Renal Agenesis in New Zealand White Rabbit

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Summary
This report describes some cases of unilateral renal agenesis, a congenital anomaly, in a breeding colony of New Zealand white rabbits, detected on physical and necropsy examination. The cases show absence of one of the kidneys, without involvement of the other parts of the genitourinary system or any other part of the body. The animals exhibited no clinical sign of renal failure. Serum biochemical and urine analysis of the animals showed a decrease in specific gravity of the urine with slight increase in the blood urea with no marked changes in other blood and urine parameters.

Introduction
Congenital anomalies of the urogenital (GU) system are not uncommon in human beings. Renal agenesis, i.e. absence of one or both kidneys, is one of the major anomalies of the GU system. Bilateral renal agenesis is often fatal whereas in unilateral cases the individual may survive with or without any complications and is compensated hypertrophy of the solitary kidney, which maintains normal renal functions. Unilateral renal agenesis is well documented in human beings (*Prasoon et al., 2004; Chaudary & Kohil et al., 1983*). However, literature highlighting the incidence of such cases in animals like dogs (*Taney et al., 2003; Agut et al., 2002*) is scanty. An animal model to study the process of developmental anomalies in GU system including renal agenesis is primarily limited to mice (*Kamba et al.2001; Gluecksohn-Schoenheimer, 1943; Mesrobian & Sulik, 1992:Maas et al., 1994*). In addition, chick embryos were reported as an important model for studying chronic renal insufficiency associated with unilateral renal agenesis (*Wenz et al., 1992*). To the best of our knowledge no report of spontaneous cases of unilateral renal agenesis has been reported in rabbits.

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Materials and Methods
In the breeding colony a few cases of spontaneous unilateral renal agenesis were observed in our conventional New Zealand white rabbits (*Oryctolagus cuniculus*) rabbits. The rabbits used for breeding were aged 6 months and weighed between 2.4- 2.6 kg. A commercial pellet diet (Golden Feeds New Delhi) and water were supplied *ad libitum*. In addition, the rabbits were provided with grain, leafy vegetables and carrots on a regular basis. The rabbits were housed in individual stainless cages (50x50x80 cm) under standard environmental conditions (Temperature 22 °C, Relative humidity 45-55%) with 10:14 hours dark: light. The animals were maintained in accordance with the guidelines for the care and use of animals in scientific research (Indian National Science Academy, New Delhi, India) under CPCSEA (Committee for the Purpose of Control and Supervision of Experimental Animals)

Case presentation
Five virgin adult male and female New Zealand white rabbits, maintained in the breeding colony were mated. The rabbits were allowed to stay in pairs overnight. The next morning one male rabbit was found dead and on post mortem examination

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the animal had a broken, paraphymotic penis, which was haemorrhagic and thought to be the cause of death. No other gross lesions were observed except the finding that the rabbit had a unilateral kidney, the right being absent. Aseptic swabs were taken for blood and urine culture to rule out other possible causes of death. The remaining four pairs delivered 15 kits, out of which two kits died at birth and had a unilateral kidney on post mortem examination. The physical examinations of the remaining 13 kits were done during the first week following birth. Of these, two kits from different does had a solitary kidney. The kits were kept under observation for any other complication and no clinical signs could be detected up to three months old. Both the sexes were affected.

Blood and urine samples were collected from those two live kits at three months of age for serum biochemical and urine analysis.

Results and Discussion

Figure 1 shows right renal agenesis in an adult male rabbit, the right ureter also being absent. The left kidney was apparently larger than normal, measuring 25 grams in weight, and giving a kidney: body weight ratio of 1:120.While in two other kits, each one day old, detected with agenesis of one kidney, the ratio was found to be 1: 166.67 and 1:157.5.

Figure 2 shows the broken, paraphymotic penis, which was haemorrhagic.

Microbial and urine culture from one adult and two kits on post-mortem revealed no specific pathogens. Serum biochemical parameters were within the reference range in two live animals with a slight increase in the blood urea value. Urine analysis revealed a slight decrease in specific gravity and an increase in protein levels.

There is strong evidence that renal agenesis is a complex of different developmental anomalies (*Taney et al., 2003; Agut et al., 2002*). Detailed study of these anomalies may provide key information on the sequence of complicated steps in the process of kidney organogenesis. Developmental studies in animal models have identified more than

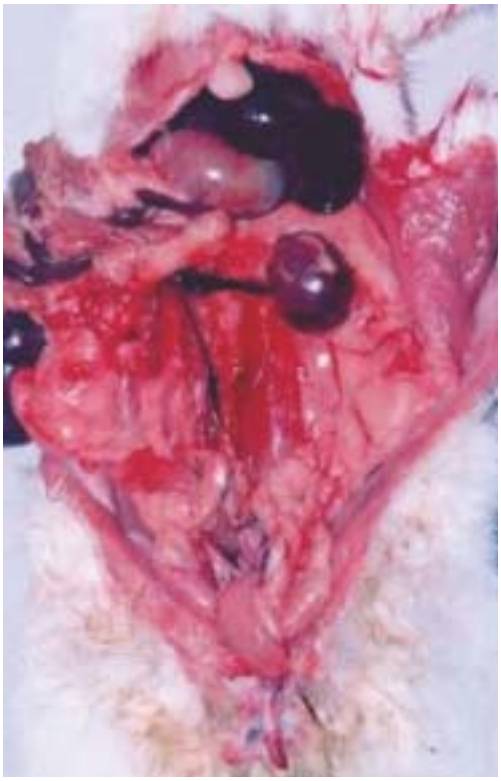

Figure 1. Gross pathology rabbit male: Unilateral kidney.

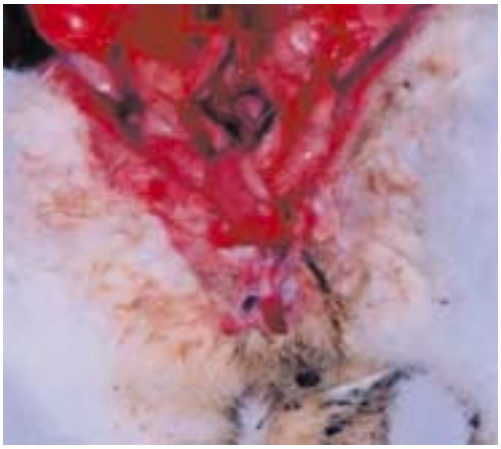

Figure 2. Gross pathology rabbit male: Broken penis with paraphimosis and haemorrhage.

40 genes regulating renal organogenesis including glial cell line-derived neurotropic factor, RET, PAX-2, Wilms' tumor suppressor gene (WT1), N-Myc, and several components of the renin-angiotensin system (RAS) (*Bates, 2000*). The interaction of environmental factors with these genes is thought to result in deformities such as unilateral renal agenesis. Mutation-induced congenital anomalies are promising tools for investigating critical genetic events in organogenesis.

Unilateral renal agenesis is most often found in association with other anomalies like Danforth Short Tail (*Sd*), (*Gluecksohn-Schoenheimer, 1943; Mesrobian and Sulik, 1992*) and limb deformity (*ld*) (*Maas et al., 1994*) etc., as described in the mouse model, which may reflect genetic or developmental commonalities of some other systems with the formation of the urogenital system. In the present cases, contrary to as described for most of the mouse models, no gross defect in any other system could be detected (although the anomaly seen in FUBI mice was pure renal agenesis without accompanying urogenital or skeletal system malformations: *Kamba et al., 2001*). Other causes of unilateral agenesis in animal models as well as in human case reports have been associated with the use of drugs or chemicals during pregnancy. In this case no drugs or chemicals that can cause renal agenesis were used in our breeding colony and therefore the cause of this renal agenesis may be associated with genes that cause congenital anomalies of the kidney and urinary tract. As random mating is practised in our breeding colony and agenesis was observed for the first time in our colony, the mode of gene transfer that causes renal agenesis could not be identified. Hence to identify the rabbits carrying such a gene we are planning to segregate the bucks and does that delivered kits with a unilateral kidney and perform a breeding programme, which would enable us to identify and develop a model for further studies.

Serum blood urea nitrogen, protein, creatinine and urine specific gravity, protein and sugar are some of the parameters indicating kidney function but there was no gross change in the above-mentioned parameters in our case except a slight decrease in the specific gravity of urine and the blood urea value and this may be due to alteration in feed and water intake or the compensatory function of one kidney.

Mice and rats are most frequently used in the study of the development of the urogenital system. However, available literature suggests that the occurrence of such spontaneous cases of renal agenesis may be rare and recurrence of such spontaneous incidence can be utilized to develop a rabbit model for renal agenesis.

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