the 1970s by the enlarged *«Club du Rein»*. The Club included Annick Pinet (who chaired the second



Fig. 2. Jean Hamburger before the Palais du Rein at the Hôpital Necker and Roger Couvelaire.





Fig. 5. Founders of the «Club du Rein»: Guy Lemaître (by courtesy of Dr J Carton) - Jean-René Michel (author's collection) - Jean Tavernier (by his courtesy)

French department exclusively for uroradiology opened in 1974 at the Hôpital Edouard Herriot in Lyon), Jacques Padovani and Michel Kasbarian of



Fig. 6. André-Noël Dardenne (author's collection)

Marseille, and Marie-Christine Plainfossé and Jean-François Moreau of Paris. Most uroradiologists in France and Italy and also in most of the countries around the Mediterranean were still not fluent English speakers. In the opinion of the author, the Belgian André-Noël Dardenne [23](1944-2007) of Brussels, was the best uroradiologist worldwide at this time. He won the quiz at the SUR meeting in 1981 and co-chaired the GU program of the 15th International Congress of Radiology with Alan Davidson in the same year. Dardenne was a member of the second wave of the Club du Rein but he never tried to be recognised by the English-speaking community.

Germany and Austria

Germany was the native country of Roentgen and many radiological innovations such as the discovery of the organic contrast media were published in German. Also the radiology industry in Germany headed by Siemens and Schering was strong. However, in Germany the internists held



Fig. 7. Minute sequence pyelogram (MSP) and Frusemide washout-test (WOT) in a patient with reno-vascular hypertension (stenosis of the right renal artery) (author's collection).

the monopoly on radiology, with the urologists in charge of urinary tract radiology. Many radiologists did not speak English and contact with other western Europeans was limited except with some of the adjacent countries and Scandinavia.

USSR and the Soviet Block.

Throughout the twentieth century the impact of Russian radiology in Europe was minimal. The emphasis of the Russians on preventive medicine led them to favor fluoroscopy and radionuclides rather than radiography. In August 1980, a panel of three French radiologists was invited to give expert lectures during a technical exhibition in Moscow. The audience posed one question to the speaker on abdominal CT, two questions to the speaker on renal ultrasound, and dozens of questions on MRI to the



Fig. 8. Retropneumoperitoneum

biophysicist.

In the satellite Eastern Republics the situation of radiologists was difficult too, but they tried to maintain personal contacts, often through their connections with industry. Because of their previous relationship until 1939 with what had become the free world, many remained closest to German culture. Those who had not emigrated to the USA or to Western Europe were often more fluent in German than in the English or French. Radiologists in Western Europe often received requests for reprints of their papers that radiologists in Eastern Europe knew from *Index Medicus, ISI Current Contents, Excerpta Medica* and *Zentralblatt* listings.



1950-1980: SIX URORADIOLOGICAL CHALLENGES

The new subspecialty of uroradiology faced six major clinical challenges in the period 1950-1980.

1. Renovascular hypertension.

In 1948 Harry Goldblatt (1891-1977) described a rare variety of hypertension related to unilateral renal ischemia called "*Renovascular hypertension*" [24]. There was great excitement about the possibility of detecting renal artery stenosis with IVU and about whether it would be curable. Evans [25] introduced the minute-sequence pyelogram to detect delayed pelvicalyceal opacification on the affected side. Amplatz [26,27] modified the examination with the urea wash-out test, which was not widely adopted because it was not sufficiently effective [28]. The German Hardt [29] proposed the injection of frusemide, but this was not sufficiently sensitive either (fig.7). The diagnosis had to be confirmed by renal arteriography and selective renal venous sampling



Fig. 10. Andreas Grüntzig



[30] was necessary to prove that the renovascular lesion was important in the pathogenesis of the hypertension [31].

Another rare cause of hypertension produced similar excitement after Jerome Conn (1907-1994) described an aldosterone secreting adrenal adenoma which upset the renin-angiotensin system in 1955 [32]. Pneumoretroperitoneum was used again in 1948 by the Spanish Ruiz-Riveras [5] using presacral oxygen injection (Fig 8) and was the reference diagnostic method to study the adrenals in suspected Cushing's syndrome and pheochromocytomas [33]. However, neither pneumoretroperitoneum nor arteriography was sufficiently sensitive to detect a tiny Conn's adenoma. Adrenal venography was developed first in Germany by Bette [34], followed by Butch [35] in Scandinavia and Joffre [36] in France (Fig. 9).

Then in 1975 the many researchers studying hypertension were shocked by two ground breaking papers published by Barbara McNeil in the same issue of the prestigious New England Journal of Medicine [37,38]. She had made a sophisticated statistical analysis of the subject and introduced the concept of the cost-effectiveness of technological innovations. Were IVU and arteriography more effective than isotopic scintigraphy? Was it even worthwhile



Fig. 12. Bruce J Hillman (author's collection)



Fig. 13. Severe distention of the upper urinary tract induced by a chronic distention of the bladder (benign prostatic median lobe). Urographic pattern 3 hours after drip infusion of 1g iodine/kg bw. (author's collection)

detecting renovascular hypertension with one of these methods if drug treatment of hypertension was very effective?

Then in 1978 a German angiographer practising in Zürich, Andreas Grüntzig (1939-1985), described his revolutionary treatment of renal artery stenosis by percutaneous transluminal dilatation [39] (Fig 10). Immediately, Francis Joffre [40], a French uroradiologist in Toulouse, devoted his research program to the new discipline of *"interventional angiography"* (Fig 11). Last but not least, Bruce Hillman [41] of Tucson, Arizona introduced *Digital Intravenous Angiography* (DIVA) performed on an innovative ©CGRmachine. This last modification of the conventional IVU protocol created a sensation at the RSNA 1981 meeting (Fig 12).

2. Urinary tract obstruction

Since it had been introduced in 1930, artificial external ureteral compression had been a common subject of disagreement between many radiologists and urologists. The value of better distension of the pelvicalyceal system helped to compensate for the low excretion rate of diiodinated contrast media but the urologists were concerned that, if compression was applied too early, mild ureteral obstruction might be overlooked. Also, patients often complained that the device caused discomfort. In France, Coliez concluded that many, but not all, French radiologists only applied compression after the patency of both ureters was demonstrated on early films [42]. Severe ureteric obstruction was seen as a "non-functioning" kidney, which was too often incorrectly considered to be irreversibly damaged and to require nephrectomy [43]. Once high doses of triodinated contrast media and delayed nephrotomograms showed the famous "Dunbar's crescent sign" and filling of the dilated pelvicalyceal system, it was apparent that many of these kidneys retained some function. In 1964 Schenker introduced the technique of drip infusion pyelography [44], freeing the radiologist to increase the contrast medium dose above the "single dose" (20ml), which did not provide a dense nephrogram and the "double dose" (40ml) which did not opacify severely dilated pelvicalyceal systems. The introduction of the Butterfly needle made intravenous injection or prolonged infusion easier and safer. In the early 1970s, Schering, France produced a 200ml-vial of diatrizoate (®Radioselectan urinaire et vasculaire 76%) which allowed the drip-infusion of 1g of iodine/ kg body weight, a standard dose recommended by the Club du rein [19] in severe obstruction, with 24 hour delayed nephrotomographic films to check for any pelvicalyceal filling before a kidney was considered to be non-functioning (Fig 13).

In 1969 Ogg and Saxton [45] developed percutaneous nephrostomy to avoid the complications of cystoscopy and retrograde uretreric catheterisation and to provide drainage of the obstructed pelvicalyceal system. According to Pollack [5], punctures of the kidney and/or renal pelvis had already been suggested by others, including the French Kapandji and the Swedish Wickbom. However the technique came into its own only when new needles and plastic materials for catheters were developed. This new technique also led to a new treatment of urolithiasis by calculus extraction following percutaneous nephrostomy under radiographic control, which had first been suggested by Ferström and Johansson [46] in 1976.

3. Urinary tract infection

Urinary tract infection (UTI) is common throughout life. The British uroradiologist C John Hodson (1915 -1985) in 1959 emphasised the importance of calycealpapillary lesions - so-called *"calyceal clubbing and scarring"* - seen in children following acute or



Fig. 14. C John Hodson by courtesy of Pr. Bruce L McClennan, Yale University.

recurrent pyelonephritis [47,48]. He dedicated his long life in Britain (at University College Hospital), in Newfoundland and then at Yale University to the relationship of these lesions to vesico-ureteral reflux and hypertension (Fig. 14).

At the same time, Renée Habib [49], pathologist to Pierre Royer's school of paediatric nephrology, which was associated with the paediatric radiologist Jacques Lefebvre [50] at the Hôpital des Enfants Malades of Paris, described a new condition which was similar radiologically but different pathologically. She called this condition "segmental hypoplasia", already known as the Ask-Upmark kidney and she believed that this lesion, which was usually found in hypertensive children who did not have a history of UTI, was congenital. These opposing theories were debated in 1978 at a conference led by Hodson and the Australian Priscilla Kincaid-Smith [51], but a consensus was not reached. For a decade at the Hôpital Necker hundreds of children and adolescents presenting with clubbing and scarring, recurrent UTI and documented vesico-ureteral reflux were referred for Hutch's ureteric reimplantation operation [52,53] (Fig 15). From this huge unpublished case collection and a retrospective study by Philippe Grenier for his medical thesis of 110 adult patients who had presented with clubbing and scarring, Moreau and Grünfeld [54] concluded that none of the theories



Figueh5/2Micturating IV cystography demonstrating late asymetrical bilateral active reflexed surchoild. (no passive reflux, right duplex kidney). (author's collection)

explained all the cases. Rather, this was a radiological syndrome complex with a variety of underlying pathogenetic mechanisms. They suggested that many of the patient files studied by both Hodson and Habib may have been misinterpreted because the search for reflux was not sufficiently rigorous [55]. Hodson and Moreau met at Yale University in June 1981 to discuss Moreau's hypothesis. Later, when Hodson met Habib [56] in Washington D.C., he told her that he had been impressed by their discussion, but sadly Hodson died before the three of them could collaborate on an editorial summarising their consensus. The British uroradiologist Hugh Saxton wrote in a personal communication emailed on December 9th, 2009: "I was his registrar at UCH and that began my interest in uroradiology. His dates were. It is one of my greatest regrets that he died before I started doing pressure measurements during voiding in children with unstable bladders. In my paper 'Spinning top urethra - not a normal variant' Radiology, 168: 147-150, 1988 you can see the sort of pressure generated by a child trying to stop themselves from leaking. The micturating cystograms carried out by David Edwards for Hodson, were mainly on children with enuresis. Many were found to have reflux in association with the clubbing and scarring which Hodson was diagnosing. Hodson was constantly frustrated by the inability

to show scarring experimentally without urethral obstruction. He 'knew' that reflux caused scarring but this last clinching piece of evidence was lacking." 04. **Haematuria**

Haematuria is always a worrying symptom because of the possibility of underlying cancer. Before IVU was widely used to investigate haematuria, cystoscopy with retrograde pyelography was the diagnostic test used to screen patients with haematuria by checking the bladder and the upper tracts. At this time, before unenhanced CT, high-quality plain films were the best method of diagnosing radiopaque calculi, the most frequent cause of painful haematuria. Urography with bolus injection of the new triiodinated contrast media and ureteric compression improved the diagnosis of many of the causes of painless haematuria, such as radiolucent calculi, transitional cell tumors, vascular malformations, schistosomiasis, etc. [57]. Bolus injection and nephrotomography also improved the urographic detection of renal masses. (Fig. 16). However, benign renal cysts which do not usually cause haematuria, are a much commoner cause of a renal mass than adenocarcinomas. When urography detected a renal mass, renal angiography was used to look for the typical hypervascularity shown by the majority of adenocarcinomas. However, some adenocarcinomas are avascular, mimicking cysts [58]. Ekelund [59] and Michel [60] suggested that



Fig. 16. Pseudo-cystic partly calcified (arrow) renal cancer. a) preliminary nephrotomogram (AO: vena cava); b) opacification of the vascularized thick wall after bolus secong injection. (author's collection).



Fig. 17. Pseudo cystic renal cancer: a) nephrotomography at a tubular stage; b) selective arteriography with angiotensin.exhiting the cancer vasculature. (author's collection)

angiotensin, a strong vasoconstrictor of normal renal arterioles, should be injected intraarterially just before the contrast medium, to show neovascularity in a hypovascular tumor or sometimes a vascular malformation which had been hidden by the normal renal vasculature [61] (Fig. 17).

At this time, developing economies were looking for cheaper methods of treatment and renal embolization was one of these [62] (Fig 18). At the First International Symposium on Interventional Radiology [63] in Algarve, Portugal in 1979, two papers on embolization of renal cancer came from the favorite agent but Merland [66] used the sticky agent, bucrylate, to treat aneurysms.

5. Renal impairment, renal transplantation.

In patients with renal failure, it is important to detect potentially reversible obstruction early in the diagnostic process. The possibility that urography with contrast media would cause further renal damage had to be balanced against the possibility of inducing severe or even lethal sepsis if cystoscopy and retrograde pyelography were used to exclude obstruction in these uremic patients. In 1962 the



Fig. 18. Embolization of a renal carcinoma by Hlava *et al*⁶¹.
(by courtesy of Excerpta Medica)

Main effects of embolization. (A) Richly vascularized tumour with (B) venous collaterals. (C) Pre-operative embolization interrupts temporarily blood flow through tumour and kidney.

Canadians MacEwan, Dunbar and Nogrady [67] broke the taboo on using contrast media in patients with impaired renal function with a paper on IVU in children with renal impairment. Schwarz [68] showed that urography with a relatively low dose of contrast medium (60ml of Hypaque 50%) in adults with impaired renal function diagnosed obstruction in a significant proportion of patients, with no long term harmful effect on renal function. Kong and Meaney [69] from the Cleveland Clinic also showed that diagnostic arteriography in their atheromatous patients with chronic renal insufficiency was safe. The British radiologists Kelsey Fry (working with the nephrologist Cattell) and Sherwood had already contributed to the understanding of the physiology of contrast medium excretion and to the relation between this process and the nephrogram and pyelogram [70,71,72,73]. They realised that "high dose urography" using a double dose of contrast medium (600mgI/kg) would improve the concentration of contrast medium in the glomerular filtrate in patients with impaired renal function and showed that they could reliably diagnose or exclude obstruction with this method [74]. They used the nephrographic pattern seen in oliguric and anuric patients to differentiate many of the causes of renal failure [75]. Subsequently, Judith Webb, with Kelsey Fry and Cattell, could not find evidence that high dose urography in well hydrated patients produced long term harmful effects on renal function [76]. In 1972, Paul van Waes [77] showed that the extrarenal hepatointestinal excretion of metrizoate through the



liver removed up to 50% of the contrast medium in three days in oliguric and anuric patients (Fig. 19). At the Necker hospital, the nephrologists [78] drew the attention of Michel and Moreau to the incidence



Fig. 20. Delayed aortogram and urogram after injection of 60ml of Télébrix 38 in the inferior vena cava in an oliguric patient with aortic aneurysm producing a retroperitoneal fibrosis. (author's collection)

of further reductions in renal function after IVU and arteriography in their azotemic patients, despite the undoubted diagnostic use of these investigations [79,80,81]. Michel and Moreau, with the urologist Dufour [43] and the nephrologists Kleinknecht, Jungers and Dominique Ganeval, recognised that there were two different clinical groups of renal impairment patients. The renal function of the patients presenting with obstructive uropathy with either acute or chronic renal failure did not deteriorate after they received large doses of contrast medium, while the renal function of the patients with chronic nephropathies who had multiple contrast medium examinations in rapid succession, (e.g. an IVU followed within a couple of days by abdominal angiography, coronary angiography or a biliary study) did deteriorate [82,83]. Interestingly, renal angiography was often better tolerated than IVU because of the smaller doses used and the less prolonged preceding dehydration. When a delay of five days was observed between two contrast medium examinations, any serum creatinine increase was transient. Because retroperitoneal fibrosis was a curable cause of subacute or chronic renal impairment, they used cavo-aorto-urography performed with a single high-dose of contrast medium injected into both femoral veins in all patients with oliguric renal failure referred for an "IVU" [84] (Fig 20). At this time, the difficult early monitoring of renal transplants meant that contrast medium procedures

J. Radiol., Electrol., 1974, t. 55, nº 1, pp. 1-15.	Mots-CLEF: : imuffisance rénale aigué nécrose corticale rénale anériographie rénale transplantation rénale rejet suraigu
Aspects artériographiques	J. F. MOREAU, D. KLEINKNECHT, J. P. GRUNFELD, F. REBOUL.
des necroses corticales rena	IES J. SABTO, J. R. MICHEL
Les nécroses corticales rénales (NCR) repré- sentent environ 2 % du total des insulfisances rénales aigués (IRA) [10]. Les états de choc, sur- tout obstétricaux, en sont l'étiologie principale. L'évolution immédiate a été transformée par la pratique d'épurations extra-rénales. L'évolution plus tardive dépend de l'étendue de la nécrose : dans les nécroses totales, qui représentent la moi- tié des cas environ, l'hémodialyse chronique défi-	pratiquement réduite à la seule observation de DEUTSCH et coll. [2]. On ne peut guère retenir les deux clichés de NCR illustrant une revue générale récente de HALPERN, consarcée à l'arté- riographie de l'insufisance rénale [5]. Les signes artériographiques des NCR sont surtout connus par le biais de l'expérimentation animale [10, 12, 16] et de la transplantation rénale. La NCR du transplante rénal est une manifestation de rejet
Angiographic patterns of renal cortical necrosis	
Renal cortical necrosis (RCN) represents two per cent of the causes of acute renal failure (ARF) [10]. It is usually related to the acute shock syndrome of major obstetrical accidents. Prognosis of the acute phase is improved by haemodialysis. The long-term prognosis depends upon the anatomical extent of the necrosis [10]. In complete necrosis which constitutes about fifty per cent of cases, chronic haemodialysis and/or renal transplantation are necessary. In partial RCN, one can except some functional recovery and long-term survival with residual renal insufficiency [10]. Renal biopsy is necessary for recognizing RCN. This diag tosis is occasionnally confirmed several weeks or months later by the appearance of renal arteriographic radictifications on plain films [10, 19, 22]. The indication for renal arteriographic aclifications on plain films [11, 12, 16] or angiograms performed on transplantation drateris of RCN are best known through animal experiments [11, 12, 16] or angiograms performed on transplantation is detail the attriographic fautures of RCN in human transplantation [8, 13] while Visix <i>et al.</i> described the same radiological pattern seen in the transplated dog [20]. The progne of this paper is to evaluate the role of renal arteriographic paper is to evaluate the role of renal arteriography in the diagnosis and the prognosis of thirteen cases of RCN of various actiologies.	
Communication présentée à la Société française de Radiologie médicale, séance du 8 avril 1973. Travail du Service de Radiologie de l'appareil urinaire (P J. R. Micruit) et de la Clinique Néphrologique (P' J. HAM- BURGER), Hôpital Necker, 161, rue de Sèvres, 75730 Paris Cedex 15.	
Fig. 21. Renal cortical necroses by JF Moreau <i>et</i>	
<i>al.</i> ⁸⁴ Fac-simile of the unique bilingual original ar-	
ticle published in the Journal de Radiologie edited	
by JR Michel and at the origin of the personal re-	
lationship between the author and Dr LB Talner of	

the UCSD calling for reprints). (author collection).

with some potential for risk were justifiable when the only alternative was scintigraphy [85,86].

The nephrologist Jean-Pierre Grünfeld. with Dieter Kleinknecht and Joseph Sabto, established protocols based on what he had learned about renal haemodynamics from Norman K Hollenberg [87] during his fellowship at the Brigham & Women's Hospital, Boston. Michel and Moreau performed selective and superselective arterial and venous catheterisation and angiography in oligoanuric patients with acute tubular necrosis or renal cortical necrosis [88,89] (Fig. 21) and in hypertensive transplanted patients [90], and the nephrologists measured the renal blood flow with isotopic rare gas [91]. Moreau and Paul Baillet in his medical thesis showed marked vasodilatation of the renal vasculature at angiography after infusion of dopamine and frusemide in the normally functioning transplanted kidney, and this was used as a short term method of treatment for acute rejection [92].

6. New alternative technologies

Nuclear medicine and ultrasonography (US) are early examples of what Clayton Christensen at the Harvard School of Economics terms "disruptive innovations" in medical imaging [93]. The term disruptive innovation describes a radical and unexpected technical innovation which creates a new market and may subsequently replace existing technology. Both techniques emerged in the 1950s while roentgenology was booming, and matured slowly until they were included in the new "Departments of Medical Imaging" in the 1970s.

i. Nuclear Medicine started just after the end of the Second World War and was at first a very militarydependent biophysical specialty. It soon developed at the Lawrence brothers' laboratory, UC Berkeley, USA, where many foreign doctors were trained. Centre de l'Energie Atomique (CEA) had been created in France by the Nobel Prizewinner Frédéric Joliot-Curie who discovered artificial radioactivity with his wife Irène, the daughter of Marie Curie. Many nuclear medicine applications were first developed at the hospital of the city of Orsay, a Parisian suburb, before sophisticated departments opened in general French hospitals [94]. The pioneers worked mainly on biochemical application, studying organ physiology with dedicated radionuclides. Scintigraphy became a clinical imaging tool when Hal Anger (1920-2005) in 1957 invented the gamma-camera at UC Berkeley [95]. Only a very few uroradiologists were experts in nuclear medicine, for example Lee Talner at UC San Diego, USA, coauthor of Sherwood's

Uroradiology [96], and later on Henrik Thomsen [97] of Copenhagen University. The first international symposium on radioisotopes in the diagnosis of kidney and urinary tract disease was held in 1969 in Belgium at the invitation of Timmermans and Merchie [98]. Donald Blaufox, a member of the SUR, who convened the second symposium in 1972 in New York City [99], was impressed by the research presented by Claudio Biachi of Italy, Mark Joekes of Britain, Claude Raynaud of France and Karl zum Winkel of Germany, none of whom were radiologists [100].

ii. Renal ultrasonography (US) based on the



Fig. 22. Renal compound US images by Sarti and Sample. (mounted on their book's cover page by the author).

principle of sonar used by the military to detect submarines was initially an echo A line. The first images of the urinary tract were obtained in 1956 by Ian Donald (1910-1987), a gynaecologist and obstetrician at the University of Glasgow who studied abdominal masses with a prototype machine [101]. Another pioneer was the Danish urologist Hans H Holm [102] who focused his research both on imaging and US-guided renal punctures, using specialized probes from Bruel and Kjaer. Renal puncture had been suggested by Lindblom [103] in 1946 but was not widely used until US could guide the needle safely [104]. Other pioneers were general radiologists like Marie-Christine Plainfossé of Paris and Francis S Weill [105,106] of Besançon, a future president of the World Federation of Ultrasound in Medicine & Biology (WFUMB). The author remembers Weill having to tolerate a lot of criticism from a sceptical audience when he presented his first paper on renal ultrasonography at the Societé Française de Radiologie in 1972. Relatively few uroradiologists practised US, examples among the membership of SUR in 1980 being Arthur Rosenfield of Yale University, USA, and JF Moreau in Paris.

A new branch of imagers, called "exclusive sonographists" in France, promoted US as being non invasive, since it did not involve contrast medium or ionizing radiation, as preferable to invasive urography and arteriography. Unfortunately, they too often lacked adequate knowledge of anatomy and radiology to be reliable and many false positives and false negatives were observed in routine clinical practice. The new concepts of operator-dependence apparatus-dependence and emerged. Manv radiologists were reluctant to adopt the algorithmic approach proposed in 1974 by Howard Pollack and Barry Goldberg [107] who suggested evaluation of renal masses with US as an alternative to IVU and/ or arteriography. The atlas published in 1980 by Sarti and Sample [108] of University of California Los Angeles shows beautifully the difficulties US pioneers faced before grayscale was developed by the Australian George Kossoff [109] in 1973 (Fig. 22). The majority of the sonographers in the 1970s used analogue compound images. High-resolution realtime appeared in the mid-seventies in the USA and much later in Europe. In 1977, digital images with 16 shades of gray and focused higher frequency probes allowed adequate resolution for examining deep organs.

To avoid the pitfalls of ultrasound, uroradiologists had to learn the strengths and weaknesses of the new method in relation to conventional radiology and to develop new algorithms for urinary tract investigation. For example, in the early days, Moreau discovered the difficulties caused by absent or ectopic kidneys [110]. With the exception of the transplant kidney [111], he used US as a secondary test after IVU in patients with normal renal function [112].

October 15th-20th 1973: Three Important Advances at the 13th International Congress of Radiology (ICR), Madrid, Spain.

Thousands of radiologists from around the world in 1973 attended the 13th International Congress of Radiology (ICR) in Madrid, Spain. At this meeting,

angiography held pride of place and the swansong of conventional radiological technology was symbolized by the CGR Futura 2000 prototype with complex tomography, videoscopy, 3D-telecommand, and automatic film processing (which never developed however was commercially). It would have been easy to overlook three important advances which were presented in small rooms with few attendees.

i. CT-scanner. The British engineer Hounsfield had been working since 1971 with the neuroradiologist Ambrose on what they termed

"computerized transverse axial tomography". They presented their work in Madrid and published the first papers on this new method of brain imaging in 1973 [113-114]. In 1974 Ledley [115] introduced the first total body ACTA-scanner in Science with the following lines: «The ACTA-Scanner has virtually unlimited potential in the evalution of any part of the body. (...) The abdominal pathologies that can be studied are almost uncountable: gastric neoplasms, pancreatic cysts and stones, gallstones, neoplasms of the liver and pancreas, bowel tumors, abdominal aortic aneurysms, renal neoplasms and cysts, atrophy of the kidneys, bladder tumors, uterine tumors, ovarian cysts, and many more. (...) there is no doubt that as the new technique is developed ACTA-grams will contribute significant information in the transverse plane, as well as in densitometric analyses. The impact of ACTA-scanning will not be limited to the diagnostic area, but will extend, at least indirectly, to general patient management and to some aspects of medical economics as well. Risk-laden, technically complex, and costly diagnostic procedures, sometimes requiring lengthy hospitalization, will in some cases be eliminated. The simple, innocuous, and noninvasive ACTA-scanning can be performed on an outpatient basis. Repeated follow-up examinations should be easily accepted by the patients, considering that this diagnostic test is carried out without discomfort. The entire field of diagnostic radiology is on the verge of revolutionary changes.»

Because of the high cost of the new equipment, many European countries limited the introduction of CTscanners with a new procedure of authorization by the government. France, Italy and the UK suffered from slow introduction of the new technology, unlike Belgium [116]. This meant that foreign radiologists



often had to provide chapters on CT for books. Struyven [117] of Brussels and Albert Baert [118] of Leuven wrote the chapter on CT in the urinary tract respectively in the Club du Rein's textbook in 1978 and in Pistolesi's Italian textbook in 1981, and Sherwood invited Alan Davidson [119] to write the CT chapter in his book.

ii. Metrizamide. The high osmolality of the ionic triiodinated contrast media was associated with many sideeffects. The Australian uroradiologist Benness [120] had already shown that there were less vascular side-

effects with methylglucamine salts than with sodium salts. but the methylglucamine agents were also hyperosmolar. The brilliant radiologist Torsten Almén [121] of the University of Lund had been working on a revolutionary generation of low osmolar iodinated contrast media since 1969. He designed the first of these, the nonionic monomer metrizamide (®Amipaque, Nyegaard & Co). Unfortunately, it was expensive, had relatively poor water solubility and was used for neuroradiology only. Pollack [5] described Almén's difficult situation: "Unfortunately, Almén was once again forced to suffer those twin



Fig. 23. Torsten Almén.

maladies so common to original thinkers, rejection and frustration. It was several years before he was able to interest any pharmaceutical company in his ideas - even with a molecular blueprint in hand. Eventually, a small Norwegian concern, Nyegaard A/S and Co., was persuaded to listen. The perspicacy of its director of research and development, Hugo Holtermann, was rewarded years later when the little known Nyegaard evolved into the giant international Nycomed organization, largely on the strength of low-osmolarity contrast media."

The Italian chemist Felder [122] synthesized the first water soluble and stable nonionic monomer, iopamidol (®Iopamiron, Bracco Spa) in the mid 1970s. In 1976, Laboratoire Guerbet developed ioxaglic acid (®Hexabrix), a low osmolality ionic dimeric contrast medium. Ioxaglate produced high density IVU images and intraarterial injections of ioxaglate were painless [123]. This astonished haemodialysis patients referred for angiography of their arteriovenous shunt, for until then this had been the most painful examination performed in a department of uroradiology [124].

[Reprinted from RADIOLOGY, Vol. 115, No. 2, Pages 329-336, May, 1975.] Copyrighted 1975 by the Radiological Society of North America, Incorporated **Osmotic Nephrosis Induced by Water-Soluble** Triiodinated Contrast Media in Man A Retrospective Study of 47 Cases ançois Moreau, M.D., A.I.H.P., Dominique Droz, I.H.P., Joseph Sablo, C.P., Paul Jungers, M.D., A.I.H.P., Dieter Kleinknecht, M.D., A.I.H.P., Nicole Hinglais, M.D., and Jean-René Michel, M.D., A.I.H.P. Nicole Hinglais, M.D., and Jean-Hene Michel, m.D., ALIN-F. opies were performed in 211 patients within 10 days of excertory uroraphy or teriography in which diatrizoate, lothalamate or loxithaliamate had been used. In specimens, osmotic nephrosis of the proximal tubular cells was found. Previous cition had been normal in 10 patients, moderately impaired in 19, and severely in 18. Tubular atrophy and/or necrosis was associated with histological features of patients. Diffuse camotic nephrosis was more often found in patients biopsid er roentgenography and also with severe renal insufficiency, but was not neces-sociated with declining renal function. The mechanism(s) by which contrast ay induce osmotic nephrosis remains unclear. may induce osr INDEX TERMS: Contrast Media, toxicity • Kidneys, failure • Kidneys, necrosis transplantation • Nephritis • Pyelonephritis Radiology 115:329-336, May 1975 WATER-SOLUBLE triiodinated contrast media (WTCM), presently used for radiological examina-tion of the urinary tract and vascular system, are usually numbe of DELAY BETWEEN X-RAY EXAMINATION cases considered safe and non-nephrotoxic (4, 12, 15, 20, 39, AND RENAL BIOPSY 43). However, acute renal failure with or without anuria 4.5) However, acute renar handle with or without another may follow excretory urography (IVP) or angiography, particularly when large doses of WTCM are used (2, 7, 14, 22, 27, 28, 30, 31, 38). These complications re-



Fig. 24. Osmotic nephrosis. facsimile of the article and histologic findings. (by courtesy of Radiology).

iii. Osmotic nephrosis. Many patients admitted with nephropathies at the Hôpital Necker had percutaneous renal biopsies just after urography or arteriography. Kleinknecht [125] often found cytoplasmic vacuolisation of the tubular cells, so-called osmotic nephrosis, induced by the non specific cellular phenomenon of lysosomal pinocytosis, which had been described by the Belgian Nobel Prizewinner Christian de Duve [126] of Louvain-en-Woluwe. When osmotic nephrosis was seen in oligoanuric patients after IVU, it led to a debate on the possible effects of the marked cellular enlargement which narrowed the tubular lumina. Could this block the excretion of urine as myeloma or Tamm-Horsfall protein cylinders can do in severely dehydrated patients? In Madrid, the radiologist Moreau, the nephrologist Jungers and the pathologists Dominique Droz and Laure-Hélène Noël presented their findings that in humans [127] and later a mouse experimental model, there was no correlation between the histological lesion of osmotic nephrosis and the nephrotoxicity of the iodinated contrast media. Even the low osmolar media, both non ionic monomers and ionic dimers, produced vacuolisation so the phenomenon did not relate to the osmolality of the contrast media or their chemical structure [128]. Jean Hamburger, who had both heard the lectures and reviewed the manuscripts before publication, supported these findings and commented that they had been more troublesome for the contrast media industry than for nephrologists. The mechanism of the nephrotoxicity of the contrast media used in uroradiology remained a mystery.

1980: Whither IVU?

The professors of forensic medicine, Derobert and Dehouve (who also was a radiologist), together with Wolfromm, an allergologist, wrote in 1964: "More patients died from lack of an IVU than patients died because they were submitted for an IVU" [129]. By the end of the 1970s, urography had become a sophisticated technique practised by uroradiologists, not urologists [4,5,130]. Ten years after Saxton's famous review [3] and Lalli's booklet on the "tailored urogram" [131], the technical aspects had been defined, the indications and the contraindications were widely accepted, and the complications and their prevention were known [132]. However, urography now faced the challenge of the alternative methods of US and CT, and the new generation of uroradiologists needed to develop strategies for using them optimally.

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les clefs de l'interprétation

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flammarion médecine

Rapida interpretazione

A AFFEL

dell' UROGRAFIA

J-F MODELI

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