6 M is probably caused by aggregation, because a gel formed from the 8·5 M solution after a few hours.

Thus, by observation of six parameters (resonances) simultaneously, the denaturation of ribonuclease in urea at *p*H 4·7 (and perhaps also at *p*H 2·8) appears to occur in a single step, whereas in KCNS or in acids (formic acid and HCl) multiple steps are observed. With lysozyme at *p*H 2·8 the exterior of the molecule unfolds in urea before the hydrophobic core. It is clear that diverse results are obtained for one protein (ribonuclease) in different denaturants and for different proteins (ribonuclease and lysozyme) in the same denaturant. The NMR technique can, however, detect the occurrence of intermediate states; it is clearly the most powerful technique currently available for structural studies of proteins in solution.

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Renin-like Activity in the Plasma of Anephric Men

Renin-like activity has been found in several extra renal tissues[1–3], and the isolated perfused rabbit uterus releases renin-like material in response to pharmacological stimulants[4]. Capelli *et al.*[5] found plasma renin-like activity in anephric women but not in two anephric men. Finding detectable renin-like activity only in the uterus at post-mortem in one female, they postulated uterus as the likely source of the plasma renin-like material. The present study provides evidence of renin-like material in male as well as female anephric patients, thus implicating a source other than uterus for some of this material.

Seven anephric patients (three male and four female) who were on chronic intermittent haemodialysis were studied. Blood samples were taken just before dialysis into heparin (10 u/ml.). Plasma renin-like activity was measured according to the method of Skinner[6], using a standard sheep substrate.

All patients had detectable levels of renin-like activity in their plasma (Table 1). One male patient showed formation of pressor material in the normal range for plasma renin (5–20 ng angiotensin equivalent/ml. plasma/h), while one female was at the lower limit of this range. Among these patients, the level of plasma renin-like activity did not appear to be related to the duration of the anephric state ($r = -0{\cdot}18$, $P > 0{\cdot}35$), but was related to patient age ($r = -0{\cdot}72$, $P < 0{\cdot}05$) and possibly to systolic blood pressure at the time of sampling ($r = 0{\cdot}58$, $P < 0{\cdot}1$).

The renin-like material was capable of acting on human substrate and therefore, presumably, of producing angiotensin in the human circulation. Plasma samples from patients 3 and 4 were treated at *p*H 4·5 (ref. 6), which left the plasma substrate intact, and then incubated alone at *p*H 7·5. Angiotensin-like pressor material was formed at constant rates of 0·3 ng angiotensin equivalent/ml./h for patient 3 and 0·6 ng/ml./h for patient 4, compared with a lower limit of normal for human plasma of 0·7 ng/ml./h (ref. 6). The substrate content of these plasmas was 900 and 1,000 ng of available angiotensin/ml. compared with the mean normal value of 1,100 ng/ml. (ref. 6).

Table 1. CLINICAL DATA AND PLASMA RENIN-LIKE ACTIVITIES IN ANEPHRIC PATIENTS

Patient	Sex	Age	Time anephric (months)	Dietary sodium (mequiv./day)	Blood pressure at sampling (mm of mercury)	Plasma renin-like activity (ng/ml./h)
1	M	21	15	50	140/70	2·3
2	M	45	17	50	130/90	2·4
3	M	20	1·5	65	160/90	7·6
4	F	31	12	90	160/110	4·9
5	F	44	5	50	150/100	2·5
6	F	49	4	65	140/86	0·6
7	F	50	3	50	160/90	1·9

To identify the renin-like material further, it was shown that the Michaelis constant for the material acting on sheep substrate was 166 and 210 ng available angiotensin/ml. substrate concentration in two experiments, compared with 190 for normal human plasma. An angiotensinase-free antibody to human renal renin (kindly donated by Dr S. L. Skinner, Department of Physiology, University of Melbourne), which blocks the activity of human plasma renin[7] but not dog renal renin (S. L. Skinner, personal communication), completely suppressed the renin-like activity in anephric plasma whether it was acting on human or sheep substrate. The pressor product of incubation was ultrafilterable, was not destroyed by boiling but rapidly destroyed by trypsin and chymotrypsin. It distributed by counter-current[8] like angiotensin I and unlike angiotensin II, vasopressin, adrenaline or noradrenaline. Pepsin treated like the anephric plasma and incubated with sheep substrate at *p*H 7·5 formed no pressor material after 24 h.

These results demonstrate that renin-like material exists in the plasma of both male and female anephric patients and is capable of reacting with homologous substrate at *p*H 7·5. The source of the material in the male patients is not known.

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