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THE AETIOLOGY OF BENIGN ENLARGEMENT OF THE PROSTATE IN THE DOG.

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(PLATES XVII.-XXIII.)

THE changes induced by oestrogens in the male reproductive organs of various laboratory mammals have suggested that spontaneous prostatic enlargement in man results from the prolonged oestrogenic stimulation of the prostate, following a primary imbalance between "male" hormone and some oestrogenic agent also elaborated in the male organism. The data available hitherto do not provide the necessary histological justification for the hypothesis, for as yet it has been impossible to demonstrate the identity of the histological changes in naturally and experimentally enlarged prostates. And since only limited and relatively indirect experimental observations can be made on human subjects, it is also clear that such a demonstration could be provided only by comparative histological studies.

The experimental prostatic changes comprise fibro-muscular growth and epithelial hyperplasia and metaplasia leading to epithelial stratification and desquamation. The first of these changes is a common finding in human enlarged prostates, and the second also occurs occasionally. Nevertheless it could hardly be claimed that the histological appearance of an experimentally altered rodent prostate is in general similar to that of the spontaneously enlarged human prostate. de Jongh (1935) and van Cappellen (1936), among others, have remarked on the fact that both in man and in rodents enlargement begins in the most cranial region of the gland, and from this correspondence have attempted to argue the aetiological similarity of the two conditions. Such homological argument cannot, however, prove very profitable, because it is undoubtedly true that the human prostate and the prostates of most experimental animals have individual anatomical peculiarities which make comparison fruitless in some cases, and difficult in all.

The dog, one of the animals in which prostatic enlargement has been produced experimentally, is the only familiar mammal other

than man known to suffer from the condition naturally. This fact is of importance, in view of the obstacles which prevent direct knowledge of the aetiology of benign enlargement in man, since it provides an opportunity of comparing the histology of the naturally occurring with that of the experimental enlargement. The present paper is concerned with this question in general, and in particular with an extraordinary specimen of enlarged prostate in a terrier. This had been preserved by Dr J. R. Baker, who handed it to us for investigation.* We wish to take this opportunity of expressing our indebtedness to him. That it has been possible to institute a comparison between this specimen and the experimentally enlarged canine prostate is due to the generosity of Professor S. E. de Jongh and his colleagues of Leyden, who placed at our disposal histological material from dogs they had injected with oestrone (de Jongh and Kok, 1935). To them also we wish to express our warmest thanks.

The size of the normal canine prostate.

According to Kracht-Paléjeff (1910-11), the author of the only adequate account of pathological enlargement of the prostate in the dog that we have been able to find in the literature, the normal gland ranges in size between a pea and a walnut, depending on age and breed. The transverse and dorso-ventral diameters of a complete section of an "enlarged" prostate kindly loaned to us by the director of the institute of pathology, Royal Veterinary College, London, are 24 and 16 mm., respectively. Only one of the nine prostates we collected (dog 2) has smaller dimensions, the corresponding measurements being 11 and 8 mm., and as spermatogenesis was in progress in this animal at the time of its death, we may conclude that it was mature. In view of the dimensions of this specimen, and of Kracht-Paléjeff's description, it may be assumed that with the exception of dog 2, all our specimens are "enlarged" prostates (table I). The condition is widely stated to be common in dogs, although, as it rarely causes any urinary disturbance, it is seldom recognised except at autopsy. Kracht-Paléjeff states that it begins usually after the fourth year of life and that the organ often grows to the size of an apple. He refers to one case recorded in the literature in which the prostate of an animal of $25\frac{1}{2}$ lb. weighed no less than 10 lb.

Whether or not the canine prostate enlarges gradually throughout life has yet to be determined; we know of no detailed data on the "normal" size at different ages. If it does so enlarge—and the fact that all the prostates we collected were larger than the supposed

* A note on the histological correspondence between this specimen and the experimentally enlarged prostate was published in *Nature* on 20th June (Zuckerman, 1936b).

normal is suggestive of this conclusion—it will be necessary to qualify the terms "normal" and "enlarged" so far as the dog's prostate is concerned.

TABLE I.

Dimensions of the prostates of ten dogs, all mature as determined either by known age or by the occurrence of spermatogenesis.

Dog no.	Transverse diameter.	Dorso-ventral diameter.	Crano-caudal diameter.	Remarks.
Vet. Inst.	mm.	mm.	mm.	
	1 80	60	60	Enlarged
	2 11	8	...	Normal
	3 24	16	...	Enlarged
	4 26	20	...	"
	5 35	29	25	"
	6 36.5	32	31	"
	7 46	38	41	"
	8 27	24	28	"
	9 28	21	24	"
	9 60	50	70	"

Material.

Tissues from the nine numbered dogs in table I form the primary basis of the observations here recorded. All the prostates investigated, except those of dogs 1 and 8, were removed from animals which had been killed, either because of senility or because they were unclaimed strays, at an R.S.P.C.A. station. The organs were removed immediately after death and fixed in Bouin's fluid. Dog 8 was sent us by Mr I. W. Rowlands, to whom we should like to express our thanks. All sections were stained with Meyer's haemalum and eosin.

Dog 1 was the terrier, $7\frac{1}{2}$ years old, whose reproductive organs had been fixed by Dr J. R. Baker in formol saline immediately after it was killed some ten years ago. The clinical history of this dog is of interest, and is relevant to the question of the aetiology of its enlarged prostate. Until it was about six years old, the animal was regarded by its owner as normal. It had never, however, been known to pursue bitches. What is described as a change in its "sexual instinct" from male to female occurred about that time, and for some eighteen months it was apparently regarded as a female in perpetual heat by the other dogs in its neighbourhood. Owing to the embarrassment so caused, the dog was destroyed, the matter being most opportunely regarded as of sufficient interest to draw Dr Baker's attention to it. Other changes noticed during the last months of the animal's life were increasing drowsiness and enlargement of the nipples.

Fig. 1 shows the ventral surface of the animal taken immediately after its death. Four pairs of greatly enlarged nipples and the swollen sheath of the penis can be seen. The significance of these changes will be considered later. The scrotum was normal and the testes were small. Histological examination, somewhat limited owing to imperfect fixation, shows that the testes were in an atrophic condition, and although a few spermatozoa can be seen, it appears likely that spermatogenesis was in abeyance or much slowed down at the time of the dog's death. Corroborative evidence for this view is provided by the epididymis, which is almost free of spermatozoa.

Figs. 2 and 3 are line drawings of the ventral and dorsal aspects of the

prostate, which was enormously enlarged, and imperfectly divided into two larger cranial and two smaller caudal lobes. Before fixation the organ must have been at least 8 cm. in transverse and 6 cm. in crano-caudal and ventro-

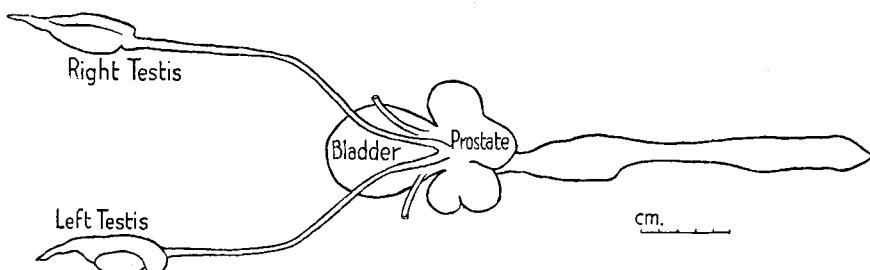


FIG. 2.—Dorsal view of genital tract of dog 1. $\times 0.24$.

dorsal diameters. For purposes of histological examination, it was divided into a number of marked blocks, each of which was cut at $10\ \mu$. Serial sections were made of the two blocks which included the crista urethralis and the openings of the ejaculatory ducts, and every fifth section was mounted. Pieces of the membranous and penile urethra were also cut and stained. Fixation of the prostate was moderately good.

The interior of the prostate comprised a mass of cysts of varying size, most of which were filled with a solid core. Some of the larger were about the size of a normal canine prostate, and several exuded pus.

Dog 2 was a normal mature animal of undefinable breed. Its prostate, which measured 11×8 mm. (table I), was cut serially at $10\ \mu$. Selected regions of the urethra and a block of the testis were also cut and stained.

Dog 3 was an aged Pekinese, with no history of urinary disturbance. The prostate, which measured 26×20 mm. (table I), was divided transversely into five equal-sized blocks and sections were cut at $10\ \mu$ from the cranial surface of each. Sections of urethra and testis were also prepared.

Dog 4 was a fully mature and healthy mongrel terrier. The prostate, which measured $35 \times 29 \times 25$ mm. (table I), was divided transversely into five equal-sized blocks and sections were cut from each. Pieces of urethra and testis were also cut.

Dog 5 was a fully mature mongrel resembling a spaniel. The prostate measured $36.5 \times 32 \times 31$ mm. Preparations were made as in the previous specimen. The cut surfaces of the prostate revealed numerous small cysts. The bladder was considerably distended, but no obvious mechanical obstruction to the flow of urine was encountered.

Dog 6 was a fourteen-year-old greyhound. The prostate measured $46 \times 38 \times 41$ mm. (table I): its surface was somewhat nodulated. On account of its size, a few selected blocks only were cut.

Dog 7 was a mongrel, in appearance somewhat like a chow. The prostate measured $27 \times 24 \times 28$ mm. (table I). Preparations similar to those of dog 4 were made.

Dog 8 was a wire-haired fox terrier aged twelve years. The prostate measured $28 \times 21 \times 24$ mm. (table I). The usual sections were prepared.

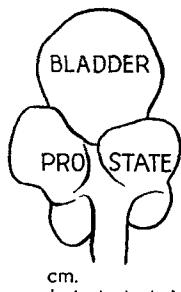


FIG. 3.—Ventral view of prostate and bladder of dog 1. $\times 0.34$.

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FIG. 1.—Photograph of ventral surface of the terrier (dog 1) whose prostate showed the effects of oestrogenic stimulation. Note the enlarged nipples and the swollen penile sheath. There is no clinical record of the onset of the skin pigmentation.

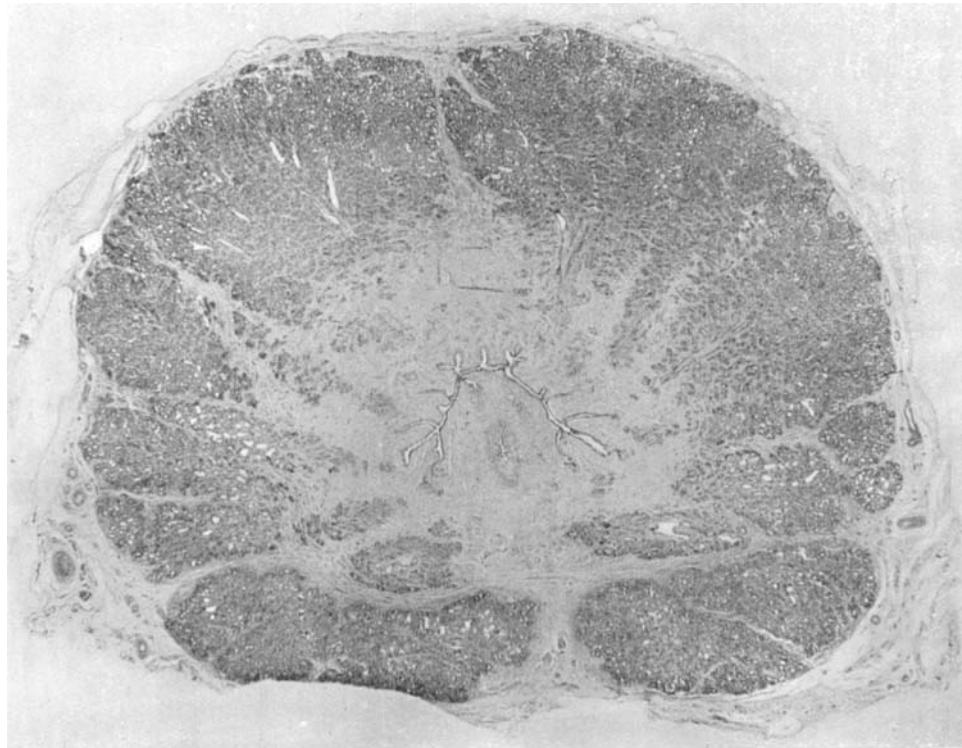
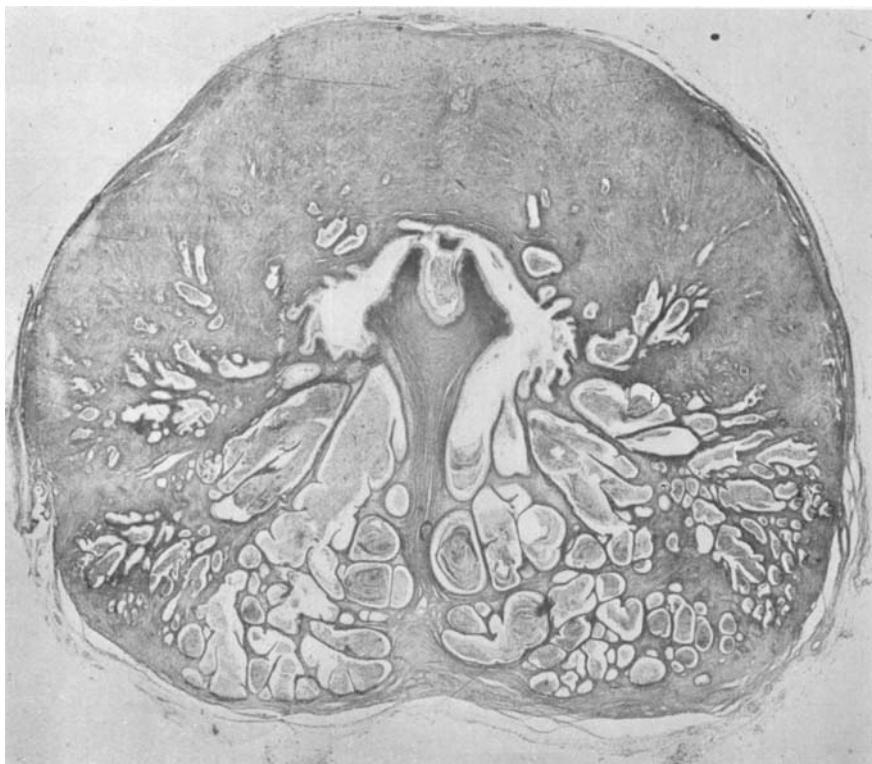


FIG. 4.—Transverse section of normal canine prostate (dog 2). The sagittally disposed uterus masculinus can be seen dorsal to (*i.e.* below) the urethra. $\times 10$.

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FIG. 5.—Normal prostatic urethra and uterus masculinus of dog. $\times 28$.FIG. 6.—Transverse section of prostate of dog which had been injected with oestrone. Note the acini distended with shed epithelial cells. $\times 7$. Specimen lent by Professor S. E. de Jongh.

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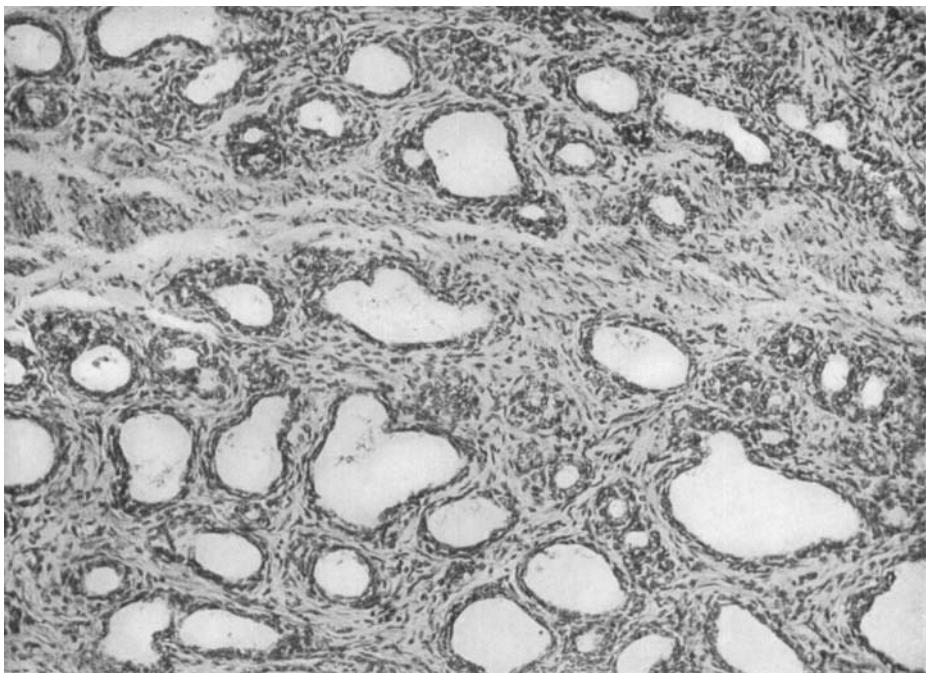


FIG. 7.—Normal prostatic glands of canine prostate (dog 2). $\times 162$.

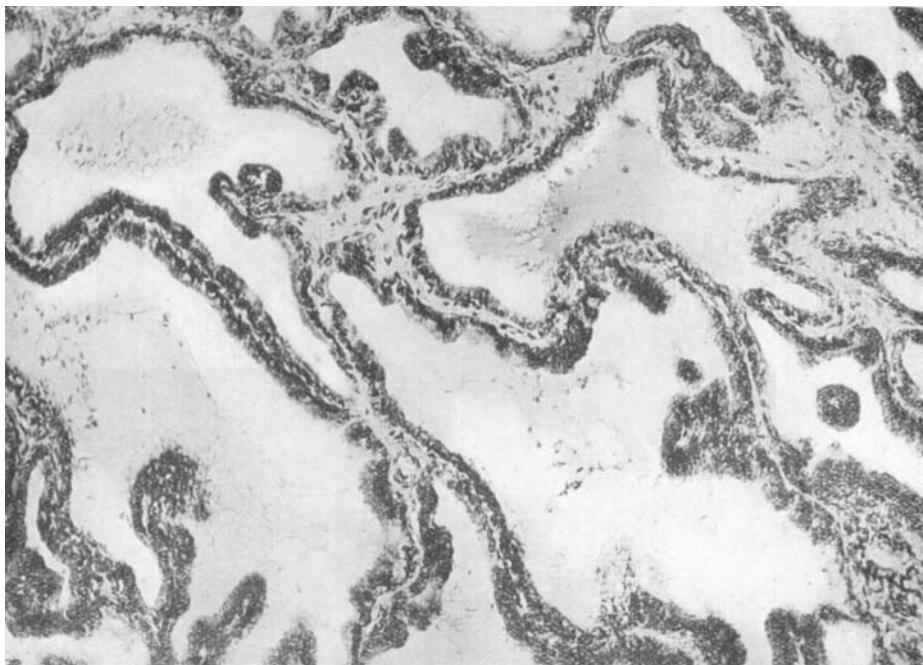


FIG. 8.—Prostatic acini in case of simple glandular hyperplasia (dog 3). $\times 162$.

PROSTATIC ENLARGEMENT IN THE DOG

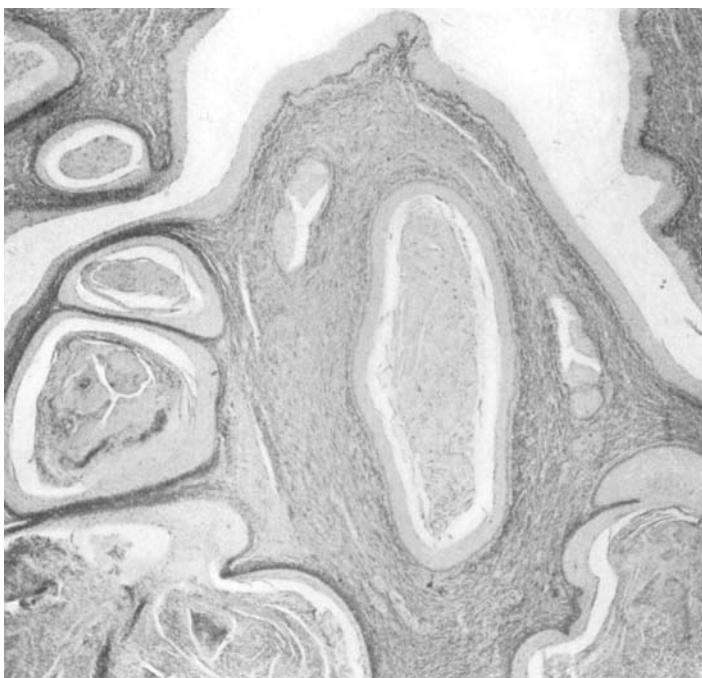


FIG. 9.—Mouth of uterus masculinus in crista urethralis of experimental dog 5516 (table II). Note the thickened utricular and urethral epithelium, with desquamation of superficial cells. $\times 32$.



FIG. 10.—Uterus masculinus and urethral epithelium of dog 1, showing excessive stratification of epithelium similar to that of fig. 9. $\times 32$.

Dog 9 was an Alsatian aged six years. The prostate measured $60 \times 50 \times 70$ mm. (table I) and contained numerous small cysts. Owing to its size only a few selected blocks were cut.

The material lent by Professor de Jongh and Dr Kok comprised sections of the prostates of the eight dogs shown in table II, all of which are referred to in their paper (1935). Some of the preparations were stained by van Gieson's method, others with Meyer's haemalum and eosin. The experimental treatment which these dogs had received is summarised in the table.

TABLE II.
Source of material received from Professor de Jongh.

No. of dog.	Age (months).	Condition.	Experimental treatment.
5519	3½	Not castrated	Daily oil injections
D	5½	Castrated	" " "
E	5	Not castrated	Nil
5516	3½	" "	2000 I.U. oestrone daily for 5½ weeks.
5517	3½	" "	2000 I.U. oestrone daily for 5½ weeks
A	5	Castrated	800 I.U. oestrone daily for 7 weeks
B	5		800 I.U. oestrone daily for 7 weeks
C	5		2000 I.U. oestrone daily for 7 weeks

HISTOLOGICAL OBSERVATIONS.

The normal prostate (dog 2, table I).

The prostate is a compact organ into whose interior a series of strong trabeculae pass from the surrounding capsule to divide it, from the histological point of view, into a series of lobules (fig. 4). The glandular elements are more prominent peripherally, the fibromuscular tissue centrally.

The glandular tubulo-alveolar tissue entirely surrounds the urethra, into which collecting tubules pass from all sides and at all levels of the prostate. Their disposition is thus unlike that of the corresponding tubules in Old World primates. In the central parts of the lobules the ducts are horizontally directed towards the urethra, and they usually appear more dilated at their peripheral ends. The glandular acini are small and lined with fairly regular columnar epithelium, which, however, is flattened in the more expanded tubules and ducts (fig. 7). This general appearance can be taken to represent that of the normal mature dog, since, as noted above, spermatogenesis was in progress in this animal at the time of its death.

The ejaculatory ducts (*vasa deferentia*) comprise a central duct with numerous simple tubular glandular offshoots, the whole system being lined by columnar epithelium, and both offshoots and ducts containing numerous spermatozoa. The ducts enter the urethra about 1 mm. above the opening of the uterus masculinus. The latter is a sagittally disposed simple diverticulum with a narrow lumen (fig. 5). It is approximately 1·5 mm. long and is lined with a low, somewhat irregular epithelium. The utricular stroma is differentiated from the surrounding fibro-muscular tissue by being slightly more chromophilic.

The œstrone-stimulated prostate (de Jongh and Kok's specimens).

The essential changes induced in the prostate of the dog by œstrone are, as in the mouse and monkey, fibro-muscular overgrowth and epithelial hyperplasia. The increase in fibro-muscular tissue is relatively more conspicuous in those specimens in which epithelial changes are least pronounced.

Changes occur in all the epithelial elements of the prostate except the ejaculatory ducts—urethral epithelium, collecting tubules, glandular acini and uterus masculinus. The available specimens unfortunately do not allow a definite decision about the ejaculatory ducts, but in so far as any conclusion is permitted, it would appear that they do not share in the general changes.

The glands of the dorsal half of the prostate are more sensitive than those ventral to the urethra (fig. 6) and, as in the mouse (Burrows, 1935), the proximal parts of the collecting tubules react sooner than the parts situated more peripherally. The essential changes appear to be, as Burrows has described for the mouse, (a) arrest of secretion, (b) epithelial hyperplasia and (c) epithelial metaplasia, the last two processes grading into each other and converting the once single layer of columnar cells into a heavily stratified and rapidly desquamating epithelium. The epithelium is no more than two or three layers thick in the most rapidly growing acini, the more superficial cells being immediately shed (fig. 13). By this process of growth the glandular system is converted into a series of cysts filled with a core of shed epithelial cells and separated from each other by fibrous trabeculae covered on each side by flattened epithelial cells (fig. 11).

The change in the utricular epithelium is essentially similar and indeed it is impossible in some sections to distinguish this diverticulum from other affected glands except by its topography (fig. 9). In one specimen the utriculus extended upwards for a considerable distance *behind* the ejaculatory ducts. As a rule, too, the epithelial proliferation occurring in the region of the utricular mouth extends irregularly into the stroma of the crista urethralis,

a condition reminiscent of the dermal extensions of benign papillomatous growths. Round-celled infiltration is conspicuous in one section.

The enlarged prostate of dog 1 (table I).

Except that the changes it demonstrates are somewhat more advanced, there is no difference between the histological appearance of this specimen and that of the experimental prostates discussed above (figs. 11 and 12). It has already been noted that when divided into blocks this prostate revealed itself as a conglomeration of cysts of various sizes, some minute, others as big as a normal canine prostate. Normal glandular tissue is completely absent. The cysts are generally separated from each other by thin trabecular strands, and are lined as a rule by no more than two or three layers of flattened epithelial cells, whose rapid division is amply attested by the solid plugs of shed cells which fill the distended cysts (figs. 12 and 14). In some places desquamation has not proceeded as far as in others and the stratified epithelium is consequently thicker. Occasionally, too, wide plates of stratified cells extend into the cysts (these may, however, represent tangential sections of the cyst walls), and sometimes the deeper layers of the cyst walls appear to be proliferating into the prostatic stroma.

As in the experimental prostate, thin crescentic tongues of lining cells, supported on a frame of fibrous tissue, occasionally project into the cysts. It cannot be doubted that the transformation of the glands into cysts was due to the accumulation of epithelial debris in their lumina, a process even better recognisable in the experimental prostates in which more of its stages are represented. The mass of cysts has so disorganised the prostate that it is impossible to unravel their relations to each other. Moreover, no collecting tubules can be recognised as such, and the urethral openings of the cysts do not appear as numerous as the glandular openings of a normal dog's prostate. Many of them may have become obliterated in the process of cyst formation.

It would be misleading to speak of an increase in the fibro-muscular tissue of this prostate. If anything the stroma is relatively reduced. Fibro-muscular tissue mainly appears as the central structure of the thin trabeculae which separate the cysts. Occasionally the cysts are more widely spaced and in regions where this occurs the stroma is more abundant. It is very likely, however, owing to the enormous size of the prostate, that the total amount of its fibro-muscular tissue is far greater than that of the normal organ. As already noted, fibro-muscular tissue also appears relatively reduced in those experimental prostates in which the epithelial changes are extensive.

Owing to the great distortion occasioned by the generalised

cystic development, the uterus masculinus cannot be recognised as such except within the crista urethralis, in which it runs a course of some 2 mm. (fig. 10). The epithelium of the diverticulum is heavily stratified, and near its mouth there is considerable proliferation of its basal layers into the stroma of the crista—a condition identical with that seen in the experimental specimens. Surprisingly few of the cysts show round-celled infiltration. Where it occurs it is presumably a secondary phenomenon similar to that seen in experimentally enlarged prostates.

The epithelium of the prostatic urethra in this specimen is even more stratified than that in the experimental prostates (figs. 9 and 10). The stratification extends distally to the external urethral opening and proximally well above the mouths of the ejaculatory ducts. Its upper limit cannot be determined owing to post-mortem shedding of the epithelium. In its distal extension the stratification is highly reminiscent of the condition met with in certain species of monkey after oestrogenic stimulation (Zuckerman, 1936b).

Over the lower half of the crista urethralis the epithelium had proliferated deeply into the stroma, forming extensive irregular blocks of stratified epithelial cells easily visible to the naked eye in section. Within these masses of cells numerous simple gland-like structures can be seen, each consisting of a circle of epithelial cells without any definite central lumen. These structures are fairly regularly disposed and, in spite of a superficial resemblance, can readily be differentiated from the cell-nests of malignant squamous growths by the uniformity of the single layer of cells of which they are formed. The metaplastic cysts of the prostate proper also display a superficial resemblance to certain other cellular formations seen in malignant epitheliomatous tumours.

The enlarged prostates of dogs 3-9 (table I).

The histology of these specimens, which appeared obviously enlarged, is very different from that of dog 1. The glandular epithelium is, almost without exception, normal, but more actively secretory than usual, and comprises a single layer of large columnar cells in all the regions examined (fig. 8). The acini are, however, very irregular in shape and variable in size, some forming relatively voluminous cysts filled with secretion (fig. 15). The glandular cells are larger and their inner borders less clearly defined than in dog 2, the "normal" specimen (fig. 7).

A few cysts lined by a low, single-layered epithelium are present in the prostates of both dogs 3 and 4; the size of these cysts is surprising in view of the apparently non-secretory nature of their epithelium. A very few glands are also lined by a low stratified

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FIG. 11.—Distended glandular acini of prostate of dog injected with oestrone, 5516 (table II).
Note the central cores of shed epithelial cells. $\times 118$.

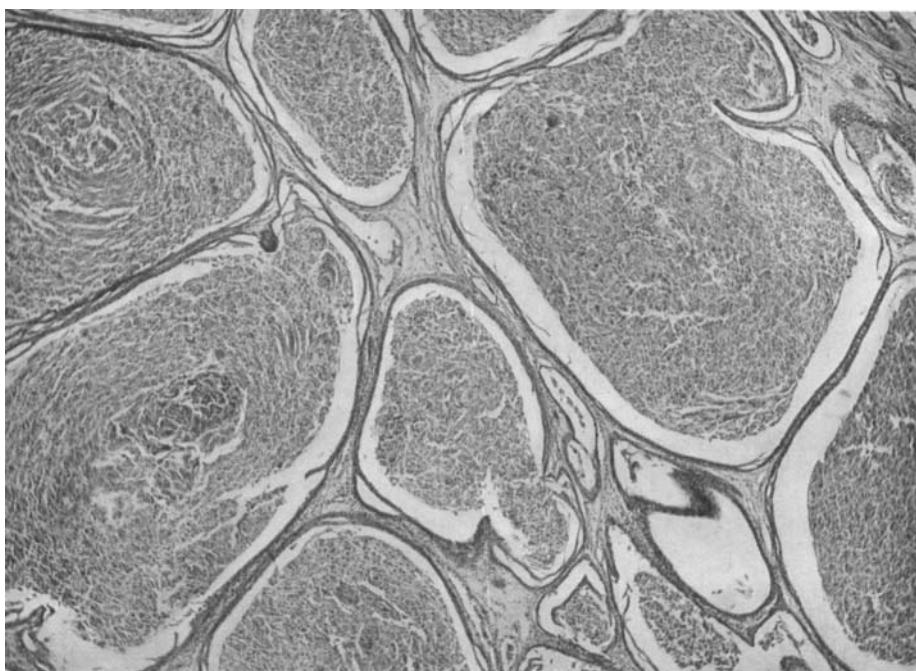


FIG. 12.—Prostatic acini of dog 4, showing the correspondence of the natural with the experimental condition. $\times 118$.

PROSTATIC ENLARGEMENT IN THE DOG

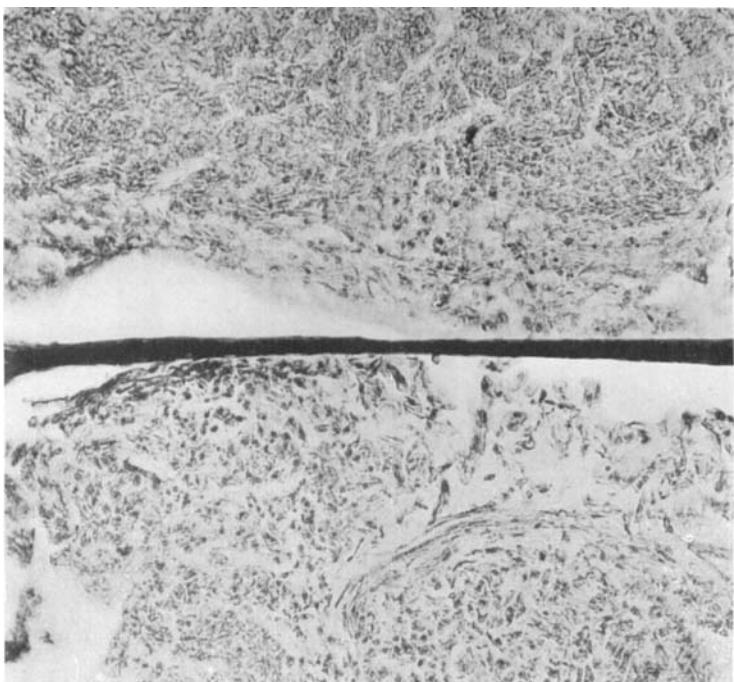


FIG. 13.—High-power view of shed epithelium in two glandular acini of experimental prostate 5516 (table II). Owing to the thickness of the section the structure of the bar of tissue separating the two acini cannot be seen. $\times 178$



FIG. 14.—Similar view in prostate of dog 1. Note the very low and flattened epithelium covering either side of the stromal plate separating the two acini. $\times 178$.

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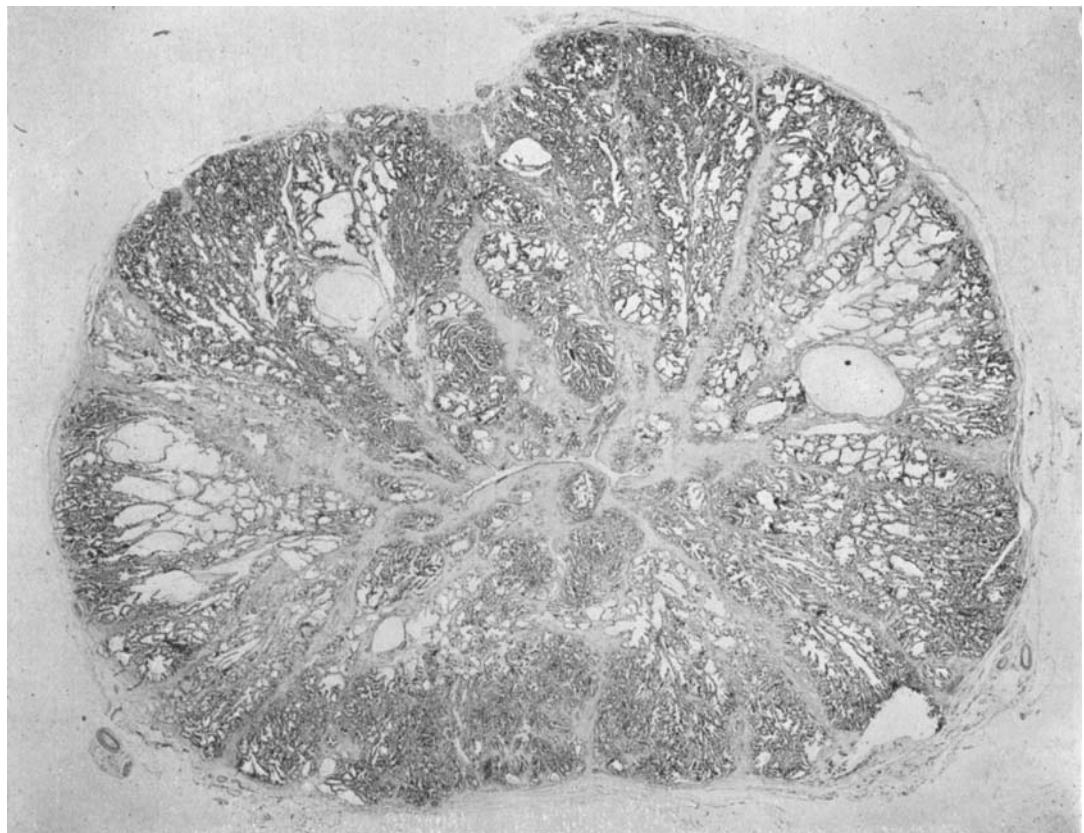


FIG. 15.—Low-power view of enlarged prostate of dog 3 showing simple glandular hyperplasia. $\times 5$.

epithelium which, however, was not being shed any more quickly than the normal single-layered columnar epithelium. Extensive disorganised glandular hyperplasia and in places considerable degeneration had taken place in the prostate of dog 9. Round-celled infiltration of the stroma is conspicuous in only two prostates (dogs 6 and 8), and in dog 8 several suburethral collections of round cells were encountered.

The general appearance of all these prostates is that of a primary glandular hyperplasia, but in so far as they are all markedly enlarged, it is not unreasonable to suppose that the total amount of stromal tissue is also increased. As a rule the stroma merely provides a frame for the walls between adjacent glands. The appearances (fig. 15) suggest plainly that these walls frequently disappear in the process of distension.

In none of the sections in which it can be found does the uterus masculinus appear abnormal. The epithelium of the ejaculatory ducts is also everywhere normal, and the lumen of the urethra, too, is not obstructed in any of the specimens. In only one instance does the urethral epithelium appear abnormal. The epithelium in the exceptional specimen (dog 4) is hyperplastic over the crista urethralis and its superficial cells are being shed at an apparently rapid rate.

DISCUSSION.

Kracht-Paléjeff describes four types of simple enlargement of the canine prostate—glandular hypertrophy proper, pseudo-hypertrophy (interstitial enlargement), cystic degeneration and enlargement, and purulent inflammatory enlargement. The last of these is of no interest in the present connection. It appears likely that the other three classes of enlargement are closely related to each other aetiologically, since glandular hyperplasia is an essential part of each. In so-called "glandular hypertrophy" the most obvious change is the increase in glandular tissue; in pseudo-hypertrophy the stromal tissue is said to be primarily affected, an increase in the glandular elements being a compensatory process; while in cystic degeneration the glandular acini become so distended through obstruction, that cysts containing up to two litres of fluid may be encountered. With the exception of the prostates of dogs 1 and 2, all the prostates we collected showed a predominantly glandular hyperplasia of the kind which Kracht-Paléjeff would presumably have classified as the first type of enlargement. The specimen lent by the director of the pathological institute of the Royal Veterinary College as an "enlarged dog-prostate," was also of this class, which presumably is a form of prostatic enlargement that afflicts many dogs as they age.

The prostatic glandular tissue in instances of enlargement of

this kind is essentially not abnormal—unless hyperactivity be regarded as an abnormality—nor, as is usually stated, does the enlargement appear to cause obstruction to the flow of urine. If the normal activity of the prostate is under the control of male hormone, as is generally believed, it is conceivable that this kind of enlargement is due to an excess of male hormone ; it may be noted in this connection, however, that there was no excess of interstitial tissue in any of the testes relating to this series of prostates. The possibility that the prostate of the dog is unusually sensitive to male hormone is readily amenable to experimental test.

In neither Kracht-Paléjeff's paper nor elsewhere in the literature have we found any reference to prostatic changes comparable with those manifested by the prostate of dog 1 of our series. As indicated above, these changes are identical with those experimentally induced by oestrogens (essentially comprising excessive and unceasing division of cells derived from the epithelium of the uro-genital sinus) : since these changes are specific to oestrogens, it is reasonable to conclude that the spontaneous prostatic enlargement of dog 1 was a response to an oestrogenic agent elaborated within the animal's body. That the male mammal normally produces such a substance is well known, and the view which we advance merely implies that the changes in question were caused either by an absolute excess of oestrogen or by a relative excess following a diminution in the level of secretion of male hormone proper.

Other evidence of oestrogenic stimulation in this animal is provided by its enlarged nipples and by the stratification of its urethral epithelium. The swollen penile sheath may also be comparable with the corresponding swelling shown by rhesus monkeys when injected with oestrone. The view that the dog's "feminine" behaviour should also be taken as evidence pointing in the same direction is, however, not warranted, since oestrous behaviour has not been clearly shown experimentally to be a specific effect of oestrogenic substances.

The occurrence of epithelial hyperplasia and metaplasia throughout the whole of the prostate in question is of great interest from the point of view of the responses of the prostate of monkeys to oestrogenic stimulation. Reports on rhesus or other monkeys injected with oestrone for more than 89 days are not as yet available ; in monkeys injected for shorter periods only the proximal parts of some of the collecting tubules are affected (Zuckerman and Parkes, 1935-36). In monkeys belonging to the genus *Cercopithecus* which had been injected for two weeks there was some mitotic activity of the epithelium of the prostatic glands proper, but no evidence of epithelial stratification and shedding. On the other hand the data provided by de Jongh and Kok for the dog

show that the general prostatic epithelium is extremely sensitive, and in many regions immediately sensitive, throughout the gland. On the basis of the theory put forward elsewhere (Zuckerman, 1936a), it would follow that in the dog all the prostatic glands are derived from sinus epithelium, which is very sensitive to oestrogens, whereas it would seem that in the rhesus monkey only part of the prostatic tubules have such an origin. Further experiment is necessary, however, to show whether or not all the prostatic tubules in the monkey would react after more prolonged treatment with oestrone. If it proves that they do, the hypothesis referred to above will require modification and the problem will be to explain the varying sensitivity both of different regions of the prostate and of the prostates of different species.

The specimens we have studied show clearly that in addition to the common simple glandular hyperplasia of the prostate which affects dogs, with its consequence of a uniform and in most cases apparently a non-obstructive enlargement, there is another form of somewhat irregular enlargement, which is caused by the action of some oestrogenic agent. It is possible that the occurrence of a few stratified glands and of excessive epithelial stratification of the prostatic urethra in some of the specimens we studied is also indicative of oestrogenic action, but this point needs further investigation with more material. It is claimed that regression of the enlarged prostate soon follows castration in dogs (Hobday, 1924). Such a result would be readily understandable on the view that while the simple glandular enlargement is due to an excess of male hormone, the oestrogenic variety results from an excess of oestrogenic substance elaborated by the testis.

SUMMARY.

Of nine prostates of mature dogs studied, only one was normal in size and histology. Seven of the remaining eight were enlarged, the enlargement being due to a simple glandular hyperplasia, possibly determined by an excess of male hormone. The ninth specimen was greatly and irregularly enlarged. In histological appearance it is different from the other specimens, but is identical with the prostates of dogs which had been treated with oestrone. This correspondence is taken as direct evidence that enlargement of the prostate may result spontaneously from an excess of oestrogenic stimulation.

The photomicrographs are by Mr W. Chesterman, to whom we should like to express our thanks. We also desire to record our appreciation of the care and skill with which Mr R. Munro prepared the sections.

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