DISCUSSION

KENNEDY (Glasgow): I have two questions for Dr. Beroniade and they relate to his patients with acute renal failure. First of all, has he any further detail for us on the state of the patients before they were given the drug? For example, has he information on the central venous pressure or on the urine urea, or on urine or plasma osmolarity. And the second question is: what other treatment had these patients had before they were given furosemide?

BERONIADE (Bucharest): In one of the tables you have the values of the diuresis before the treatment was applied. This varied between 30 ml/day and 180. You have the values of the pH which was between 7.24 and 7.41. The plasma sodium was as low as 126 mEq/l. Generally, before the furosemide treatment was started, the patient was re-equilibrated from an electrolytic point of view, by infusions of electrolyte solutions.

The second question, I think, was about the treatments associated with furosemide. In three cases, the dialysis was the first treatment, without any response. But in the evolution some other cases needed one or two dialysis sessions in spite of the fact that we had some diuretic response to the furosemide. Then, as I said, it is very difficult to say the result is spectacular but I think furosemide might be accepted as a reliable treatment of acute renal failure.

The CHAIRMAN (Kerr, Newcastle): You did not have data on plasma or urinary osmolarity, or urine urea of those patients with acute renal failure?

BERONIADE (Bucharest): They were generally very low. I cannot quote a figure but about three or four times the normal in the blood.

FRITZ (Bonn): I have two questions for Dr. Beroniade. We had nearly the same experience as you with high doses of furosemide in chronic renal failure and we were sure that this was chronic renal failure, because in all our patients, osmolarity of the urine was lower than 400 milliosmols per litre and we also tried, like you, to replete the patients beforehand with infusions. We had these patients for many weeks under our control before we started. Our doses of furosemide were even higher. We used doses up to 1500 mg per day and we had a very good diuresis in 12 of more than 20 cases, with inulin clearance lower than 5 ml per minute.

But I have two questions for you: we saw in three cases, after very good success, a sudden breakdown of renal function. The patient died and we were not able to save his life with haemodialysis. Very suddenly they had the appearance of intoxication. Did you see anything similar?

On the other hand, we had one patient with inulin clearance of 3.5 ml over more than nine months with such high doses as 1500 mg daily, without any dialysis. And the second question: did you see relatively late therapeutic results? We had a few patients with whom we had to wait two to three weeks until they responded to furosemide.

The CHAIRMAN: Did you have any toxicity and any very late results?

BERONIADE (Bucharest): The first question: in one patient, we noticed a period of some numbness. I did not quote this case. But I should mention the other case which started with very good diuretic response—I mean 1000 ml a day—and after that, we have seen, as you noticed, that the patient’s kidney function very rapidly went down and down and the patient died.

SIMOES (Lisbon): I should like to put this question to Dr. Beroniade. I think it is extremely difficult to evaluate drugs in the treatment of acute renal failure if you do not tell us precisely
when you gave the drugs, in which stage of the acute renal failure you gave the drugs. Many doubts have been raised in my mind, after hearing your paper, and would you suggest for instance that the drug should be given in the first part of renal failure, in the oliguric part, or do you suggest that the drug be used, for instance as mannitol has been used, as a diagnostic procedure, or even as a prophylactic procedure? Have you used the drug in the polyuric phase? At that phase it is extremely difficult to evaluate its results.

The Chairman: We can limit that, to just one question. Do you think it should be used to abort renal failure at the early stage, or later, when the patient is oliguric?

Beronia (Bucharest): The cases we have treated were all between the third and the sixth day of oliguria. It was not exactly at the beginning, because the patients are not hospitalised on the first day in this series. But as I told you I think that at the beginning you must equilibrate the patient. That is what we have tried to do.

Linton (Glasgow): I should like to ask Dr. Maher two questions. First of all, he is no doubt aware that there is considerable disagreement as to whether dialysis, and particularly forced diuresis, are of value in the treatment of poisoning with the intermediate acting barbiturates. I wonder whether he feels that the amounts of fall in the blood levels obtained by these methods are in fact greater than might be explained by the amount of barbiturate one can recover either from the diuresis or from the bath. Our observations suggest this.

The second question is about glutethimide poisoning. I wonder whether he has seen any episodes of apnoea which are reported very commonly in the literature and, secondly, what his survival rate is in glutethimide poisoning? I think that because of the tendency to report fatal cases, the presently quoted mortality rate for glutethimide poisoning is unduly high.

Maher (Washington): The difficulty in answering your first question of evaluating the amount removed in relation to the delta blood level depends on how well one equilibrates since both short-acting barbiturates and glutethimide get into body fat; if you remove the drug only from the circulation, the quantity recovered will not look very impressive in relation to the dose ingested and there will be a sharp fall in blood levels, but then there is a rebound. We discussed this earlier and I am not sure of the answer.

Now your second question: apnoea. I think we were the first to call attention to it. We had seven cases and they are particularly dangerous if you are doing gastric lavage. It may be due to pharyngeal spasm.

The mortality is certainly not nearly as high as the first series that we had. We have now seen some milder cases but I would think that it is one of the most fatal of the poisons, however, perhaps 10% as a figure off the top of my head.

Koralnik (Geneva): I want to ask a general question to Dr. Maher or the people on the floor. Is it possible to do at the same time a forced diuresis and peritoneal dialysis? We have tried that and several times the diuresis went down even if the balance, water balance, electrolyte balance, was positive.

Maher (Washington): It is certainly more difficult to achieve the forced diuresis during either peritoneal or haemodialysis. You will be dialysing out the osmotic agent. We have, however, achieved diureses of 15 ml per minute with secobarbital using acid.

Unidentified Member: I should just ask Dr. Maher to comment on the use of oil as dialysis fluid. Do you have any opinion on that?

Maher (Washington): Certainly the work of Earl Gynn and Shinaberger make this look quite effective for glutethimide poisoning. We think that charcoal—the work from Dr. De
DISCUSSION

Myttenaere from Brussels—is an even more effective way of removing it. We have not ourselves used the lipid.

McGowen (Belfast): I think Professor O'Dwyer's drawing attention to potentially good results, in some cases with acute glomerulonephritis, is particularly important. I had one patient who, four years ago at the age of fourteen, had virtual anuria for six weeks and severe membranous glomerulonephritis on biopsy. Four years later she is perfectly well with normal urea and creatinine and normotensive. We have looked at her biopsy again and it still looks terrible.

Could I use this as a plea that any case of apparently acute renal failure, whatever its origin—because this is often difficult to ascertain—should be given the benefit of dialysis and, indeed, very many cases with chronic renal failure are worth dialysis because they, too, may subsequently recover useful function.

Alwall (Lund): I should like to make some comments on your very interesting paper. In 1963, we published our experience from 1946 to 1961 and we had a similar series with better overall prognosis than in other cases of acute renal failure. But maybe the situation will change later on. Nowadays, we have the opportunity of a chronic, regular dialysis in such cases.

Secondly, I am surprised that the kidney size was normal. In all our cases I think—or most of them—the kidney size was increased and became normalised later on. If we see a case of acute glomerulonephritis with normal size kidneys, we think it may be an acute exacerbation of a chronic glomerulonephritis.

Thirdly, we also had a misleading biopsy, an open biopsy. The pathologist said there were no glomeruli left and three weeks later diuresis started.

O’Dwyer (Dublin): Professor Alwall, when I used the phrase ‘normal kidney size’, I intended to emphasise that we were not dealing with patients who had reduced kidney size. I agree with you that many of the kidneys are somewhat larger and they do reduce later on. But I meant to emphasise that you would not make this diagnosis ordinarily if they had reduced kidney size.

May I just make a comment on your biopsy? We had the opposite experience in one of these autoimmune patients who in fact turned out to have periarteritis nodosa and he came in with acute renal failure of unknown origin and we biopsied him and got a perfectly normal biopsy which encouraged us to go on dialysing this poor man for a very long time. But he did eventually die and he had periarteritis nodosa of a rather segmental type—large vessels were involved—and we had just picked out a normal piece of tissue. So we had the opposite experience to you.

Cameron (London): Two questions for Professor O'Dwyer: your slide on histology. Can we assume that when you said ‘benign’, you meant the usual appearances of recoverable acute glomerulonephritis in children and ‘proliferative’ meant epithelial proliferation with crescents?

And the second question: This is especially relevant for those units who have not maintenance dialysis facilities. How long, on the basis of the time that your patients who did recover, took to recover, with crescents, would you go on dialysing such a patient, given ideal conditions and the patient in reasonable condition?

O’Dwyer (Dublin): The answer to your first question is in the affirmative. Yes, the benign lesions were those that one associates with ordinary benign acute glomerulonephritis with perhaps some endothelial proliferation, and the proliferative were epithelial proliferations with crescent formation, and in some cases hyalinisation of the glomeruli.

The last question, as to how long. I suppose this is very empirical, but I think that they should get a trial of six weeks anyhow to make up your minds, and there may be circumstances in which you would go longer than that. But I would say, as a general rule, they should be kept going for six weeks.

257