For non-random mating populations (such as those with inbreeding) it may be shown that $\bar{w}$ could decrease under selection even for one locus. Then, Fisher's fundamental theorem does not apply to the discrete-generation model.

C. C. Li

Department of Biostatistics,
University of Pittsburgh,
Pittsburgh, Pennsylvania.

[1] Fisher, R. A., *The Genetical Theory of Natural Selection* (Clarendon Press, Oxford, 1930).
[2] Fisher, R. A., *Ann. Eugenics (London)*, **11**, 53 (1941).
[3] Li, C. C., *Biometrics*, **13**, 225 (1957).
[4] Li, C. C., *Genetics*, **42**, 583 (1957).

PHYSIOLOGY

Evidence for a Non-Plasma Source of Urea in Sweat

THE ratio of the concentration of urea in the sweat to that in the plasma (s/p) is known to be greater than unity. Schwartz[1] attributed this gradient to back diffusion of water because he found that raising the plasma urea concentration had little effect on the s/p ratio for urea. Recent evidence[2,3] suggests that (*a*) s/p for urea is not entirely independent of plasma urea concentration; (*b*) s/p for urea is independent of s/p osmolality in man and the cat (for example, the s/p urea is greater than 1 in the hyperosmotic sweat obtained from the hairless footpad of the cat); (*c*) compounds related to urea by virtue of similar volumes of distribution (ethanol, antipyrine, creatinine) or similar molecular configuration (thiourea, methylurea, acetamide) all behave differently from urea in sweat in that none of these compounds is present in sweat at higher concentrations than in plasma.

Because of these arguments it was concluded that factors apart from back diffusion of water play a part in establishing the urea gradient in sweat. The present study was designed to determine whether plasma is the sole source of urea in sweat.

An isotope dilution study was performed on cats and human volunteers. 30 to 50 μc. of urea labelled with carbon-14 was administered orally to the human volunteers, all of whom received oral neomycin as an intestinal antiseptic. The cats received 50 to 100 μc. of the isotope intravenously. Two to three hours after administration of the isotope sweat was collected as previously described[2]. A thermal stimulus was used to produce sweat in the human subjects.

The labelled urea was analysed by a modification of the technique of Walser[4] as follows: portions of plasma or sweat were placed in a modified Warburg incubation vessel, acidified with 0·1 normal hydrochloric acid and shaken for 5 min, following which the mixture was neutralized with 0·1 normal sodium hydroxide. After the vessel was chilled in ice, 1 ml. of buffered urease was added and the stopper (from which was suspended a polyethylene well containing 0·2 ml. hyamine) was inserted. The reaction mixture was shaken in a 37° water bath for 30 min, and 10 per cent sulphuric acid was then injected into the reaction mixture through the stopper. After the flask had been shaken at room temperature for 1 h the centre well was placed in a toluene liquid scintillation mixture and counted. Efficiency was determined using toluene labelled with carbon-14 as an internal standard. Unlabelled urea was determined as previously described[2].

Table 1 compares the sweat to plasma concentration ratios of labelled urea and total urea in four men and eight cats. In all experiments but one the s/p for labelled urea was less than the s/p for total urea. The mean s/p for labelled urea was 1·08 in man and 1·03 in the cat, values similar to the s/p for methylurea (1·06) and acetamide (1·04) in the cat[3].

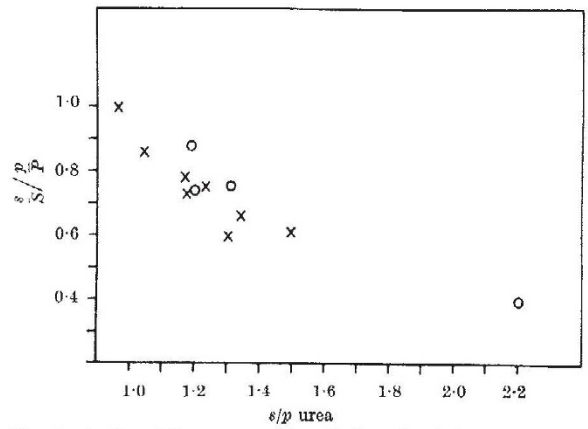

Fig. 1. A plot of the urea specific activity ratios between sweat and plasma against the sweat to plasma urea concentration ratio. ○, Man; ×, cat. (Abbreviations: s/S, p/P, specific activity of urea in sweat and plasma respectively; s/p, sweat to plasma urea concentration ratio.)

Fig. 1 shows the ratio of the specific activity of sweat to that of plasma plotted against the ratio of urea concentration between sweat and plasma for each experiment. In both man and the cat there is dilution of the labelled urea, the magnitude of which appears to be related to the s/p for urea. (In five of the eight cats lacrimal fluid was collected and analysed. The mean ratio of specific activity between lacrimal fluid and plasma was 0·99. In three of the four human subjects, urine was collected during the sweating period and the mean specific activity ratio was found to be 1·06, similar to Walser's[4] finding of 1·10.)

Table 1. RATIOS OF CONCENTRATIONS OF UREA LABELLED WITH CARBON-14 AND TOTAL UREA BETWEEN SWEAT AND PLASMA (s/p) IN SAMPLES FROM CATS AND HUMAN BEINGS

Cat	s/p for labelled urea	s/p for total urea
1	1·03	1·23
2	1·06	0·96
3	1·05	1·38
4	1·02	1·30
5	0·98	1·18
6	1·02	1·15
7	1·05	1·49
8	0·99	1·03
Mean	1·03	1·24
Man		
J.J.	1·01	1·20
C.B.	1·12	1·31
M.A.	1·12	1·19
O.B.	1·10	2·20
Mean	1·08	1·43

Because the labelled urea in sweat was diluted by unlabelled urea, these studies suggest that a fraction of the urea in sweat is derived from sources other than plasma or interstitial fluid. Furthermore, because this non-plasma source accounts for that urea in sweat in excess of the plasma urea concentration it would appear that back diffusion of water plays a minor part in establishing the urea concentration in sweat.

These studies do not indicate the non-plasma source of urea. Two possibilities include synthesis of urea by some segment of the sweat gland or a pool of urea in the skin (perhaps the cornified epidermis) which is immiscible with the circulating labelled urea, but which may be partially miscible with the sweat.

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SAUL W. BRUSILOW

Department of Pediatrics,
Johns Hopkins University School of Medicine,
Baltimore, Maryland.

[1] Schwartz, I. L., Thaysen, J. H., and Dole, V. P., *J. Exp. Med.*, **97**, 429 (1953).
[2] Brusilow, S. W., and Gordes, E. H., *Amer. J. Physiol.*, **209**, 1213 (1965).
[3] Brusilow, S. W., and Gordes, E. H., *Fed. Proc.*, **25**, 468 (1966).
[4] Walser, M., and Bodenlos, L. J., *J. Clin. Invest.*, **38**, 1617 (1959).