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Postnatal growth of the mouse bladder

S. P. JOST

Department of Anatomy, The University of Manchester, Stopford Building, Oxford Road, Manchester M13 9PT, England

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INTRODUCTION

There is little information about bladder growth in mammals, particularly with regard to specific parameters. The present investigation therefore attempts to describe the postnatal growth of murine bladder size and weight and their relationship to overall body weight. This report is part of a continuing comprehensive study intended to improve knowledge of normal growth of the bladder as a whole, and of the urothelium in particular, in an effort to further understanding of abnormal patterns of urothelial growth.

MATERIALS AND METHODS

Parasite-free $B_6D_2F_1$ mice were used throughout and animals were housed in conventional plastic cages, lined with wood shavings. Pregnant female mice were regularly monitored for their newborn and the birth dates of male offspring were recorded. When about three weeks old, animals were weaned and fed a pelleted, standard mouse diet *ad libitum* ('PMD' Diet; Oakes Ltd, Congleton, Cheshire) and had continual access to tap water containing residual Milton. All animal rooms were regulated to provide a constant relative humidity of 45–50 %, a constant temperature of 20–22 °C and a constant 12 hour dark/light cycle (artificial daylight from 0700 to 1900 BST).

The following four parameters were investigated:

(*a*) Body weight (in grams) of the animal at a given age.

(*b*) Bladder weight (in grams) of the empty bladder at a given age.

(*c*) Bladder size, i.e. area covered (mm^2) by the serosal surface of the opened bladder, placed on graph paper, at a given age.

(*d*) Bladder weight relative to body weight, i.e. the ratio (as a percentage) of bladder weight to total body weight, using the average values obtained from five mice of a given age.

Animals were killed by ether overdose, the abdominal cavity exposed and the entire bladder removed. The organ was immersed in a petri dish filled with physiological saline. Each experimental group consisted of five bladders. Each bladder was incised across the bladder neck and drained of urine. Excess fluid was absorbed by filter paper prior to recording the wet weight of each bladder. The previous incisions were lengthened so that the organ could be gently flattened on millimetre graph paper, with the urothelium uppermost. Contours were carefully drawn around the area covered by the flattened (but unstretched) organ, using a sharp pencil, and the serosal surface area was determined.

RESULTS

Results are depicted in Figures 1–4. Each point of the graphs was based on results from five mice. The average variability of results did not exceed ±5% per point.

Body weight of $B_6D_2F_1$ male mice increased steadily with age (Fig. 1), ranging from 2 g for newborn mice to about 30 g for 10 weeks old mice. The isolated sample of 1 year old mice had a body weight of 38 g. Body weight doubled within the first two weeks and again at four weeks, as well as at seven weeks. The bladder also clearly grew both in terms of surface area or size (Fig. 3) and of wet weight (Fig. 2). Bladder surface area ranged from 30 mm^2 (newborn) to about 70 mm^2 (10 weeks), thereby taking six weeks to double in size. For 1 year old mice, the value was 90 mm^2. Bladder wet weight increased from 0·01 g (newborn) to approximately 0·04 g (10 weeks), doubling within four weeks and again at nine weeks. After one year the bladder weighed 0·055 g.

The ratio of bladder to body weight (Fig. 4) declined steadily from its original value of 0·6%. The ratio reached stability at about five weeks of age at roughly 0·15%, remaining unchanged at one year.

DISCUSSION

Male mice were chosen for the entire investigation, of which the present report forms a part, because female mice undergo hormonal fluctuations known to affect the proliferative behaviour of epithelia. The recording of birth dates permits the age of the animals to be estimated to within 12 hours, which might represent a source of variation in the early postnatal age groups.

Regarding the determination of serosal surface area, it should be noted that this area may differ from the urothelial surface area, especially in the contracted condition. Both the invagination of plaque areas from the luminal membrane into the cytoplasm as vesicles (Hicks, 1975; Hicks, Ketterer & Warren, 1974) and the gross pleating of the urothelial surface effectively reduce the actual urothelial surface upon contraction of the bladder.

The present observations show that the bladder is a relatively large organ at birth, reaching adult proportions comparatively rapidly. Firstly, although the overall pattern of weight gain appears to apply to both body weight and bladder growth, body weight increases by a factor of 10–15 by ten weeks of age (as compared with the newborn), whereas the wet weight and the size of the bladder increase by factors of only about 4 and 2·5, respectively.

Secondly, the bladder weight constitutes a relatively large proportion of the total body weight in early postnatal life. This proportion is highest at birth and decreases thereafter until a stable ratio is attained at about five weeks. These observations are supported by the findings of Martin & Wong (1981) who report that the neonatal

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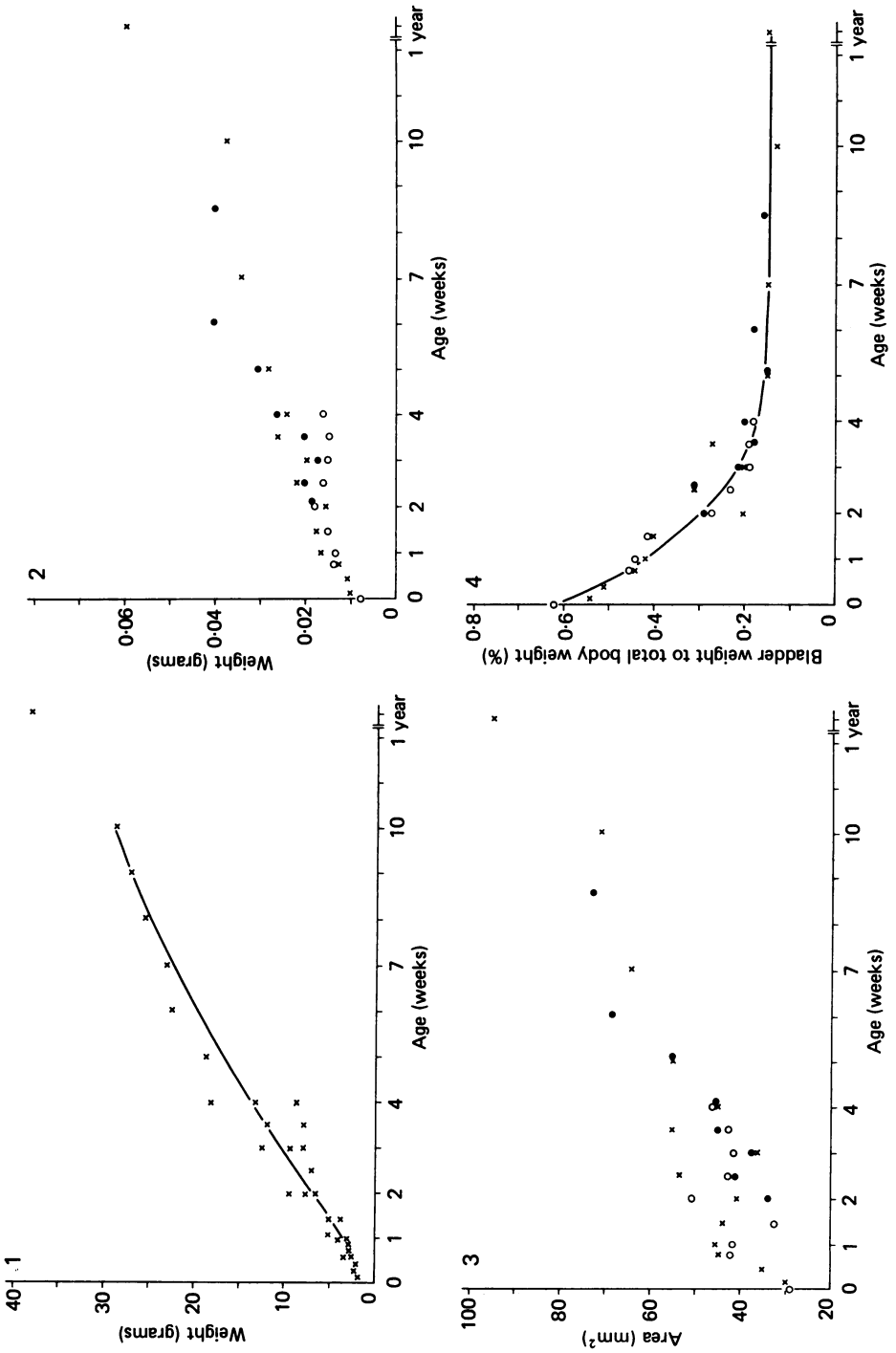
Fig. 1. Development of body weight in $B_6D_2F_1$ male mice.

Fig. 2. Development of bladder weight in mice. Symbols as in Figure 3.

Fig. 3. Development of bladder size (surface area) in mice. Data from different experiments are designated by different symbols (×, ○, ●).

Fig. 4. Development of the ratio between body and bladder weights. The ratio is expressed as the percentage proportion of the bladder weight to total body weight. Symbols as in Figure 3.


1
Weight (grams)
40
30
20
10
0
0 1 2 4 7 10 1 year
Age (weeks)
2
Weight (grams)
0·06
0·04
0·02
0
0 1 2 4 7 10 1 year
Age (weeks)
3
Area (mm²)
100
80
60
40
20
0 1 2 4 7 10 1 year
Age (weeks)
4
Bladder weight to total body weight (%)
0·8
0·6
0·4
0·2
0
0 1 2 4 7 10 1 year
Age (weeks)

bladder of the guinea-pig has a surprisingly large capacity, compared with the adult, as well as a high basal cell count in the urothelium.

The remarkable constancy of the ratio of bladder to body weight after the age of five weeks in mice could imply that the rates of growth become similar from this age. The possibility should be borne in mind, however, that as a result of fat storage in older animals, body weight may increase in the absence of growth (Enesco & Leblond, 1962).

Considering the long biological time span between ten weeks and one year, the relative increases in murine body weight, bladder weight and bladder size are small, especially when compared with the considerable growth occurring during the first weeks of life. This interpretation is supported by the finding that the ratio of bladder weight to body weight remains unchanged at one year (0·15 %).

Since the bladder shows a greater increase in weight (×4) than in size (×2·5), during the first ten weeks of life, this suggests that a large proportion of growth is due to the production of smooth muscle and connective tissue elements. In the mouse, marked urothelial growth, as measured by the tritiated thymidine labelling index and mitotic activity, takes place only during the first ten days of postnatal life (Jost, 1984; Jost & Potten, 1985). The levels of proliferation rapidly decline thereafter and reach a plateau of very low labelling and mitotic indices (Farsund, 1975; Jost, 1984; Jost & Potten, 1985). In the guinea-pig, the urothelium reaches its adult state and basal cell count after the third postnatal week and shows very little mitotic activity thereafter (Martin & Wong, 1981). In the dog, Harvey (1909) reported that the depths of the urothelium and of the whole bladder wall were 172 and 5326 μm, respectively, thus the urothelium forms a fairly small component of the bladder wall. Hence, as both bladder size and bladder weight continue to increase beyond this early period of appreciable urothelial proliferation, the later gain is likely to be due to the growth of non-urothelial components. A urothelial contribution, however, cannot be ruled out entirely if at this age (10–14 days) the emphasis of growth were to shift from the production of new cells or possible endoreduplication of DNA (both detectable by tritiated thymidine) to an increase in the mass of individual cells (not detectable by tritiated thymidine).

Enesco & Leblond (1962) investigated the growth of a number of tissues in the developing rat. Although they did not examine the bladder, they observed that most tissues undergo enormous postnatal growth. However, the adrenal gland and the lung grew postnatally with a similar order of magnitude to that described here for the murine bladder, although the possibility of species differences should be borne in mind. It might be argued, therefore, that there is an advantage for the animal if these latter tissues are fairly mature at birth. As early postnatal food is of a liquid nature (mother's milk), this might require a fairly functional bladder (as well as an intact bladder epithelium) well before weaning to protect the animal internally from potentially hostile urine as well as to discharge urine adequately. In addition, mice are known to mark out territories with the help of urine, which may represent another functional reason for early maturity of the bladder.

SUMMARY

Data are presented on the postnatal growth of the mouse bladder. Both bladder size (measured as surface area) and bladder wet weight increase steadily with age, respectively reaching 2·5 times and 4 times their newborn values by the age of ten

weeks. Despite this growth, which may be due principally to non-urothelial components of the bladder, the body weight rises 10–15 fold above the newborn levels. The ratio of bladder weight to the total body weight steadily declines from a peak value in newborn mice to a stable plateau reached at about five weeks of age. The results indicate that a fairly mature bladder exists at birth.

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REFERENCES

ENESCO, M. & LEBLOND, C. P. (1962). Increase in cell number as a factor in the growth of the organs and tissues of the young male rat. *Journal of Embryology and Experimental Morphology* **10**, 530–562.

FARSUND, T. (1975). Cell kinetics of mouse urinary bladder epithelium. I. Circadian and age variations in cell proliferation and nuclear DNA content. *Virchows Archiv, B Cell Pathology* **18**, 35–49.

HARVEY, R. W. (1909). Variations with distension in the wall and epithelium of the bladder and ureter. *Anatomical Record* **3**, 296–307.

HICKS, R. M. (1975). The mammalian urinary bladder: an accommodating organ. *Biological Reviews* **50**, 215–246.

HICKS, R. M., KETTERER, B. & WARREN, R. C. (1974). The ultrastructure and chemistry of the luminal plasma membrane of the mammalian urinary bladder: a structure with low permeability to water and ions. *Philosophical Transactions of the Royal Society of London*, B **268**, 23–38.

JOST, S. P. (1984). Cell growth and renewal in developing and adult bladder epithelium of the mouse. M.Sc. thesis, University of Manchester.

JOST, S. P. & POTTEN, C. S. (1985). Urothelial proliferation in growing mice. *Cell and Tissue Kinetics*. (In Press).

MARTIN, B. F. & WONG, Y. C. (1981). Development and maturation of the bladder epithelium of the guinea pig. *Acta anatomica* **110**, 359–375.