Advent of Percutaneous Renal Biopsy

There was a paper studying kidney histology on hypertensive patients but it was an operative technique but there had been performed needle biopsies before, especially Perez in Cuba had published a work on "kidney puncture", he called it, on kidneys of normal size, and he published it in 1950 so it was actually published a year before our first paper.

We did our first biopsy in May '49, and we didn't know of Perez' work because it was in Spanish and in a canceralogical paper published in Havana. Alwall performed a kidney biopsy in 1944 and he didn't publish it until 1952 because the patient had died and originally he thought that the patient died from the biopsy but later he changed his opinion and found that he had probably died of the x-ray procedure involving contrast medium.

Relationship to Early Liver Biopsies

It's true that, of course, liver biopsy, which Iversen and Roholm published in '39 just before the war, was a main inspiration, but at that time Iversen had asked me to look after uremic patients. He had given me a small room where I could have the patients and study the physiology. And at that time we occasionally got anuric patients from the psychiatric department in another hospital where they treated barbiturate poisonings mostly and the first patient who was biopsied in our hands was such a patient where there was no other renal disease than the anuria probably caused by prolonged shock, and he also had carbon monoxide poisoning. It was not clear with the patient, you don't know what's happening in his kidneys so it was natural to extend the liver biopsy technique.

The Biopsy Needle

The same needle as we used for liver biopsies at the approximate place where we expected the kidney to be. The needle had a stylet inside so you could introduce the needle through connective tissue onto the kidney.

Then you removed the stylet and placed the syringe on the needle and then you pushed the needle forward into the kidney tissue and cut a cylinder of kidney tissue.

Then to keep it, not to lose it during the final procedure, you created a vacuum in the syringe and took out the syringe and needle together and the kidney tissue would end up... (under the piston).

Reaction to the First Biopsy

We were very proud of this tiny piece of tissue and Iversen and I went down to our pathologist, because he had been in more or less

the same situation with his liver biopsy, and told him here we have something you have never seen before, fresh kidney tissue from a patient with an unknown renal disease. But to our great surprise it didn't ring a bell with anybody in the pathology department. He called it "keyhole" and sure it is keyhole pathology and I'm still surprised that it worked so well as it does and I have the impression that the reason we can use it at all is that it's a long piece of kidney tissue and not from only one tiny spot. It wouldn't work nearly as well if you didn't have a couple of centimetres of kidney tissue.

The First French Renal Biopsy

He (Hamburger) invited me down to do a biopsy on a nephrotic patient there and the biopsy was quite successful. I came out with a nice piece of kidney tissue and nothing happened to the patient but I think I shocked the French doctors because after that they started using open biopsies, cutting down on the kidney, and with great difficulty extracting kidney tissue. It is not so easy as it sounds to take renal tissue in an open biopsy.

Early Dialysis Machines

Nils Alwall had a machine which was working and Kolff in Holland had a similar one. In those two machines there was a great drawback in that you were not quite sure where the patient's blood was. Sometimes it was all in the machine and sometimes in the body. So when I was in the United States and saw the plate dialyzer developed by Skeggs and Leonard I found out that here you had a constant or easily controllable volume and I thought that this must be the ideal. On top of that with Kolff dialyzers you had to rely on sausage skin for membrane used as a rather thick cellophane. With the Skeggs and Leonard kidney you could easily choose the membrane yourself and I found some very thin cellophane which was only a few microns thick.

The First Renal Biopsy

I saw exactly the same things that are seen today in what you call acute tubular necrosis and my contribution to the diagnosis I think could be that I got the pathologist to put the diagnosis in quotation marks because the strange thing was there was not much necrosis to be seen, not in the first one nor in the later one.

One of the problems was that we didn't really know how fresh kidney tissue looked. We could at least see that the glomeruli looked perfectly normal and that the tubules were dilated, and especially in the distal tubules there were some peculiar looking casts with a brownish reddish pigment in them. Furthermore, there was some cellular interstitial infiltration and some edema.

Homer Smith's Laboratory

It was a very great experience to me and medical life in the United States at that time was quite different from what I'd experienced in the University of Copenhagen and the Municipal Hospital. When it got too hot and humid in New York, the whole lab moved to Maine, to a desert island, which had a wonderful climate and wonderful nature and the object of our studies was to try to find out what happened to kidney function in seals who were diving, which was quite difficult. The diving experiment was created by putting a funnel on their snouts. When they dive the seals had the same reflexes and the pulse rate went down to 30 or 40 per minute. We had the seals on a dock with a sort of fence around it. We took them up to the lab, put a catheter in the bladder and needles in the flipper veins and gave them inulin and paraminohippuric acid and then tried to see what happened. It was very difficult. One of the difficulties was that there was no plastic tubing at that time so we used needles.

I did some clearance studies, osmotic clearances which was purely kidney physiology and nothing to do with the patients but I would like to add that while on the desert island the reason it was such a wonderful experience was that there was a group of kidney physiologists who worked with different animals. We worked with the seals, some worked with sharks, some with chickens, some with lobsters and once a week there was a lecture given by the different people, who demonstrated their work. It was very inspiring. I enjoyed it tremendously.

Interest in Nephrology

The reason for going into renal work, originally not so much pathology as renal physiology, was that in the late 40s we had access to papers from the United States, especially Homer Smith, who by the way would have been 100 years old this month. This opened up all the possibilities to measure filtration rate, renal blood flow, tubular mass and that is where we started out – in this completely new field, where we could, under different conditions study the kidney function.

It was not really nephrology. It was a small part of internal medicine, where could offer patients with kidney diseases was nothing more than endless bedrest and diet and that was about all. I was interested in the low protein diet. I had a patient who had a chronic interstitial nephritis and I made a prescription book with different dishes and I went to the Institute for Technology and tried to make bread with a low protein content. It made the patients happy that somebody looked after them and talked to them and corrected their acidosis and gave them a diet book but of course it didn't really mean anything for the prognosis.

I think there were several things we did that would not be accepted today. It is very difficult today to do something that has not been done before.

Intestinal Dialysis Experiments

The technique I can describe, the result is a little bit more difficult. I introduced a tube, a nasal tube, down into the duodenum and put a rectal tube in the other end and then I flushed the complete interstine with different solutions and it turned out that if you had a lactose solution flushing the interstine, you could remove urea, sodium, potassium and glucose but you could not remove uric acid, creatinine and phosphate. So it was more or less a cosmetic treatment. But I made the patients look better after I had given them transfusion and removed their acidosis but it was not a really effective treatment of uremia so I gave it up.

Technical and Treatment Advances

It's true that as we saw more of the first biopsies that the techniques was not very good and most of biopsies we saw were 7 microns thick in the sections. It made a very big difference when Paul Kimmelstiel told us to cut much thinner sections so that you can look through the glomerular capillaries.

Finally, the problem was solved by some knife made in Japan which made it fairly easy to cut 2 micron thick sections. Apart from the purely technical side it is very important to have technicians who are interested and capable of doing very fine work.

The nephrology picture has changed over the years. When we started in the 40s the most common renal disease was called pyelonephritis which probably a misdiagnosis for all kinds of renal disease which showed renal atrophy and interstitial nephritis. We saw quite a few analgesic nephropathies but that disease seems to have been eradicated more or less.

Acute renal failure patients have diminished somewhat and the reason why we had so many was probably lack of knowledge of treatment by salt and water. They were underhydrated or overhydrated and improvement in understanding of the specialty has stopped the great influx of acute renal failure. Of course you still see them after accidents, crush injuries and what have you but one of the most frequent objects for studying by kidney biopsy is actually the threatening rejection of renal grafts and it is very easy to perform the biopsy because the kidney is very accessible but it is more difficult to study the tissue. I could wish that we had more secure methods of diagnosis in early rejection.

I could wish that we could prevent more kidney diseases because a growing number of patients who need chronic dialysis is going to be a problem, economically and otherwise and we are not very good at preventing kidney diseases. Luckily we have had some improvement in the treatment of some patients, we can treat glomerulonephritis by plasma exchange and we can treat lupus nephritis and polyarteritis by immunosuppressant drugs but in ordinary acute post-infectious

glomerulonephritis we have relatively few. We can give some antibiotics but when it starts there is not much we can do.