presenting by the breech. The membranes were not ruptured on this occasion, and the operator, with his hand, kept the presenting part high in the pelvis until a general anaesthetic had been administered. The membranes were then ruptured and a breech extraction was easily performed 25 minutes after the delivery of the first child. The second twin, a male, weighed 6 lb. 2 oz. (2.8 kg.). The placenta had to be removed manually. Both babies made satisfactory progress.

Case 4.—The patient, a gravida-4 aged 36, was admitted to hospital as an emergency case four weeks before term. After a labour lasting two and a half hours a male child weighing 3 lb. 7 oz. (1.56 kg.) was born. Intravenous ergometrine, 0.5 mg., was given with the birth of the anterior shoulder; a twin pregnancy was diagnosed as soon as this child had been delivered. Vaginal examination showed the second twin to be presenting as a vertex, and the operator kept the presenting part high in the pelvis whilst a general anaesthetic was administered. The membranes were then ruptured and a male child weighing 3 lb. 12 oz. (1.7 kg.) was delivered by forceps; the placenta was expressed quite easily. The first child made satisfactory progress, but the second suffered from repeated cyanotic attacks for several days; the appearance of the second twin strongly suggested mongolism, but this diagnosis has yet to be established.

Discussion

There is convincing evidence that intravenous ergometrine, provided it is given with the crowning of the foetal head or birth of the anterior shoulder, will reduce the risk of post-partum haemorrhage and shorten the duration of the third stage of labour (Martin and Dumoulin, 1953). Certain drawbacks to its use have been noted. Grimes *et al.* (1948) and Priver *et al.* (1949) have reported side-effects such as nausea, headaches, and vomiting, while Martin and Dumoulin noted a significant increase in the incidence of manual removal of the placenta. For the past two years, in our hospital, intravenous ergometrine has been used widely but not routinely in the control of the third stage of labour. During this time there have been 74 cases of twin pregnancy, and nine of these have been undiagnosed. Four out of the nine patients were given intravenous ergometrine as the first baby was being delivered, and details of these cases have been given. One of the eight babies born to these women died, and, although we cannot be sure, we suspect that the death was at least in part caused by the strong uterine contractions which followed the administration of ergometrine; this drug is known to cause tonic contraction of the uterus and is therefore liable to interfere with placental circulation and so lead to foetal anoxia. As a result of the difficulty experienced in the delivery of the second twin in Case 2, we made a point, in the later cases, of not rupturing the second sac of membranes until we were in a position to carry out immediate delivery of the second twin. By conserving the sac of membranes there is less likelihood of the uterus contracting firmly down on the second twin.

So far we have been fortunate in that none of the undiagnosed second twins has been lying transversely. Were this to happen, then the operator might well be faced with a difficult intrauterine manipulation where the uterus had contracted down firmly on the foetus. There might then be a risk to mother as well as to child.

A number of authors have now reported the use of intravenous ergometrine in large series of cases, but, so far as we are aware, no one has acknowledged the complication to which we draw attention in this paper. In our experience the hazard is a real one and must be taken into account when an assessment is made of the advantages and disadvantages of the use of intravenous ergometrine in the control of the third stage of labour.

Summary

Attention is drawn to the complication of the undiagnosed second twin when intravenous ergometrine has

been given in the control of the third stage of labour. This complication occurred four times in two years at the Princess Mary Maternity Hospital, and one baby died. Details of the four cases are given.

It is suggested that when this complication occurs every effort should be made to avoid rupture of the second sac of membranes until the patient is under an anaesthetic and immediate delivery of the second twin can be undertaken. With an intact sac of membranes there is less likelihood of the uterus contracting down on the second twin and interfering with placental circulation.

We are indebted to Professor Harvey Evers for permission to publish details of cases which were under his care.

REFERENCES

- Grimes, W. H., Bartholomew, R. A., Colvin, E. D., and Fish, J. S. (1948). *Sth. med. J.*, **41**, 980.
Martin, J. D., and Dumoulin, J. G. (1953). *British Medical Journal*, **1**, 643.
Priver, M. S., Harris, J. M., Krohn, L., and Boros, H. H. (1949). *West. J. Surg.*, **57**, 586.

RENAL CLEARANCE OF CREATININE AND UREA IN THE WEST AFRICAN

BY

R. A. KENNEY, Ph.D., B.Sc.

*Colonial Medical Research Committee's Laboratory for
Hot Climate Physiological Research,
Oshodi, Lagos, Nigeria*

We have previously reported from this laboratory the low levels of plasma urea (Phillips and Kenney, 1952) and the low output of urea following the ingestion of 30 g. of this substance (Kenney, 1953) encountered in the West African subject. The clearance data reported in this paper were obtained in order to provide a further standard of comparison with the European subject. Precise investigation of the renal partial functions, glomerular filtration rate, and the rate of renal plasma flow (Kenney, 1954) had demonstrated the identity of these values in the African and European subjects.

Methods

Ten African subjects were used. All were familiar with the procedure of venepuncture and were trained to empty their bladders completely and spontaneously at frequent fixed intervals. The subjects were typical members of the local labour force, in regular employment and enjoying a good standard of nutrition by African reckoning—that is, a diet containing about 70 g. of protein a day, about one-third of which was meat.

The subjects reported to the laboratory at 8 a.m., after their normal morning meal, and rested in bed for a period of two hours. During this time their water intake was adjusted so as to provide a low urine flow of less than 1 ml. a minute at the start of the experimental period. At the end of this time the bladder was emptied and urine collection started. Urine samples were obtained every 15 minutes for a period of 90 minutes. During this time two or three blood samples were taken by venepuncture with the minimum of stasis. The blood was stored in a heparinized vessel and the plasma separated off by centrifugation for subsequent analysis. During the period of urine collection water was given by mouth in volumes sufficient to raise the urine flow from its original low level to about 5 to 6 ml. a minute. In this way a series of urine samples were obtained over the wide range of urine flows.

Urine and plasma samples were analysed for creatinine and urea by the following methods.

Urea.—The method of Karr (1924) was applied to both urine and tungstate filtrates of plasma in appropriate dilution. The final colorimetric estimation was carried out in a Coleman junior spectrophotometer set at a wavelength of 5,000 Å.

Creatinine.—Diluted urine samples and tungstate filtrates of plasma were treated by an alkaline picrate method (W. S. S. Ladell, 1951, personal communication), the final estimation being carried out in the Coleman junior spectrophotometer set at a wavelength of 5,200 Å.

Results

From the values for plasma concentration, urine concentration, and urine flow were calculated the clearance values for the two substances by the usual formula. The results obtained are set out in the Table, together with the mean values and the standard deviations of the observations. The table also records the mean values obtained on a group of European subjects examined under the same conditions. The values for urea clearance have been divided into two groups—those obtained at urine flows less than 2 ml. a minute and those obtained at higher rates of flow. In both cases the true clearance value is recorded; the empirical standardization of the values obtained at low flows has not been employed.

Urea and Creatinine Clearance Values

Subject	Creatinine Clearance ml./min.	Urea Plasma Concentration mg./100 ml.	Urea Clearance ml./min. flows > 2 ml./min.	Urea Clearance ml./min. flows < 2 ml./min.	Urea Clearance/Creatinine Clearance
Os ..	121	15.0	—	52	0.43
Wm ..	117	13.5	44	43	0.37
Sa ..	141	12.7	36	50	0.31
Jo ..	145	10.6	36	—	0.25
Go ..	85	10.2	42	37	0.41
Pa ..	168	10.7	36	21	0.15
Ma ..	102	11.9	35	46	0.43
Ge ..	129	16.7	34	31	0.22
La ..	141	18.8	80	54	0.44
An ..	120	19.6	63	46	0.44
Mean ..	127	13.9	45	42	0.345
s.d. ..	23	3.4	16	11	
European values: Mean ..	122	26.7	70	54	0.48
s.d. ..	12	4.7	8	9	

Discussion

The value obtained for the creatinine clearance is in very good agreement with the values commonly observed in the European subject. It appears that creatinine is as adequate a method of determining the rate of glomerular filtration rate as is the more popular inulin or mannitol clearance, and if this be accepted the glomerular filtration rate in these subjects agrees well with the "world average" for this function quoted by Smith (1951). The creatinine clearance was completely unaffected by the rate of urine flow.

It will be observed that the values of urea clearance are nearly identical whether observed at high or low rates of urine flow. The African subject, therefore, fails to show the "augmentation" phenomenon which is characteristic of urea excretion in the European subject (this is supported by the values recorded in the table).

The absolute values of the urea clearance are low, being only about two-thirds of the normal standard. The average ratio of urea clearance to glomerular filtration rate at random urine flows in 37 normal subjects observed by Raaschou (1948) was 0.65 (range 0.458–0.776). Shannon and Smith (1935) obtained a value of 0.64 (range 0.59–0.67), and Blegen, Haugen, and Aas (1949) reported a mean value of 0.59. The ratio observed in this laboratory for the European subject lies at the lower extreme of the range reported by the Danish workers. This may, however, merely be a reflection of a preponderance of low rates of urine flow in the present European data. In the African

subject, even at high rates of urine flow, the clearance value is less than that observed at flows below the augmentation limit in the European subject.

It is well known that the level of dietary protein affects the rate of urea elimination, and for this reason the comparison of African with European data may not be valid. The European subjects investigated had a daily protein intake of about 100 g. (half of which was of animal origin) compared with an intake of 70 g. for the African (about one-third of which was meat). The plasma concentration of urea will, however, be conditioned by the same factor, and, since it is the clearance value which is here being considered, the effect of the lower elimination may be to some extent compensated. Although Jolliffe and Smith (1931) and Shannon, Jolliffe, and Smith (1932) have demonstrated a fall in urea clearance on low-protein diets, this fall has been accompanied by a fall in the filtration rate; in the present series there was no indication of reduced filtration rate.

The possibility that there is a real difference between the mode of urea elimination in the African and the European is the subject for further investigation, with particular reference to the secretory phase of urea elimination which has been demonstrated in the European subject (Barclay, Cooke, and Kenney 1947; Kenney *et al.*, 1950).

REFERENCES

- Barclay, J. A., Cooke, W. T., and Kenney, R. A. (1947). *Proc. int. physiol. Congr.*, 17, 58.
 Blegen, E., Haugen, H. N., and Aas, K. (1949). *Scand. J. clin. Lab. Invest.*, 1, 191.
 Jolliffe, N., and Smith, H. W. (1931). *Amer. J. Physiol.*, 99, 101.
 Karr, W. G. (1924). *J. Lab. clin. Med.*, 9, 329.
 Kenney, R. A. (1953). *British Medical Journal*, 1, 600.
 — (1954). In preparation.
 — *et al.* (1950). *J. Obstet. Gynaec. Brit. Emp.*, 57, 17.
 Phillips, P. G., and Kenney, R. A. (1952). *Lancet*, 2, 1230.
 Raaschou, F. (1948). *Studies of Chronic Pyelonephritis, with Special Reference to the Kidney Function*. Ejnar Munksgaard, Copenhagen.
 Shannon, J. A., Jolliffe, N., and Smith, H. W. (1932). *Amer. J. Physiol.*, 101, 625.
 — and Smith, H. W. (1935). *J. clin. Invest.*, 14, 393.
 Smith, H. W. (1951). *The Kidney*. Oxford Med. Publ., New York.

FAT UTILIZATION IN ADULTS ON A DIET OF COWS' MILK

BY

R. HECKER, M.B., M.R.A.C.P., D.T.M.&H.

AND

W. H. H. ANDREWS, D.M., D.T.M.&H.

(From the School of Tropical Medicine, Liverpool)

Although extensive investigations into the absorption and excretion of fat in infants, both breast-fed and on cows' milk, have been carried out by Holt *et al.* (1919a, 1919b, 1919c), we have found no reference to fat absorption by adults on a milk diet. During the course of another experiment we were required to live on a diet of cows' milk for one month, and below we record our fat absorption and excretion taken over three days of the fourth week.

The fat content of a milk diet is much higher than that of a normal mixed diet. Wollaeger *et al.* (1946) found that on normal mixed diets the amount of fat ingested by adults may be increased to 208 g. a day without gross change in the percentage absorbed, an average of 9% only of the ingested fat being excreted. Annegers *et al.* (1948) studied the effect of varying quantities of fat added to a mixed diet, and found that, within normal limits, neither the quantity nor the type of ingested fat influenced the amount of excreted fat in any individual subject. A normal fat