The Biphasic Course of Regression in the Chick Mesonephros

The chick mesonephros regresses rapidly after the egg has been incubated for about 15–16 days. There are marked decreases in mesonephric size[1], weight[2–4], and function[5], concomitant with increases in the amount of connective tissue, the number of lipid and pigment granules[1,6–10], the number and size of lysosomes[8], and specific activity of acid phosphatase[11]. On the other hand, the first signs of regression appear at about 12 days, when the only obvious histological changes are decreases in glomerular volume, tubule diameters, and vascularization[1,12]. Regressive changes involving a decrease in cell size, yet with little autolysis, also occur during post-partum involution of the rabbit uterus[13].

In general, growing tissue undergoes a progressive dehydration[14,15], but degenerating tissue becomes relatively hydrated as its structure deteriorates[16,17]. The present investigation examines whether the regressing chick mesonephros becomes relatively dehydrated, consistent with the general growth of the embryo, or whether it becomes relatively hydrated, consistent with its own destruction. Measurements were made of the weights of mesonephroi and the volumes of nephric units to distinguish between the hydration changes resulting from a shrinking of nephric lumina and those from the loss of mesonephric tissue.

Experimental. The fresh weights of mesonephroi and metanephroi (non-regressing controls) from 140 embryos were determined after blotting the excised and rinsed organs on filter paper (Figure 1). The paper was covered with fine-meshed bolting cloth to prevent its absorption of the organ.

Their dry weights were measured after heating the mesonephroi and metanephroi for 2 days at 60 °C, and could not be decreased detectably by drying at 100 °C. The difference between the fresh and dry weight is referred to as the 'total water content' (Figures 2 and 4). That % of the fresh weight attributable to the total water content is called the 'relative water content' (Figures 3 and 4).

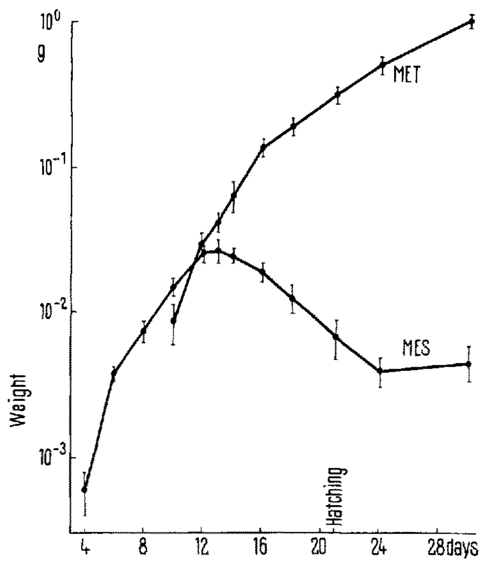

Fig. 1. Fresh weights of the mesonephroi (MES) and metanephroi (MET) versus age. Each point (average ± standard deviation) represents the weight of at least 11 paired left and right organs. Note that the graph is semi-logarithmic.

Volumes of mesonephroi and their individual ducts, tubules, and capsules were calculated from area measurements of over 24,000 tracings from serial sections (Figure 2). One typical mesonephros was studied for each age group. The measurements were made by a planimeter which was placed on a cardboard carriage that could be moved from one tubule tracing to the next to record the sectional areas of the tubules. The accuracy of these measurements was verified by the close correspondence between the tubule diameters calculated from them and direct diameter measurements. Details of this technique and its evaluation appear elsewhere[18].

The 'relative luminal volume' is that % of the total mesonephric volume (calculated from planimetric meas-

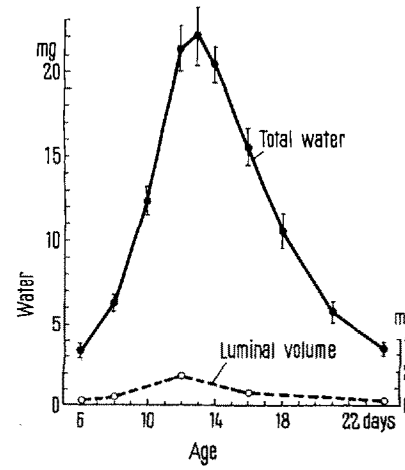

Fig. 2. Water content and nephric luminal volume (total volume of the duct, tubules, and capsules in mm^3) versus age in the mesonephros. The 2 curves are on the same scale if it is assumed that the specific gravity of the luminal content is near unity. Calculated for paired left and right mesonephroi. The vertical bars each represent ± variance of mean for at least 11 weight determinations.

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urements of the peripheries of the sections) occupied by the total duct, tubule, and capsule luminal volumes (Figure 3).

The period of regression appeared in two distinct, and physiologically significant, phases: a shrinkage phase and a degeneration phase. The shrinkage phase occurred between 12 and 16 days of incubation – Hamburger-Hamilton stage 38–42[19]. (Variability between mesonephroi, and the arbitrary times of measurement make these boundaries only approximate.) This phase was characterized by the onset of weight loss, a slight decrease in the relative water content, and an abrupt decrease in the relative luminal volume (Figures 1 and 3). Here the loss of water probably was the most important contributor to weight loss. The dry weight decreased only 12% between 12 and 16 days, yet the water content decreased 27%. In spite of the fact that nephric luminal volumes decreased 60% during this phase, on a volume-to-weight basis only about 20% of the water loss could be accounted for by shrinkage of nephric lumina (Figure 2). Allowing for artifactual contraction in the histological specimens, this

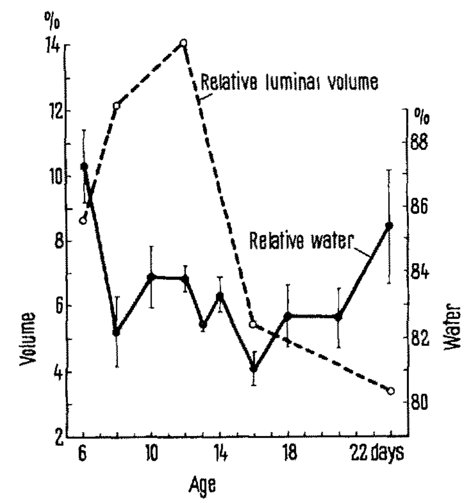

Fig. 3. Relative water content and relative nephric luminal volume versus age in the mesonephros. Both curves are drawn to the same scale, but the origins are shifted to facilitate comparison. Calculated for paired left and right mesonephroi. The vertical bars each represent ± variance of mean for at least 11 determinations.

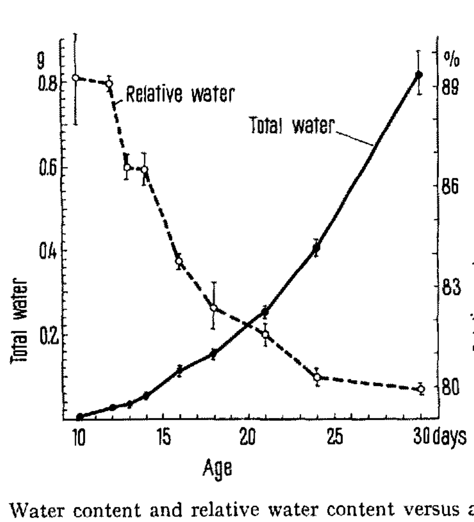

Fig. 4. Water content and relative water content versus age in the metanephros. Calculated as for the mesonephros (Figures 2 and 3).

could be as much as 30%[20]. Histological evidence suggests that constriction of blood vessels, invasion by connective tissue, and the continued maturation of some cells account for most of the water loss[12].

The degeneration phase of regression (approximately between 16 and 24 days of incubation – Hamburger-Hamilton stage 42 until 3 days post-hatching) is readily characterized by histological changes[1,6–10] and loss of protein[11,21]. Although water content and volume decreased (as in the shrinkage phase), there was a 5% increase in the relative water content (Figures 2 and 3).

The accuracy of the weight and water measurements on the mesonephros is in part supported by independent data for the metanephros, since both organs were weighed by the same technique. During metanephric growth, weight and water content increased at a constant rate, but the relative water content decreased at a constant rate (Figure 4). The relative water content at 30 days was approaching the probable adult value of 78–80%, as estimated from data on the water content of other vertebrate kidneys[22].

It is concluded that the mesonephros enters a shrinkage phase several days before the destruction of tissue appears. During this first phase small changes may be seen in the cells with the light microscope[7], but they are most evident on the subcellular level[8,11]. Pieces of 16-day-old mesonephros are capable of renewed mitotic and functional activity when transplanted to the chorio-allantoic membrane[12]. Thus, during the shrinkage phase some features of regression are reversible, which suggests that this phase may be identical with the period of reversible change preceding irreversible cell death in excised or injured tissues or cells[16,17,23].

Zusammenfassung. Vergleiche zwischen wachsenden und zurückgebildeten Mesonephrosen im Hinblick auf Nass- und Trockengewicht und totales nephritisches Luminalvolumen ergaben, dass die Rückbildung in 2 Phasen verläuft: (1) Während 12 bis 16 Tagen durch beginnenden Gewebeverlust, Organschrumpfung und relativen Wasserverlust (20–30% im nephritischen Lumen). (2) Während 16 bis 24 Tagen ist der relative Wassergehalt höher, wobei histologische Andeutungen einer Degeneration sichtbar werden.

J. E. MORRIS[24]

Department of Zoology, University of California, Los Angeles (California 90024, USA),
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[24] Present address: The Wenner-Gren Institute, Norrtullsgatan 16, Stockholm Va, Sweden.