III. General section.

Observations on the structure of the tubules.

The nephron segments and the collecting tubules.

The nephron segments. The capsule of Bowman is of uniform structure. The epithelium is sometimes thicker in some parts of the capsule, but this feature seems very variable and has probably no morphologic significance (cf. Mac Nider 1927). The shape also varies, but there seems to be no regularity in the distribution of the forms.

The neck is individual in its occurrence, too.

The proximal tubule often shows slightly differentiated parts with regard to diameter, transparency and granule content. Some of these differentiations seem to be individual variations, but one is certainly of greater significance: a distinct terminal segment in some *Carnivora*. This is well known in the cat and the dog (cf. p. 320 and 325), where the terminal segment is usually very distinct. A similar, thickened terminal segment exists in *Ursus* (p. 327), *Lutreola* (p. 330), sometimes in *Mustela* (p. 329) and in *Phoca hispida* (p. 336). It is thus a wide-spread feature in the *Carnivora*, though it is absent in *Arctitis*, *Lutra* and sometimes in *Mustela*. It must be assumed that there is also a terminal segment differentiated in those carnivores where it is apparently lacking. In these forms it is probable that its existence cannot be ascertained owing to the uniform diameter of the proximal tubule.

In several forms belonging to other groups there is a terminal segment which is most often narrower than the preceding part of the proximal tubule. It is usually more transparent than the latter (shrews, Pl. 3, fig. *1*; rabbit, *Sciurus*, *Mus*, Pl. 2, fig. *3*; sometimes in the cow, horse), but in *Pipistrellus* it is more opaque. The transition seems to be gradual in these forms. In the white rat (Pl. 1, fig. *5*) and in *Hystrix* (Pl. 2, fig. *1*) the transition is abrupt, and the terminal segment is thicker than the preceding part of the proximal tubule. In all these forms it is possible to see cell boundaries in the terminal segment, but not in the other parts of the proximal tubule. In many mammals there is thus a terminal segment which is anatomically distinguishable and probably comparable with that of the carnivores. It is reasonable to suppose that, in the

other mammals also, there is a similar differentiation of the proximal tubule, though it is indistinguishable in the maceration preparations used by me.

Suzuki (1912) has divided the proximal tubule into 3—4 parts on the basis of their structure. Of these parts the distal one is probably the same as the terminal segment. The segments distinguished by him in the proximal part of the proximal tubule seem somewhat doubtful. His investigations refer to guinea-pig, mouse, rabbit and hedgehog.

The thick segment is as a rule differentiated into a thicker and a thinner part. Sometimes it is uniform. This is especially the case in cortical nephrons, but it may also be so in all nephrons of a kidney (*Jaculus*, young calf, young rabbit, young cat).

The distal tubule is often composed of distinct segments. The first of these, the intercalated segment (Pl. 3, fig. *2*, *3*), is often structurally identical with the thinner part of the thick segment. In this case it would perhaps be appropriate to refer the intercalated segment to the thick segment, and not to the distal tubule. From a practical point of view it is, however, better to refer it to the distal tubule, as the beginning of the latter is usually most accurately determinable if the point of attachment to the capsule is taken as the boundary between thick segment and distal tubule. The other distinct segments of the distal tubule (cf. esp. *Erinaceus* and cow) vary so greatly in occurrence and appearance that it is not possible to give any general scheme.

The distal tubule is usually not provided with numerous projections. Especially in the small forms and in young specimens there are very seldom as many projections as Peter has found in several larger forms.

The collecting tubules. As described in the introduction there are two main types of collecting tubules, the collecting tubule with direct junctions, and the arcade. These types have been described by several writers, especially by Peter (1909), who has reviewed the earlier literature. After him only v. Möllendorff (1930, p. 15—18) seems to have treated this subject. He considers the arcades to be more primitive.

To answer the question as to the nature of the arcades, it is necessary to find out their essential characters. The most important are that their first, ascending part does not lie in the medullary ray, as does the descending part, and the fact that the deepest nephrons open in the very beginning of the arcade. That the ascending part of the arcade has the situation mentioned is pointed out by Peter (1909) and v. Möllendorff (1930), and after thorough examination of a number of kidneys of rabbit and cow I can confirm this. Occasionally this matter has been examined in other species also, without any exception appearing. This is important, as the collecting tubules with direct junctions lie entirely in the medullary

rays when they pass through the cortex. The order of junction by the nephrons indicates more directly which type is primitive, however. In the hitherto examined *Amphibia*, reptiles and birds, the nephrons open into the collecting tubule in the order in which they were formed, the oldest nephrons opening nearest to the base of the collecting tubule (see especially HUBER 1917, also ZARNIK 1910). This must be considered the original mode.   This same order also normally occurs in the collecting tubules with direct junctions in the mammals. In the arcades this order is reversed. This must be considered secondary. In most land vertebrates the kidneys are composed of lobuli (ZARNIK 1910, HUBER 1917, v. MÖLLENDORFF 1930). In these the collecting tubules are situated at or near the surface of the lobuli, together with the afferent veins; the artery and the efferent vein of the lobulus are separate from these two and often lie in the centre of the lobulus. The part of the lobulus containing the collecting tubules corresponds to the medullary rays in mammals (cf. v. MÖLLENDORFF 1930, FREUDENBERG 1931). The artery and vein are situated separate from these; v. MÖLLENDORFF considers them as the centre of mammalian renal lobuli. (TRAUT 1923 and HUBER 1928 take another view of the lobular composition in the mammalian kidney, but it does not affect the following argument even if their view is accepted). The position in the medullary rays must then be considered primitive for the mammalian collecting tubule. It seems reasonable to think that the ascending part of the arcades, to which nothing seems to correspond in other vertebrates, has either been secondarily formed, or has changed its place secondarily.

The mammalian collecting tubules deviate from the reptilian type in one further respect. In the latter the initial collecting tubules open into the collecting tubules, and not only into their end branches, but also into the more basal parts (fig. 23 *A*, cf. ZARNIK 1910 and HUBER 1917). In the mammals the initial collecting tubules normally join only the end branches of the collecting tubules, and there is usually a long portion of them receiving no nephrons (fig. 23 *B*). The mammalian type is certainly secondary, and may be supposed to have developed either through the complete reduction of the deepest nephrons in the reptilian type, or through the displacement of their junctions towards the end of the collecting tubules (instead of this last possibility a cleavage of the collecting tubules might be supposed, so that the branchings have moved downwards). Fig. 23 *C* is a schematic representation of a collecting tubule in a bird (after HUBER 1917). If a moderate displacement of the deepest junctions occurs, a typical mammalian collecting tubule without arcade results (fig. 23 *D*). If the displacement is much greater in the deepest nephron than in the next deepest, the former may come to open into

the collecting tubule above the latter. Such types of collecting tubules
are sometimes found (fig. 9: *2*, p. 307). If there is some displacement
in the higher nephrons, but none in the deepest, a type will result similar
to that shown in fig. 11: *5*, p. 319). It is also possible to assume that the
deepest nephron may be displaced in such a way that it joins the initial
collecting tubule above it instead of the collecting tubule. The resulting
type (fig. 23 *E*, cf. fig. 11: *8—11*) has a small arcade. If such a process
is taken one step further (fig. 23 *F*, cf. figs 9: *2, 4*; 11: *13*; 13 *C*, p. 325)
a more typical arcade is formed. As the distal tubules and the initial
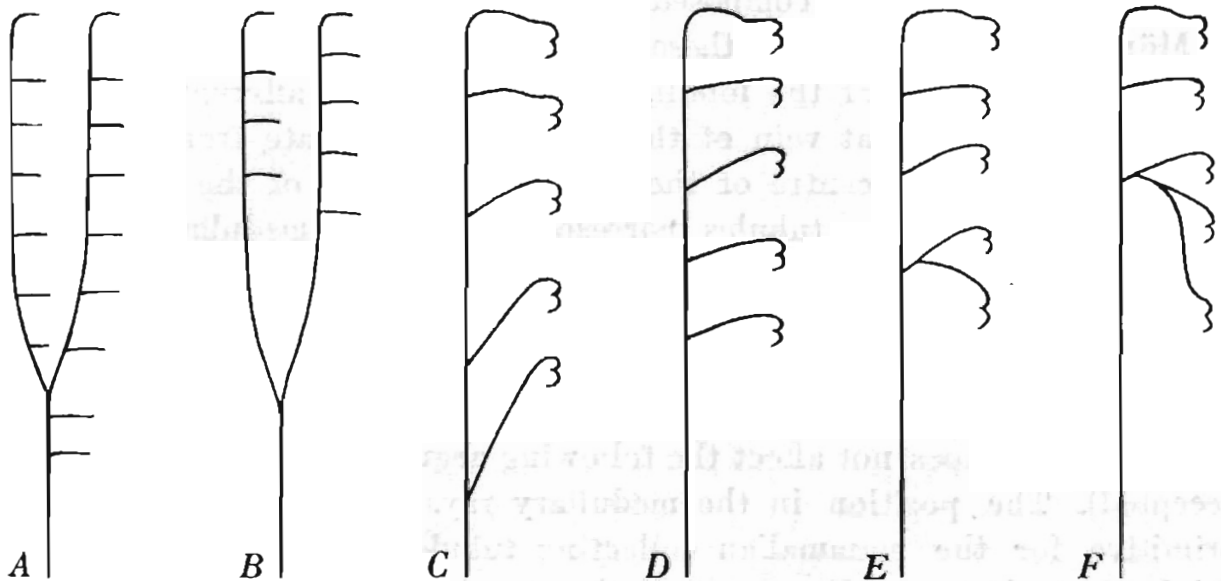

Fig. 23. Schemes of collecting tubules. Explanation in the text.

collecting tubules lie between the artery and the medullary ray the new
portion of the collecting tubule thus formed will not lie in the medullary
ray, but in the neighbourhood of the artery. This assumed process is
thus capable of explaining the three main characteristics of the mam-
malian collecting tubules: The junction-free segment, the situation of the
arcade, and the reversal of the order of junctions in the arcade. The
small aberrations described above may be attributed to small irregularities
in the process. Another relatively common type is that shown in figs.
9: *3*, p. 307, 11:*12*, p. 319. This is explained by assuming that the deeper
nephrons have not all been displaced on to the same higher initial col-
lecting tubule. Thus, two branches are formed. This type seems to be
the normal one in *Echidna* (ZARNIK 1910).

It seems to me very probable that such a process of displacement of
the peripheral junctions along the collecting tubules is, at least in a
phylogenetic respect, responsible for the formation of the characteristics
of the mammalian collecting tubules.

It is difficult to ascertain if the ontogenetic mode of development
supports, or can be explained in accordance with this hypothesis. The

opinions on the development of the collecting tubules are very conflicting (cf. PETER 1927 c and HEIDENHAIN 1923, 1937). With respect to the formation of the arcades there seems to be agreement, but the process of arcade formation as described by PETER (1927 c), though not conflicting with my view, gives no support to it, either. It might seem that the assumed displacement towards the periphery of the nephron junctions is in opposition to the opinions of HEIDENHAIN (1923, 1937), who considers that a cleavage of the collecting tubules occurs in embryonic stages. It is, however, not impossible to think that such a displacement of the peripheral junctions may occur in addition to a cleavage of the collecting tubules.

The distribution of the typical arcades is of interest. They occur mainly in herbivores, especially the larger ones. In insectivores, carnivores and some small rodents there are seldom typical arcades. In *Arctitis* and *Ursus* there are, however, well-developed arcades (p. 324 and 328), as well as in *Pteropus* (p. 283). This indicates that the diet is of greater importance than the phylogenetic relationship in this respect. In this connection it may be mentioned that the initial collecting tubules are usually reduced in length or absent in nephrons joining arcades.

The thickness of the collecting tubules is probably also correlated with the mode of living. Generally it is smaller in carnivores than in herbivores, but exact information is lacking. Of special interest in this connection are the very thick collecting tubules in *Pteropus*, and the relatively thick ones in *Ursus*.

It is almost certain that typical arcades have been developed independently in several mammalian groups (e. g. *Megachiroptera*, *Ursus*, *Arctitis*, *Oryctolagus*, other rodents). This development has, of course, been facilitated by the fact that indications of arcades probably exist in all mammalian kidneys, and according to my view, that the process of displacement takes place already in the formation of the typical mammalian collecting tubule without arcade.

The cortical nephrons; long and short loops.

PETER (1909) has shown that cortical nephrons occur in *Sus* and *Homo*. Their occurrence is interesting, as they differ from the other nephrons in some important respects. The proximal tubules do not descend to the stripe boundary, the thin segment, usually confined to the inner zone and the inner stripe, may occur in the cortex, or be absent, the loops turn in the cortex, and usually the thick segment is not differentiated into a thicker and a thinner part. The cortical nephrons thus upset the whole structural scheme of the kidney. All the peculiarities they show

also exist in the embryonic stages of all nephrons (cf. HUBER 1905, PETER 1927 b). From this fact it might perhaps be inferred that the existence of cortical nephrons is a primitive feature.

With regard to this the distribution of the forms with cortical nephrons among the mammals must be taken into account. Cortical nephrons in considerable numbers have hitherto been found in *Ornitho-rhynchus*, *Echidna* (ZARNIK 1910), *Pteropus*, *Hystrix*, *Castor*, *Microtus*, *Evotomys*, *Arvicola*, *Arctitis*, *Elephas*, *Sus*, *Hippopotamus*, *Alces*, *Rangifer*, *Papio*, *Macacus*, *Homo*. A few cortical nephrons exist in the kidneys of the cow (some specimens), *Dama dama*, the horse according to SIEWERT (1927), and in one specimen of the rabbits examined by me. With the exception of the monotremes only forms feeding exclusively or mainly on plants have cortical nephrons. It may also be noted that most of them are relatively large forms (exceptions: *Pteropus* and the voles). As an insectivorous and carnivorous diet is certainly primitive in the mammals this distribution indicates that the occurrence of cortical nephrons, at least in the *Monodelphia*, is secondary and may be looked upon as a secondary retention of an embryonic feature. As regards the *Monotremata*, it is impossible to have a well-grounded opinion on this subject.

It seems also probable that in the *Marsupialia* and *Monodelphia* there are originally both long and short loops, i. e. the medulla consists primarily of outer and inner zone. Long loops are absent in *Hystrix*, *Castor*, *Elephas*, *Hippopotamus*, *Papio*, exceedingly few in *Ornithorhynchus*, *Echidna*, *Pteropus*, *Arctitis*, *Rangifer*, *Tragulus*, *Macacus sylvanus*. The long loops are few in *Microtus*, *Evotomys*, *Arvicola*, *Sus*, *Alces*. It is apparent both that the long loops are reduced in number in many herbivores but usually not in forms from arid habitats, and that there is a strong connection between the occurrence of cortical nephrons and the reduction of the long loops. It seems probable that the two latter features are, at least in part, consequences of a reduction of the thin segment (cf. p. 384).

In several carnivores all, or nearly all, loops are long (cat, dog, *Mustela*). The long loops are numerous in the other carnivores also, except in *Ursus* and to some degree in aquatic forms. The rodent *Psammomys* has only long loops. This preponderance of the long loops is shown macroscopically by the strong development of the inner zone, and is connected with the considerable length of the thin segment in these forms (cf. p. 388). The absence of short loops must also be considered as a secondary feature. The most primitive condition as regards the relation of long and short loops and cortical nephrons thus seems to be that still existing in the *Insectivora* and most small rodents, and in many other forms, too.

In this connection it may be noticed that those kidneys that contain

numerous cortical nephrons seem to have a very large cortex in proportion to the medulla. This is the case in *Sus*, *Rangifer*, *Alces* and *Elephas*, where the cortex forms about $^9/_{10}$ of the kidney volume. It seems very probable that all or most kidneys with such extreme cortical preponderance contain cortical nephrons in large numbers.

The dimensions of the nephron segments.

The length of the nephron segments.

The proximal tubule. The nephrons and their segments usually vary considerably in length in the single kidney also. The proximal tubule is more easily studied in this respect than entire nephrons, owing to the difficulty of isolating the latter. A series of measurements has been made in *Mus flavicollis*, "young male", (table 22 a, b, p. 308), which is large enough to permit of a more detailed discussion of this subject. In this specimen there is no distinguishable difference in length between high proximal tubules and middle ones. Both categories show a moderate variation, and the measurements form a distribution not greatly deviating from the normal distribution. The deep proximal tubules, on the other hand, show a very skew distribution, and there are, perhaps, other irregularities in the distribution (though the material is not large enough to base definite conclusions upon it) with respect to the occurrence of more than one maximum. The mean length of the deep proximal tubules is distinctly higher than that of the higher ones. Taking all proximal tubules together, the distribution is also distinctly skew. This skewness is produced by the fact that a few of the deepest proximal tubules (and, indeed, all the corresponding nephrons) are much longer than the others. These longest nephrons have loops reaching or nearly reaching the area cribrosa, and are the first nephrons of the kidney to develop. In early stages of the kidney development they are, of course, much longer than the other nephrons, as is clearly shown in embryos and young (cf. HUBER 1905, PETER 1927 c). In *Mus flavicollis* this relation is retained later, and in fact is demonstrable even in the oldest specimens examined. From the series of *Mus flavicollis* it might be inferred that the greater length of the deep nephrons is due not to their position and order of development but to the fact that they have long loops. It is, however, evident that the deepest nephrons in *Psammomys* (cf. also *Mustela*) are very much longer than the high nephrons, though in *Psammomys* there are long loops only.

Similar circumstances to those in *Mus flavicollis* are common. Thus, the deep proximal tubules are longer in shrews, bats and small rodents

(cf. also *Sminthopsis* and *Antechinomys*). There are, however, types where this is not the case. The dog may be taken as an example. Here, as is evident from the data p. 326, the deep proximal tubules are not longer, but shorter than the average. On the other hand, the high proximal tubules are the longest. As it is rather difficult to examine a great number of tubules in this species, owing to their comparatively great length, it has not been possible to obtain a clear picture of the length distribution of the deep proximal tubules. It is possible that the nephrons reaching the area cribrosa have proximal tubules decidedly longer than those of deep nephrons turning at a higher level. It is, however, certain that the distribution of proximal tubule length is quite different in the dog as compared with *Mus*. In the sheep the circumstances seem to be much the same. In the cow and the camel the high proximal tubules seem to be, relatively, still longer than in the dog. On the other hand the rabbit and the cat seem to hold a more intermediate position between the mouse and the dog in this respect.

It seems that almost all the small mammals have their proximal tubule lengths distributed according to the "mouse type". This is understandable if it is remembered that they have simple kidneys with a distinct papilla. The deepest nephrons have loops reaching the apex of the papilla. The longer the papilla is the longer these nephrons must be, and it is natural that the proximal tubules are lengthened with the nephrons. In cat and rabbit, for example, the papilla is not so long, relatively, as in the smaller types examined, and the deep nephrons are thus relatively shorter. This tends to make the longest deep proximal tubules relatively shorter, too. In types showing kidneys with a crest the depth of the medulla is further reduced (cf. p. 404). The length of the high proximal tubules is determined by the fact that they normally end at or near the cortico-medullary boundary. As the depth of the cortex increases proportional to the depth of the medulla, the length of the high proximal tubules is increased proportional to the length of the deep proximal tubules. This is what has happened in the "dog type".

The latter type is common among the larger kidneys. There are, however, a number of large kidneys which do not belong to this type, for instance the kidneys of *Sus*, *Elephas*, *Alces*, and probably some others. In these the high proximal tubules are distinctly shorter than the average, and the deep ones are at all events not shorter than the average, and usually longer. It is interesting to note that in all these kidneys there are cortical nephrons. In these nephrons the normal relations to the medulla have been lost, and as the proximal tubules do not reach the medulla they have the possibility of being shorter than might be expected from the thickness of the cortex.
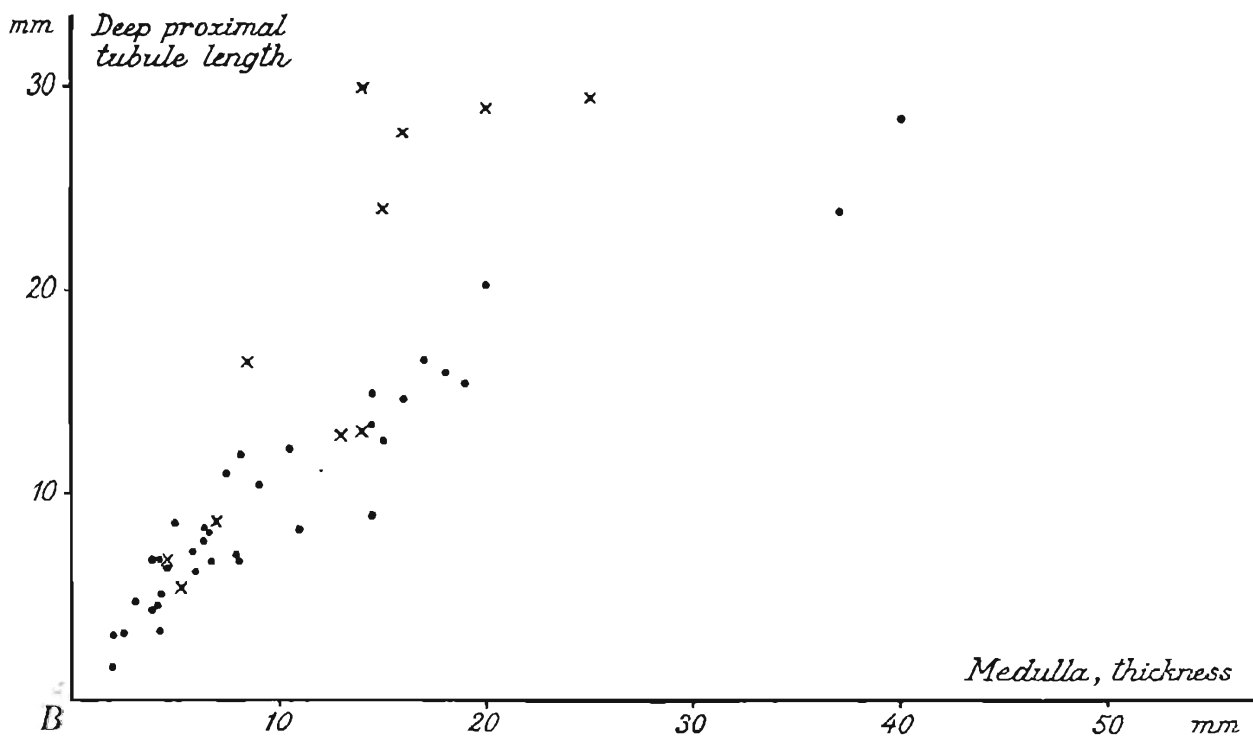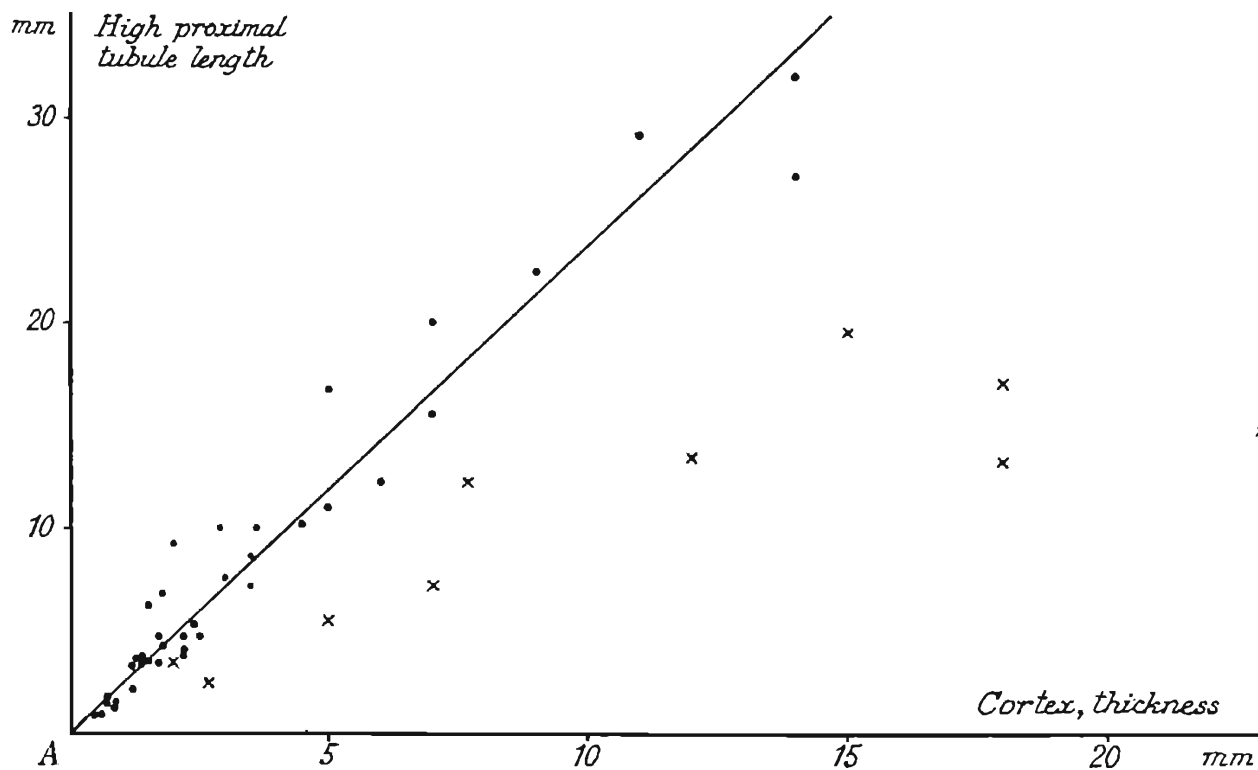
Fig. 24. Graphs showing the relation between proximal tubule length and thickness of the cortex and the medulla. In *A* the straight line through the origin represents the equation: Proximal tubule length = 2.4 × cortical thickness. The crosses represent in *A* kidneys with cortical nephrons, in *B* kidneys without or with few long loops.

These relations are shown in fig. 24 *A* and *B*. In fig. 24 *A* the mean lengths of the high proximal tubules in the examined forms are plotted against the thickness of the cortex. These quantities are directly pro-

portional in most species, but those species that have cortical nephrons diverge distinctly from the others. They also show a much greater variation. On an average the high proximal tubules are about 2.4 times as long as the cortex is thick, when there are no cortical nephrons.

In fig. 24 *B* the longest deep proximal tubule measured in each kidney is plotted against the thickness of the medulla. Here too, there seems to exist a linear relation between these quantities, except in kidneys where there are no long loops. The correlation between these quantities is, however, not so close, though this is probably due to random variation. It is, of course, difficult to find the longest tubules among the highly variable deep proximal tubules. Sometimes one of the longest has been found, but often this has not been the case. That the kidneys without long loops often have relatively long deep proximal tubules indicates that the proximal tubules in these cases constitute a greater part of the nephron length than in kidneys where the deepest nephrons have long loops. This is confirmed by the calculation of the composition of the deepest nephron in *Sus* (p. 351).

The thin segment. There is relatively little material available to show the mode of length variation in the thin segment. It is, however, clear that normally there is a distinct difference between nephrons with short and with long loops. In nearly all specimens where numerous nephrons have been measured the thin segment in short loops shows slight variation (shrews, small rodents). In long loops, on the other hand, the variation in length of the thin segment is great. There seems normally, or at least often, to be a distinct gap between the length distribution of short and of long loops. In kidneys containing cortical nephrons these relations are altered. The thin segment of the high nephrons is much more variable in length, and as there are often few or no long loops the distribution will be more continuous.

The thick segment seems in respect of its length distribution in the kidney to show two different conditions. In some cases the thick segments of the deep nephrons are about as long as or longer than those of the high nephrons (e. g. shrews). In other cases the thick segments are decidedly shorter in the deep nephrons. The former condition seems to be the rule in kidneys where the deep proximal tubules are much longer than the high. The latter condition, on the other hand, occurs where the deep proximal tubules are shorter or only slightly longer than the high ones. In both cases the ratio of the lengths of proximal tubule and thick segment rises the deeper a nephron is. The rising of this ratio seems to run parallel with the rising of the relative length of the thin segment. It seems reasonable to suppose that this is not accidental. It may be that the thick segment becomes shortened proportional to the

proximal tubule, because the thin segment is relatively lengthened. This view is supported by the fact that in kidneys devoid of long loops the thick segments of the deep nephrons are relatively long. The problem is, however, complicated by the fact that the thick segments of the high nephrons are not strictly comparable with those of the deep nephrons. The latter ones are entirely or almost entirely formed by the thicker part, whereas the high thick segments are formed by the thinner part also. In addition it must be mentioned that the cortical nephrons have relatively short, and often very short, thick segments, though they have no or very short thin segments.

The distal tubules seem on the whole to vary parallel with the proximal tubules, but their variability is often small. The difficulties in deciding where the distal tubules end are so great that it does not seem possible to say anything definite about them.

The diameter of the nephron segments.

The proximal tubule. In a kidney the longer proximal tubules are usually thicker than the shorter ones. This is evident from the tables of those species which show distinct length variations in the proximal tubules (e. g. bats, *Mus flavicollis* and *sylvaticus*, *Lutreola*, *Elephas*, *Alces*). Sometimes it is not possible to trace such a tendency, and sometimes the opposite condition is indicated, but this indication is so slight that it is impossible to show that it is not due to random variation. From the measurements it is also clear that the diameter of the proximal tubules is usually higher in kidneys with long tubules than in those with short. Thus it would seem that, generally, the diameter of the proximal tubules rises with their length. The diagram fig. 25 shows to what degree this is true. It is based on all measured proximal tubules from mature or nearly mature specimens. This material consists of two groups, those which have been examined fresh, and those which have been available only after preservation in alcohol. The former group has been treated as follows. In each kidney the proximal tubules have been classified according to their length after correction for swelling or shrinkage. The class interval is, for the shortest tubules, 0.5 mm (up to 4 mm tubule length), then 1 mm (up to 13 mm tubule length), and for the longest tubules the class interval is 2 mm. The mean diameter of the tubules of each class is calculated. When more than one specimen of a species have been investigated, the average of the means of the individuals is taken for each class. Each such class mean is represented by a cross. When alcohol material only has been available, the procedure has been the same, with the exception that a correction for shrinkage during

μ Proximal tubule diameter
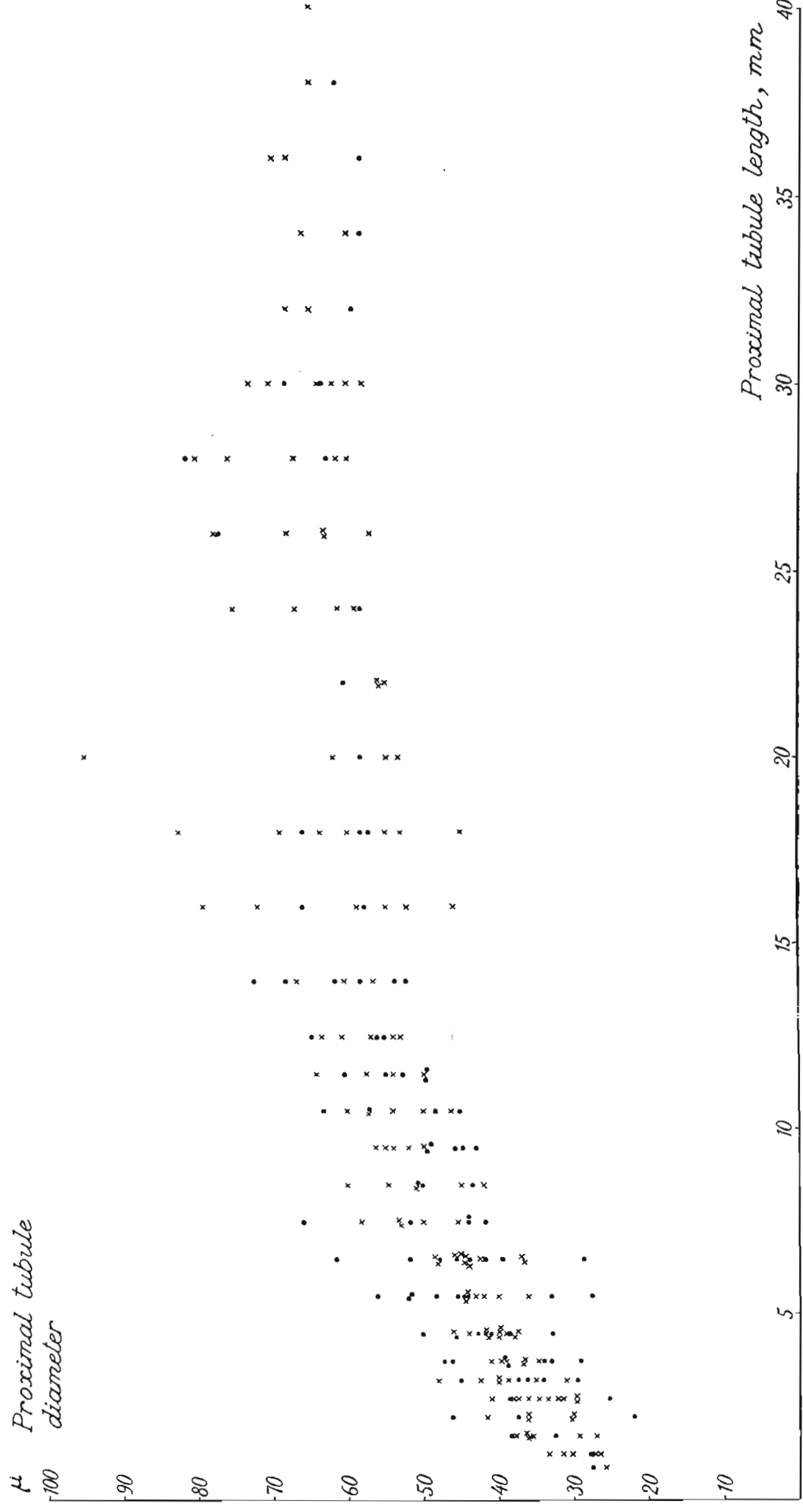
Proximal tubule length, mm

Fig. 25. Explanation see p. 379.

fixation has been introduced. Both the lengths and the diameters of the proximal tubules have, after correction for the shrinkage through maceration, been multiplied by 1.1. Then the procedure has been entirely the same as for the other tubules. The class means of each species have been represented by dots. It is evident that there is no great difference in distribution between the crosses and the dots. In fig. 26 *A* the classes have been put together, so that the class intervals are twice the original (except the end classes, which consist of three classes each) and the means of both crosses and dots together have been calculated. From fig. 25, and perhaps more clearly from fig. 26 *A*, it is evident that the diameter of the proximal tubules rises on an average fairly rapidly with the tubule length in short tubules. When tubules are longer than about 15 mm the rise in diameter is very slight when the tubule length is increased.

The relation between the outer diameter of the tubules in maceration specimens and the inner diameter of the tubules in the living animal is not known. It seems, however, almost certain that, in one kidney, tubules showing a large diameter after maceration must on an average have had a larger inner diameter in life than tubules showing a smaller diameter after maceration. The thickness of the tubule epithelium probably changes very little from one nephron to another. When kidneys from different species are compared it also seems that, on an average, the tubules which are thicker after maceration have in life had wider lumina. From this it seems reasonable to conclude that the lumen diameter of the mammalian proximal tubule rises relatively rapidly with rising tubule length in short tubules, but is only slightly altered in long tubules. That the diameter rises with the tubule length seems relatively understandable (cf. p. 408; the rise in intracapsular pressure caused by the increase in length is compensated by the rise in diameter). The limit for this rise is not so easily explained, but it seems probable that there is some connection with diffusion processes, and that, after a certain limit has been reached, the tubule becomes less effective as the lumen becomes wider.

PETER (1909, p. 299) thought the tubule thickness to be independent of tubule length. His relatively limited material did not allow of another conclusion. CONWAY (1937) finds this opinion probable on *a priori* grounds. He finds, however, from PETER's data a slight rise in diameter with rising body weight. This relation seems to be only a consequential one. In types where the tubule length is small and the body weight high the tubule diameter follows the tubule length (e. g. seals, whales).

In some species the tubule diameter is especially high in proportion to the length (bats, old cats, some pigs). This is probably due more to uncommonly thick epithelium than to great lumen width. In cats the epithelium often contains masses of "fat". In "Cat, male, kidney weight
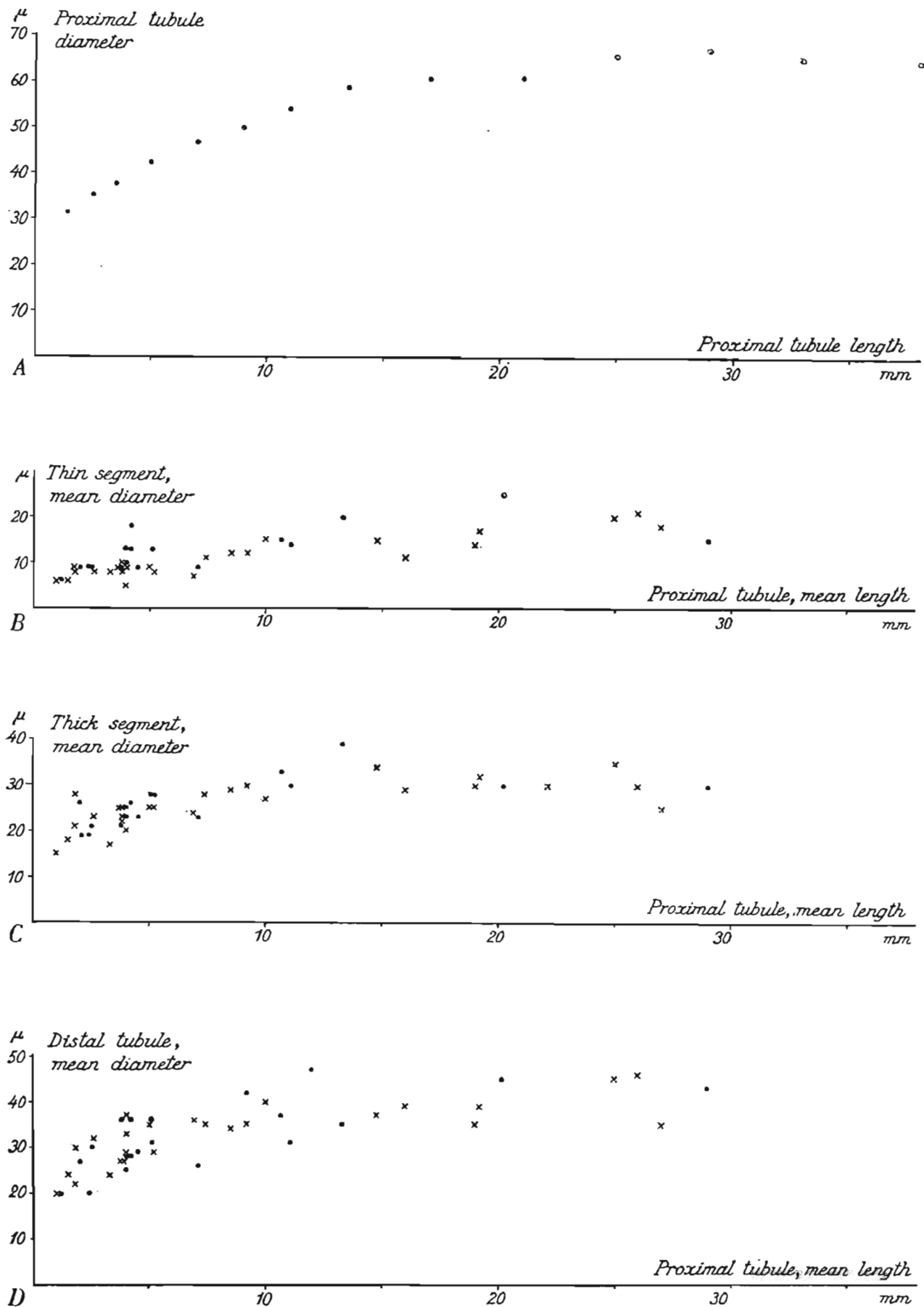
Fig. 26. Explanation see pp. 381—383.

17 gm'', which had very thick proximal tubules, sections showed much higher epithelium than in a younger cat with normal tubule diameter. The latter showed about the same epithelium thickness as a rabbit

similarly treated. In *Pipistrellus* and the pig with great tubule diameter there was also a notable number of "fat" drops in the epithelium of the proximal tubules.

The thin segment. The proximal tubules show rising diameter with increasing length, also within one kidney. This is not the case with the other segments of the nephron. The thin segment is sometimes thicker in long loops than in short (*Psammomys*), but as a rule this difference is small, especially when regard is taken to the often very great increase in length. There is, on the other hand, a distinct increase in diameter when kidneys with long nephrons are compared with those with short. To show this the mean thickness of the thin segment in each kidney has been plotted against the mean length of the proximal tubule (fig. 26 *B*). Of course it would have been better if the mean length of the thin segment could have been used. The value of this is, however, usually unknown, and is relatively closely correlated with the mean of the proximal tubule. It is clear that the diameter of the thin segment increases distinctly with increasing nephron length, and probably more rapidly and continuously than the proximal tubule.

The thick segment. The same procedure has been used to get the diagram fig. 26 *C*. The diameter of the thick segment also rises distinctly with increasing mean proximal tubule length, and this in face of the fact that within one kidney the length of a thick segment is often inversely proportionate to the thickness. This is certain, at least in those kidneys where the thick segments of the deep nephrons are shorter than those of the high ones.

The distal tubule. This segment shows similar conditions to the thick segment, as far as different kidneys are compared (fig. 26 *D*).

With regard to the thick segment and the distal tubule it would have been possible to use the mean lengths of these segments instead of the mean length of the proximal tubule. The picture is then essentially the same.

The quantitative composition of the nephron.

The relation of the lengths of the segments.

The relative length of the different segments usually varies considerably from nephron to nephron in a kidney. This makes it difficult to obtain reliable figures for the mean composition of the nephrons, which represents the composition of the kidney with respect to the different segments. Only in a few cases has it been possible to calculate such figures. When this has not been possible there are, however, usually other data which permit a comparison between different forms. Usually

high and deep nephrons deviate in the same manner. This is evident
when the figures for the composition of high and very deep nephrons
are compared. Those kidneys where the thin segment is relatively
short in the high nephrons also show this to be the case in the
deep ones. This is also seen from the common occurrence of cortical
nephrons in kidneys without long loops (cf. p. 374). That the thick
segment in high and deep nephrons varies parallel is almost inevitable,
as its length in both types is dependent on the thickness of the
outer zone. Thus the composition of the kidney may, in a comparative
sense, be judged by the composition of the high, deep or mean nephron,
the occurrence and number of cortical nephrons and the relative pro-
portion of long and short loops. Though the mean nephron is the best
measure to use for comparisons the high nephron may well be taken
when sufficient data for calculating the former are lacking. In each case
the indications of the other data may be used in addition.

The examined forms may be divided into herbivores and carnivores
(including the insectivores). *Arctitis, Ursus* and *Chiromys* are excluded,
as the two former may be considered intermediate in this respect, and
the diet of the latter seems not to be sufficiently known. There are data
as to the composition of the high nephron in 17 species of the carnivore-
insectivore group, and in 19 species of the herbivores (table 48, p. 419). The
proximal tubule constitutes 39.9 ± 0.82 % of the nephron length in the
former group, and 53.4 ± 2.18 % in the latter. Thus, the proximal tubules
are relatively shorter in the carnivores than in the herbivores, and the
difference is significant. The much greater variability in the herbivores
is mainly due to the fact that some desert rodents (*Perodipus, Dipodomys*
and *Jaculus*) have very short proximal tubules. The three more distal
segments taken together are, of course, relatively longer in the carnivores
than in the herbivores. This seems to be the case with the thin and
the thick segment regarded separately, as well as with the distal tubule.
The available material is scarcely large enough to allow of any estima-
tion as to which is relatively longest in the carnivores.

The data as to the mean tubule composition are few, but they show
that the two groups are as distinctly different in this respect as with
regard to the high nephrons. The proximal tubule constitutes 37.6 ± 1.56 %
of the mean nephron length in 7 carnivores and insectivores, and
52.9 ± 3.39 % in as many herbivores. The difference is 15.3 ± 3.71 % and
is significant despite the small number of data.

The long loops seem on the whole to be more numerous in the carni-
vores. This indicates that the thin segment is shorter in the herbivores,
and this is emphasized by the common occurrence of cortical nephrons
among them.

In all respects *Ursus* and *Arctitis* resemble the herbivores, at least more than typical carnivores. *Chiromys* seems more like the insectivores.

The desert rodents, on the other hand, deviate markedly from the majority of the herbivores in most respects.

In the carnivore group the *Insectivora* seem to deviate by having relatively short thin segments. This is shown both in the high nephrons, the mean nephrons and the number of long loops. The *Microchiroptera* seem to be characterised by very short proximal tubules. The material is, however, so small that any attempt to subdivide the carnivore group must be very uncertain.

It may be mentioned that the two small insectivorous marsupials, which are not included in the above discussion, resemble the monodelphian insectivores closely.

The localisation of water reabsorption in the nephron.

In the above it is shown that the composition of the nephrons is different in herbivores and carnivores. As there is a general difference in the composition of the urine between these groups this indicates a parallelism between the quantitative composition of the nephrons and their function. It is, then, possible that a comparison between the composition of the urine and the nephrons may help to localise the processes in the nephrons.

This problem has been solved, in the *Amphibia*, at least in its essentials, by direct methods (cf. RICHARDS 1938). In the mammals some of the most important problems concerning the function of the proximal tubule have been solved by WALKER, BOTT, OLIVER and MACDOWELL (1941), also by direct methods. (Since the terminal segment may possess other functions than the preceding part of the proximal tubule, which is the part investigated, the assumption that their results are valid for the whole proximal tubule does not seem warranted.) These authors have also attempted to analyse fluid from the distal tubule, but they do not consider the available material sufficient for any conclusions. The other segments of the nephron do not seem accessible to their technique.

Several authors have attempted to make clear the functions of the different parts of the nephron in the mammal by studying the excretion and distribution within the nephrons of dyes (e. g. HEIDENHAIN 1874, BENSLEY & STEEN 1928, HOLTON & BENSLEY 1931, EDWARDS 1933, GERSH 1934, 1936, GERSH & STIEGLITZ 1934, KEMPTON, BOTT & RICHARDS 1937, ELLINGER 1940) or substances normally excreted (e. g. GLIMSTEDT 1942). The results of these investigations seem often very difficult to interpret, and are often conflicting.

In some cases a comparison between structure and function of the kidney in different forms has been used to localise the processes in the nephrons. A survey of this method and its results has been given by MARSHALL (1934, 1935).

PÜTTER (1911, 1926) has attempted to build an entire theory of kidney function on a comparison between the volume and composition of the urine, and the nephron composition. To that end he has evaluated PETER's measurements quantitatively. His methods and results show the danger of such a proceeding when the material is inadequate (cf. p. 390). PÜTTER's hypothesis has received little attention (cf., however, v. MÖLLENDORFF 1930).

Another theory, based on a comparison between physiological and anatomical facts, seems to have been generally accepted. This theory has been most fully formulated by BURGESS, HARVEY and MARSHALL (1933) and MARSHALL (1934) (cf. STARLING & VERNEY 1925, CRANE 1927, KORR 1939). It maintains that the hypertonicity of the urine as compared with blood arises in the thin segment, the latter reabsorbing water under the action of pituitrin.

The main facts supporting this theory are the following:

1. The thin segment is typically developed in mammals and birds only.
2. The water reabsorption is increased by pituitrin in mammals and birds.
3. The urine may be hypertonic only in mammals and birds.

The basis for this theory is not very broad. Point 1 may be considered established, though it is not impossible that there are some reptiles not yet examined, which have thin segments. Points 2 and 3 are based on the examination of a few forms, and these forms do not seem significant in this respect. That such a freshwater form as *Alligator* does not respond to pituitrin with increased water reabsorption is no proof of the general inability of reptiles to do so. There is, of course, no need for freshwater animals to develop or retain a mechanism for conserving water. It is possible that the reptiles are able to conserve enough water without forming hypertonic urine, even when living in arid habitats or in the sea. As long as such forms have not been thoroughly examined it cannot, however, confidently be said that the reptiles lack this capacity.

In the bird kidney most nephrons have no thin segment, and many of the thin segments existing are very short (LINDGREN 1868, HUBER 1917, FELDOTTO 1929, my own investigations, unpublished). If, under the influence of pituitary extract, water is reabsorbed in the bird kidney by the thin segment only, most of the nephrons either do not function in this case or they form hypotonic urine.

According to GIBBS (1929 a, p. 59) the uric acid may amount to 17.5 % of the weight of the ureter urine in the fowl. The urine is then "sticky, solid" (GIBBS 1929 b, p. 598). It seems impossible that this urine, formed under the influence of pituitrin, could be a mixture of a little concentrated portion from the nephrons without thin segment and a more concentrated portion from the nephrons with it. The latter portion would then be so concentrated as to be entirely solid. Under the action of pituitrin the output of uric acid is considerably increased, which makes it very improbable that only a part of the nephrons is functioning.

Nor when the bird kidney forms a watery, but osmotically concentrated urine (KORR 1939) does it seem probable that only the nephrons with thin segment are at work. If all nephrons are functioning this would mean, according to the above theory, that some of the nephrons produce a highly concentrated fluid, which is then very much diluted by the admixture of dilute urine from the majority of the nephrons. This does not seem probable.

It must, then, be concluded that it is not probable that the water reabsorption in the bird kidney, influenced by pituitrin and leading to hypertonicity of the urine, takes place in the thin segment only.

It is somewhat doubtful if this conclusion has any bearing on the same problem in the mammals. The thin segment is undoubtedly homologous in birds and mammals, but this does not necessarily mean that the function is identical in both groups. As the structure is very similar it seems, however, most likely that the function is so, too. It may then be inferred that the thin segment of the mammalian nephron is probably not the place where the hypertonicity of the urine arises.

PETER (1909, p. 335 et seq.) states that the thin segment is better developed in mammals with concentrated urine, and infers that the thin segment is the portion of the nephron which concentrates the urine. PETER's material seems to be too small to allow of any definite conclusions in this respect. Nor has he attempted to discover if any other segments show similar conditions.

It seems possible that the material now available can be used to examine the problem with greater prospects of reaching well-founded conclusions. A great difficulty is, however, the scarcity of comparative physiological data, even with respect to the osmotic concentration of the urine. Thus, it is necessary mainly to rely on conclusions drawn from the mode of life of the forms in question.

It is well known that the urine of carnivores and herbivores is very dissimilar in many respects. In the former the urine is usually more concentrated and acid, and there are many other differences too (cf., e. g., CHAUSSIN 1920, NOLL 1924, FUSE 1925, PINCUSSEN 1925, 1934). Thus, it

is difficult to draw any conclusions as to the localisation of distinct processes from a comparison between herbivores and carnivores with respect to urine and nephron composition.

The problem seems somewhat simpler if more similar forms are compared. It is shown by HOWELL and GERSH (1935) that *Dipodomys* has very concentrated urine. This is certainly also the case with the other desert rodents examined, *Perodipus*, *Jaculus*, *Psammomys* (table 48). The ratio of the mean lengths of the proximal tubule and the thick segment is in these four forms 1.18 ± 0.106. Some other small rodents, which seem comparable to the above except in not being desert forms, have been examined, namely *Sciurus*, *Epimys rattus*, *Mus musculus*, *flavicollis* and *sylvaticus* and *Microtus agrestis*. The ratio of proximal tubule and thick segment in this group is 2.00 ± 0.051. The difference is 0.82 ± 0.118 and is significant despite the low number of data. It is not possible to make a similar comparison for the mean length of the thin segment, as there are no figures for it in *Psammomys*. There can, however, be little doubt that the thin segment is also relatively longer in the desert rodents than in the normal small rodents.

There are no detailed investigations concerning the excretion in the desert rodents, and there is also no complete knowledge of it as regards the other small rodents. It is thus impossible to say quite definitely that the concentration is the only difference between the urine of these forms, though it seems probable that it is the most important one.

The camel, which excretes a concentrated urine, apparently has longer thick and thin segments than the cow.

Little is known about the urine of the shrews and the bats. It seems reasonable to assume that they are similar, except that the bats should be expected to excrete a more concentrated urine, as they certainly lose relatively great quantities of water during flight (cf. EISENTRAUT 1937, p. 66). Both the thin and the thick segment seem to be longer in the bats.

Pachyura, which lives in drier habitats than the other shrews examined, shows relatively longer thin and thick segments than they do.

The carnivores seem to have, on the whole, more concentrated urine than most herbivores. The thin and the thick segment are relatively longer in the carnivores.

In the seal the osmotic concentration has been found not to exceed that occurring in terrestrial carnivores (PORTIER 1910, IRVING, FISHER & MACINTOSH 1935, SMITH 1936). This is certainly also the case in those whales that feed on vertebrates. The urine has been examined in dead whales, and the freezing-point depression has been stated to be moderate (SCHMIDT-NIELSEN & HOLMSEN 1921, MORIMURA 1925, SUZUKI

1925). It would seem, however, that the forms feeding on invertebrates are constantly forced to excrete large quantities of osmotically concentrated urine, as their food contains much osmotically active substance, and is probably mixed with sea water. In *Balaenoptera* the thick segment is unusually long, but the thin segment seems to be rather shorter than in most carnivores.

From the above it seems that the thick and the thin segment are normally longer in animals excreting a concentrated urine than in other forms. This indicates that both segments are connected with water reabsorption. The relative shortness of the thin segment in *Balaenoptera* suggests that the thick segment is more essential in this respect than the thin segment. (*Hystrix*, which lives in relatively arid habitats, has short thin segments, as shown by the absence of long loops, which may also indicate this. As there are no investigations of the urine of *Hystrix*, and its habits do not seem sufficiently known, this case may be considered doubtful.)

It is clear that if both the thin and the thick segment participate in water reabsorption, the thin segment cannot be the main place where the hypertonicity of the urine occurs. It seems more reasonable to assume that water, and perhaps also solutes, are reabsorbed from the fluid in the thin segment not against, but along with the concentration gradient. The structure of the thin segment seems well suited to a more passive exchange of this kind through its walls. The reabsorption against the concentration gradient would then occur in the thick segment. It must, however, be remembered that the data presented here do not exclude the possibility of the distal tubule sharing the reabsorptive capacity with the thick segment. On the contrary, this may well be the case, and it does not seem impossible that at least some part of the collecting tubules is similarly active[1].

The carnivores, and doubtless the insectivores also, excrete an acid urine in contrast to the herbivores. This may be connected with the fact that these groups have longer distal tubules than the latter (cf. ELLINGER 1940). It is, however, doubtful if this difference between carnivores and herbivores is in reality so marked as it might seem, as the distal boundary of the distal tubule is almost always difficult to distinguish, and possibly the last segment of the distal tubule sometimes forms a part of the arcade. The distal tubule is usually thicker in the herbivores, also.

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[1] This view is consonant with most of the investigations on the excretion of dyes.

The surface area and the volume of the nephrons.

The surface area and the volume of the glomeruli have been estimated by several authors (e. g. Saéki 1926, Vimtrup 1928, Rytand 1938).

The measurements of Peter (1909) and Inouye (1909) have formed the basis for some attempts to calculate the surface area of the different segments of the nephron and the total surface area of the nephrons (Pütter 1911, 1926). The investigations of Peter and his co-workers aimed primarily at a thorough knowledge of the qualitative structure of the kidney. This is no doubt the reason why only a relatively small number of measurements have been made by them. These measurements are not a sufficient basis for such a detailed quantitative analysis as that attempted by Pütter. Peter's material has often shrunk considerably, as he sometimes mentions. As an example of the very serious errors introduced when the shrinkage is not taken into account, the following case may be mentioned. Pütter (1926, p. 95) gives the kidney weight of the rabbit as 13 gm and the number of the nephrons as 285 000 (op. cit. p. 91). The average nephron he calculates from the data given by Peter has a volume of almost 0.01 cmm. The joint volume of all nephrons is then not over 3 ccm. As the nephrons form at least $^3/_4$ of the volume of the kidneys (cf. Glimstedt 1942) this value is less than a third of what it ought to be. The main reason is undoubtedly that Peter's material has shrunk. If the calculation is otherwise correct (i. e. the nephron number the same in the rabbit kidneys used by Peter and Pütter), which is possible, but not certain, the surface area calculated by Pütter is about half the correct value. When figures with such doubtful value are used as absolute and are then correlated with equally uncertain physiological data, such a procedure can only discredit quantitative anatomy.

As I have not measured the nephron number, my measurements of the nephrons are not suited to calculations of the absolute total surface and volume of the nephrons. I have, however, in table 49, p. 422, given the relative surface and volume of the segments of the average nephron in some species, where fairly reliable estimates of the dimensions of the average nephron have been obtained. In these cases the average nephron number of the species has also been given, when reliable data exist. The product of this number and the nephron volume should approach the kidney volume. The agreement is fairly good. When calculating the percentage of the segments the capsule has been excluded, as its relative size varies greatly and to some extent obscures the regularity of the nephron composition in other respects. Among the other nephron components the thin segment and the distal tubule show the largest varia-

tion. This is undoubtedly to some extent due to errors of estimation, as these parts are more difficult to examine quantitatively than the others. The thin segment is, however, undoubtedly very variable, as is shown by its varying relative length in the high and mean nephrons (table 48). Table 49 brings out distinctly how small a part of the total nephron surface and volume is formed by the thin segment. Even in *Dipodomys*, where it is uncommonly developed, it does not seem to form more than 5—6 % of the nephron volume. This is still more striking when regard is taken to the fact that, of this volume, the epithelium forms only a small part, certainly less than 20 %. As, in the other segments of the nephron, the epithelium forms the greater part of the volume, the epithelium of the thin segment probably constitutes less than 1 % of the epithelium volume of the kidney in most cases, and very often, in herbivores, less than 0.5 %.

The surface index. v. MÖLLENDORFF (1922, 1930) has examined the relation between the surfaces of the proximal tubule and the glomerulus. This relation, the "Nierenindex", is obtained by multiplying the capsule surface by 3 (or, in the mouse, by 1.3) to obtain the glomerular surface, and dividing the surface of the proximal tubule by the product. Apart from the factor 1/3 this index is the same as that given by me in the tables under the heading "Ind.". One of the difficulties of this line of thought is evident at once. The purpose is to give a ratio of the reabsorbing and the filtering surfaces of the kidney. According to v. MÖLLENDORFF the glomerular surface should then be proportional to the capsule surface in the mammals (except in the mouse). According to the conceptions on which VIMTRUP (1928) has founded his estimations of the glomerular surface, this surface is proportional to the volume of the capsule (when the diameter of the blood-capillaries is constant). This is also in accordance with NASH (1931). Still another difficulty (emphasized by v. MÖLLENDORFF 1922) is that the *inner* surface of the nephron and not the *outer* must be considered as the reabsorbing surface. These surfaces are undoubtedly not strictly proportional (cf. p. 381).

It would thus seem that the following ratios might be regarded as estimates of the ratio of the reabsorbing (or secreting) and filtering surfaces, as well as v. MÖLLENDORFF's index: 1. The ratio of the surface of the proximal tubule and the volume of the capsule. 2. The ratio of the volumes of the proximal tubule and the capsule. 3. The ratio of the length of the proximal tubule and the surface of the capsule. 4. The ratio of the length of the proximal tubule and the volume of the capsule.

The relative size of the capsule is very varying, also within the species -and even within the kidney. The capsule is certainly larger when the glomerulus is distended with blood than when it is empty. It seems very

probable that the capsule reacts differently and probably within wider
limits than the other parts of the nephron when the material is swelling
or shrinking. During dissection and measuring the capsule is more liable
to deformation than other parts (cf. p. 261). All these factors make the
data on the size of the capsule far less trustworthy than those on the
other parts of the nephron. This explains, at least in part, the sometimes
extreme differences within the species between the indices of different
specimens (e. g. *Microtus*, p. 301, 302) and the great variability normally
occurring within each kidney. This fact diminishes the importance of
this index. It is, however, fairly constant when the indices of mammals
of different size and habit are compared (table 48, p. 419). This might
indicate a special significance for it. I have calculated the ratios 1—3[1]
for each species also, and the ratios 2 and 3 are constant in the same
sense and to the same extent as the index. The ratio of the surface of
the proximal tubule and the volume of the capsule seems to diminish
with increasing tubule length, but apart from this the variability is not
greater than in the index. Thus, a comparative review of the index in
the mammals gives us no reason to suppose that it is an especially
important "constant" for the kidney.

v. MÖLLENDORFF has tried to show that the index is constant within
the kidney (apart from random variation). This is sometimes true, but
in other cases the index is higher in high nephrons than in deep (e. g.
Mus flavicollis, "young male", table 22 c, p. 309). The contrary seems to
be true in some cases (*Sminthopsis murina*, p. 267, *Pachyura etrusca*, p.
280, *Pipistrellus nilssoni*, p. 284). Though I have not made any detailed
investigation in this respect, it does not seem that the ratios 1—4, given
above, show definitely less constancy within the kidney, than the index.

v. MÖLLENDORFF assumes that the index is low in aquatic mammals,
and ought to be high in desert forms. This seems not to be the case.
The index is not higher in the desert rodents than in normal forms, and
there is no significant difference in this respect between the aquatic
forms and terrestrial mammals. As far as the values indicate anything,
it might seem that the ratio of the surfaces of the proximal tubule ·
the capsule is not correlated with the concentration of the urine. 1
would seem to mean that the reabsorption in the proximal tubule is
correlated with the final concentration of the urine. Such a conclus.
is, of course, very uncertain.

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[1] The ratio 2, the "volume index", has been calculated from the means of t
tables by dividing the product of the square of the diameter and the length of t
proximal tubule by the cube of the diameter of the capsule. The figure thus obtain
is multiplied by 1.5. An equivalent of the ratio 1 has been obtained by dividing tl
"volume index", and of the ratio 3 by dividing the "index" by the diameter of tl
proximal tubule.

Age changes in the kidney.

In the present investigation no consistent examination has been made of the differences in kidney structure due to age differences. In some species small young have been examined in addition to mature specimens of different ages. In other cases the age of single specimens has been known or estimated. This material allows some notes on this subject.

The kidney form sometimes shows modifications in this respect. In the cat the newborn young can hardly be said to have a prominent papilla. The papilla then becomes more prominent, but in the oldest specimen a reduction of the prominence has probably taken place (fig. 11, p. 319; cf. also MARSCHNER 1937, p. 376). Such a process is probably at work in other *Felidae* also (*Lynx*, lion). The cause of this is that, in the young, the medulla grows, which makes the papilla project. Later the increase in depth of the medulla stops, but the cortex, and to some degree the outer zone, increase in volume. This increase is not a simple enlargening of the outermost parts; growth takes place in the inner parts also, and apparently in all directions. Thus, the cortex expands parallel to the surface also, the base of the medulla is obliged to follow this expansion and the papilla is partly drawn in.

The continued growth of the cortex and outer zone, and the cessation of increase in depth of the inner zone, seem to be a common phenomenon. It is evident in the rabbit and *Mus flavicollis*, and the data as to the cow and Man (TOLDT 1874, PETER 1927 c) indicate its presence. The macroscopic modifications are, however, small in most mature mammalian specimens. That the cat shows so distinct modifications seems to be due to the fact that the cat kidney is enlarged in old males (cf. HALL & MACGREGOR 1937).

As there is no formation of new nephrons after the earliest postembryonic stages, the growth of the kidney depends on the growth of the tubules. These increase in length as well as in thickness (rabbit table 13, pp. 290—292, *Mus flavicollis* table 22, pp. 308—311, cat table pp. 321—324, cow table 44, p. 358). If there is no increase in the diameter of the tubules the length of the nephrons will be directly proportional to the kidney weight, provided there is no material change in their composition. If the growth is equal in all dimensions of the nephrons, the increase in length will be proportional to the cube root of the kidney weight. It seems probable that in reality the increase in nephron length will lie between these extremes, but there is not enough material available to show exactly the conditions in any species.

The proportions of the nephron are not constant during growth. The proximal tubule constitutes about 30 % of the nephron length in the

12-day-old kitten, some 30—35 % in the young female cat and about 45—50 % in the old male (pp. 320—321). Quite similar conditions are found in the rabbit (p. 292) and the cow (p. 358). In all of them the proximal tubule is relatively short in the very young specimens. Except in the cat it does not seem that the composition of the nephron is distinctly modified with age in mature specimens (rabbit, *Mus flavicollis*), except that the thin segment probably does not increase as fast as the other segments, as the inner zone is relatively little increased.

In the kitten there are a great number of short loops, but in the older specimens there are none, or very few. Similar circumstances must exist in all forms with long loops, as in an embryonic stage there are generally only short loops. The development of short loops into long takes place at an early stage in post-embryonic life, as there is a relatively constant ratio of short and long loops also when young specimens are included, in rabbit, *Mus flavicollis*, cat, and cow.

The segments of the nephrons become more tortuous in old specimens, probably as a consequence of growth. This is especially the case with the proximal tubule, in which the pars recta also may become very tortuous (rabbit, Pl. 1, fig. *4*; white rat, Pl. 1, fig. *5*). The distal tubule seems often to be more irregular, and its surface has more marked projections in old specimens.

It may be mentioned that the old kidneys often contain much very tough connective tissue, which together with the greater length and more tortuous course of the tubules makes it very difficult to obtain satisfactory preparations from them.

The form of the mammalian kidney.

Survey of the literature.

The problems concerning the form of the kidney, especially the relation between the simple kidney and the renculi kidney, have been discussed by many writers.

HUNTER (1787) correlated the renculi kidney with water-life. This notion has later been discussed and accepted by CUVIER (1840) and DAUDT (1898). As GERHARDT (1911) points out this correlation is not so close as was assumed by earlier writers. He also shows that there is no connection with hibernation, as had been assumed by CUVIER. Many aquatic animals have smooth kidneys (*Castor, Fiber, Lutreola, Halicore*), and many terrestrial forms have lobated kidneys (*Elephas, Ursus, Bos*). This problem has also been discussed by ANTHONY (esp. 1919), who assumes that the renculi kidney is dependent on two factors: 1. Such

factors that intensify urine formation (life in cold climate, water-life, absence of sweat glands), 2. Body volume. The larger an animal is and the more active the factors mentioned under 1. are, the larger its kidney surface will tend to be. This hypothesis pays no regard to features of kidney structure other than the surface, and the theory behind it is erroneous. ANTHONY (and before him DAUDT 1898) assumes that the surface augmentation is called for by increased urine volume. Indeed, he says that the secreting surface must be increased. The kidney surface has, however, no demonstrable relation to the secreting surface of the kidney. As no other types than the renculi kidney are considered there are also numerous exceptions to the rule given by ANTHONY. Anyhow, his theory marks an advance, as it takes into consideration the important factor of body size.

PETER (1909), HOLLATZ (1922) and v. MÖLLENDORFF (1930) assume that the relation between the volumes of the cortex and the medulla is the deciding factor with respect to kidney structure. The larger the cortex is in proportion to the medulla the more the kidney ought to be divided into lobes. From the investigations of DENZER (1935) it is evident that this is not the case.

ZARNIK (1910), gives another view on this problem. He assumes that there is an upper limit for the length of the nephrons (op. cit. p. 145). The nephrons must be distributed within the kidney in such a manner that, in large kidneys too, this upper limit is not exceeded. This may be accomplished by the dividing of the renal substance into renculi in large kidneys, or by the elongation of the kidney in those with tubi maximi. Thus, his theory in the first place attempts to explain the derived kidney forms in large animals, but he points to the probability that this upper limit for the nephron length may be different in different circumstances.

The opinion of ZARNIK has, to my knowledge, been cited only by FREUND (1912). In his paper of 1939, however, he does not mention it. Other authors seem not to have regarded it at all. The reasons for this are probably the following. The formulation of ZARNIK's theory is very short, and there are no reasons given as to why there should be such a limit. Neither are there any investigations to show that there is any real connection between kidney type and nephron length. Another obstacle to its wider recognition is probably that it is printed as a small part of a chapter on "Beziehungen der Echidnaniere zu der Niere der höheren Säugetiere". I myself did not find the passage before my opinions in this respect had already been worked out.

On the whole it may be said that, hitherto, none of the opinions advanced as to the relation of the kidney types to environmental or

other factors has been generally accepted. Most of them have only considered the difference between simple and lobated kidneys. This uncertainty as to the factors at work is also expressed by the latest handbooks (v. MÖLLENDORFF 1930, p. 262, VAN DEN BROEK 1938, p. 831, FREUND 1939, p. 89).

The problem of the relation between mode of life and kidney form has thus been discussed very early on, and it has later usually held a central place in the interest of kidney investigators.

This is perhaps the reason why most authors have been relatively little interested in the question as to which kidney type is primitive in the mammals. It is seldom that clear opinions on this subject are found. This is quite natural for the pre-Darwinian writers, but is somewhat remarkable in later authors.

The simple kidney has been considered primitive by GEGENBAUR (1901) and GERHARDT (1911, 1914). None of them says this in so many words, but it is evident from their arrangement of the kidney types. A certain obscurity is, however, caused by their erroneous conception as regards the kidney of the *Monotremata* (cf. p. 265), which GEGENBAUR considers to show sauropsidan features (op. cit. p. 467).

ZARNIK (1910) is led to think that the simple kidney is primitive by his study of the *Echidna* kidney.

The contrary view seems to be held by FREUND (1912), as he speaks of "verschmolzene Nieren", but he does not state this direct. In 1939 he only gives the two opposing theories without defining his own point of view.

MIJSBERG (1923) considers the human kidney primitive as compared with the simple kidneys of the monkeys (but in 1931 he seems to have altered his opinion). The same opinion is held by various authors studying the position of Man among the mammals (BOLK 1921, WOOD JONES 1929, WESTENHÖFER 1942).

ELLENBERGER and BAUM (1926) assume the renculi kidney to be primitive, as does ZUBER (1935).

With respect to these very divergent opinions it is natural that the authors of handbooks, e. g. WEBER (1927), v. MÖLLENDORFF (1930) and v. D. BROEK (1935), hesitate to give any definite opinion on this subject.

Those authors who think the renculi kidney to be primitive seem to do this for two reasons. The most important of these is the belief that embryology supports this view. This subject is treated on pages 397—399.

The other reason is that in many cases the surface of the kidney is grooved in embryonic stages and also in early post-embryonic life, but becomes smooth with age. This is especially the case in Man, but occurs also in the cow, the elephant and possibly in other forms with lobated

kidneys. This has been taken to indicate that a real fusion of lobes, leading to simple kidneys, has occurred. This is not the case; the modification is entirely superficial (cf. p. 345 and p. 356). This view has had the more influence as the interest of the authors has centred around the contrast smooth — lobated, leaving other conditions out of account.

The embryonic development of the form of the mammalian kidney.

It seems that most of those authors who incline to the view that strongly lobated kidneys are primitive in mammals do so on the assumption that embryology supports such a view. Below I will shortly examine this matter. This is necessary mainly because some authors, to my knowledge ELLENBERGER and BAUM (1926, p. 511), HAHN (1921), ZUBER (1935), HERTWIG (1910, p. 502), and KINGSLEY (1917, p. 369), plainly state that the kidneys of all mammals are lobated during the embryonic stages. None of them gives any report of any personal investigations to support their statements, or any reference to the papers of other authors on this subject. Thus it is difficult to say how they may have come by this opinion. However, the statements as to this subject are so widely scattered in the literature of kidney embryology, and FELIX in HERTWIG's handbook (1906) gives such brief information on the matter, that it is difficult to reach a well-founded opinion without personal investigations or relatively extensive studies of the literature in question.

FELIX (1906) does not discuss this matter separately, but from the following passage (op. cit. p. 344) it is evident that, in his opinion, simple kidneys are not lobated during their development: ". . . beschränkt sich die neogene Zone der einfachen Niere auf die Peripherie des Gesamtorganes". On the other hand he writes concerning the lobated kidneys: ". . . bei der zusammengesetzten Niere zerfällt die neogene Zone in mehrere . . . die neogenen Zonen breiten sich infolgedessen nicht bloss an der Peripherie der Niere aus, sondern dringen bis zum Nierenhilus vor und scheiden dadurch die ganze Nierenanlage in die verschiedenen Renculi." This is almost word for word what RATHKE (1861) has written on this matter (cf. also TOLDT 1874, p. 132).

I have not been able to find any statements on this subject referring to embryos of monotremes or marsupials. In three embryos (or pouch young) of *Didelphys* (kidney lengths 2.4 mm, 5.5 mm and 8 mm) there is no sign of superficial or internal division, and a papilla is developed. The case is the same with an embryo of *Philander sp.* (kidney length 1.7 mm). In an embryo of *Phascolarctus cinereus* and one of *Choeropus* (kidney lengths 8 mm and 6 mm) the medulla is also undivided, but no

papilla is developed; in the latter some slight furrows can be seen on the surface, but without causing any division of the cortex.

I have examined some embryos of insectivores and bats, but I have not found any statements in the literature. At most there are very slight furrows on the surface, and there is no division of cortex or medulla. (Examined are *Talpa* embryos with kidney lengths 0.8 mm, about 1.1 mm, 2.6 mm; *Erinaceus* embryos, kidney lengths 1.5, 2.8 and about 5 mm; a *Centetes* embryo with kidney length 1.3 mm; *Myotis* and *Plecotus* embryos, kidney lengths 1.0 and 4 mm).

Concerning the rodents there are statements by several authors. It is quite clear that the kidneys of the following are never lobated: Rabbit (Löwe 1879), rat and mouse (Hamburger 1890 and Chiewitz 1897), *Spermophilus* (Völker 1922). In addition to this I have examined several embryos of rabbit, *Mus* and *Microtus*, and have never found any traces of a real division, but only occasional, superficial grooves.

There seems to be little information as to carnivores in the literature. Toldt (1874) gives some figures of kidney stages of cat and dog. No division is shown. In a series of five cat embryos (kidney lengths 1.3 mm, 4.5 mm, 6.5 mm, 7 mm, 9 mm) the kidneys are smooth exteriorly, and both cortex and medulla are undivided. There is no papilla.

In *Equus* (Schurian 1925) the kidney is at first quite smooth and undivided. Later, several grooves appear, but mostly they disappear before or after birth. Schurian did not investigate the interior structure, but it seems most probable that the medulla is always undivided (cf. Chiewitz 1897). This is the case in a horse embryo that I have investigated (kidney length 25 mm). As previously (p. 365) mentioned, a *Diceros* embryo has strongly lobulated kidneys.

Concerning *Sus* the statements are divergent. Toepper (1896) and Hauch (1903) state that the kidneys are undivided exteriorly, but Toldt (1874) is of the opinion that they are lobated in embryos. As the former authors mention that there are occasionally some grooves on the kidney surface, the difference between them and Toldt is perhaps chiefly in the mode of expression. The medulla is already in early stages divided into several papillae. Both of the two hog embryos that I have examined have exteriorly smooth kidneys (lengths 1.2 mm and 15 mm). The larger of these kidneys has a divided medulla. As regards the ruminants there are several investigations of the domestic animals, and Lönnberg (1903) has described some stages of antelopes. The kidneys are all smooth or slightly grooved exteriorly, and the medulla is undivided. This is also true of the sheep kidneys. *Bos*, however, which has lobated kidneys in post-embryonic life, in an early stage has both interiorly and exteriorly lobated kidneys (Toepper 1896, Hauch 1903, Petit 1924 c). In addition

to this it may be mentioned that in a cow embryo investigated by me, with kidneys only about 5 mm long, these are distinctly divided into two lobes. It is obvious that the number of the lobes increases during foetal life, as it is always relatively large later on. PETIT (1925, p. 24) mentions an embryo in *Trichechus* with quite smooth kidneys. Both in *Pinnipedia* and *Cetacea* the kidneys are lobated very early (cf. especially CHIEWITZ 1897 and OMMANEY 1932). OMMANEY describes how the number increases during foetal life in *Balaenoptera*.

In the *Primates* only little is known about this subject. *Gorilla* and *Hylobates* (DENIKER 1886, p. 247 and 251) and *Anthropopithecus* (WESTEN-HÖFER 1942) seem to have undivided kidneys in the embryo stages, but one specimen only was examined of each. In Man the earliest stages of the kidneys are undivided, or only slightly divided. Early in foetal life the lobes become more distinct and more numerous; thus it is obvious that a cleavage of the kidneys occurs (cf. especially HEIDENHAIN 1937).

From the above it seems quite clear that there is no case yet reported of a simple kidney having really lobated stages. Indeed, there is abundant evidence to the contrary. Those kidneys that are lobated or have several papillae in the adults are usually lobated early in foetal life, or at any rate the medulla is divided. Thus it is evident that, far from supporting the opinion that lobulated kidneys are primitive, the ontogenetic development of the mammalian kidneys indicates that the simple kidney is primitive and the lobulated kidneys have developed from undivided ones.

The phylogenetic development of the mammalian kidney types.

The reviews of the kidney form of the different orders show that the simple kidney with one papilla is the primitive type in the following groups: *Monotremata*, *Marsupialia*, *Insectivora*, *Chiroptera*, *Dermoptera* (GERHARDT 1914), *Pholidota*, *Xenarthra*, *Rodentia*, *Carnivora fissipedia*, *Hyracoidea*, *Tubulidentata* (HYRTL 1872), and *Primates*. In *Pinnipedia* and *Cetacea* there are only renculi kidneys, and it must be considered most probable that this type is primitive in these groups. The same applies to *Proboscidea*. In *Artiodactyla* either the crest kidney or the kidney with papilla is the most primitive type. Among the *Perissodactyla* and *Sirenia* there occur different types, but their distribution within the orders gives no clue to the primitive condition from which these types may be derived.

Renculi kidneys and lobated kidneys occur in *Carnivora (Ursus, Lutrinae), Pinnipedia, Cetacea, Proboscidea, Artiodactyla (Bovinae), Perissodactyla (Rhinocerotidae), Sirenia (Rhytina), Primates (Homo)*. It seems

very improbable that these forms should possess a kidney type more primitive than all other mammals. The occurrence in several isolated, in many respects secondarily modified types speaks strongly against the primitiveness of the renculi kidney. This is the more evident as all these forms are either large or aquatic animals.

On analogous reasons it is highly improbable that the kidney with several papillae or with tubi maximi is primitive.

If all the mammalian groups are considered there can be no doubt that the simple kidney with one papilla is the most primitive type existing, and represents the type occurring in the ancestor common to all mammals. The exclusive occurrence of simple kidneys in *Monotremata, Marsupialia* and several monodelphian orders is especially important in this respect, and very cogent reasons would be needed for abandoning this view, firmly based on comparative morphologic facts as it is. As shown above (p. 399) the embryology, too, supports this view.

If it is thus considered proved that the simple kidney with a papilla is the original type in the mammals, one can with more assurance trace the modifications to which the mammalian kidney has been subjected.

The crest kidney is easily derived from the kidney with a papilla, by shortening the papilla. This derivation has been assumed by as early scholars as GEGENBAUR (1901) and GERHARDT (1911, 1914). There are a great number of transitional forms between these types, and this transition must be considered to have occurred independently in most mammalian groups. The crest is usually of moderate length, but is sometimes very long, as in *Giraffa* and *Halicore* (where, however, it is divided into two parts).

The kidney with tubi maximi seems usually to have developed from the crest kidney. This is probably the case with the kidneys of this type in the *Artiodactyla* and *Perissodactyla*. Tubi maximi have probably developed in a kidney with papilla in some instances, e. g. *Coelogenys*. There are numerous transitional stages towards the tubi maximi kidney (*Dasyprocta, Rangifer, Hystrix, Papio*). The *Hippopotamus* kidney shows an extreme development of this type, as here the tubi maximi are branched. In the elephant tubi maximi occur in the renculi. Tubi maximi have obviously developed independently in several groups: In *Simplicidentata* (probably more than once), *Dicotyles, Hippopotamus, Tragulus, Cervidae* (perhaps in several groups), *Perissodactyla, Elephas, Macacus.*

The type with several papillae has usually originated from the crest kidney, too, but seems also to have been derived from the kidney with one papilla. The former condition obtains in *Sus* and *Phacochoerus* and apparently in *Gorilla* and *Anoa*, the latter in *Castor,*

The *Anoa* kidney leads on towards the renculi kidney. Another stage

in this development is represented by the cow kidney. It seems most probable that all renculi kidneys have developed via the type with several papillae but undivided cortex, but it is, of course, possible that an entirely simple kidney has been divided at once into renculi. There is no evidence as to this; such a process could, however, hardly be traced now if it had taken place in the past. The renculi kidney shows a spectacular further modification in the *Cetacea*, where the number of the
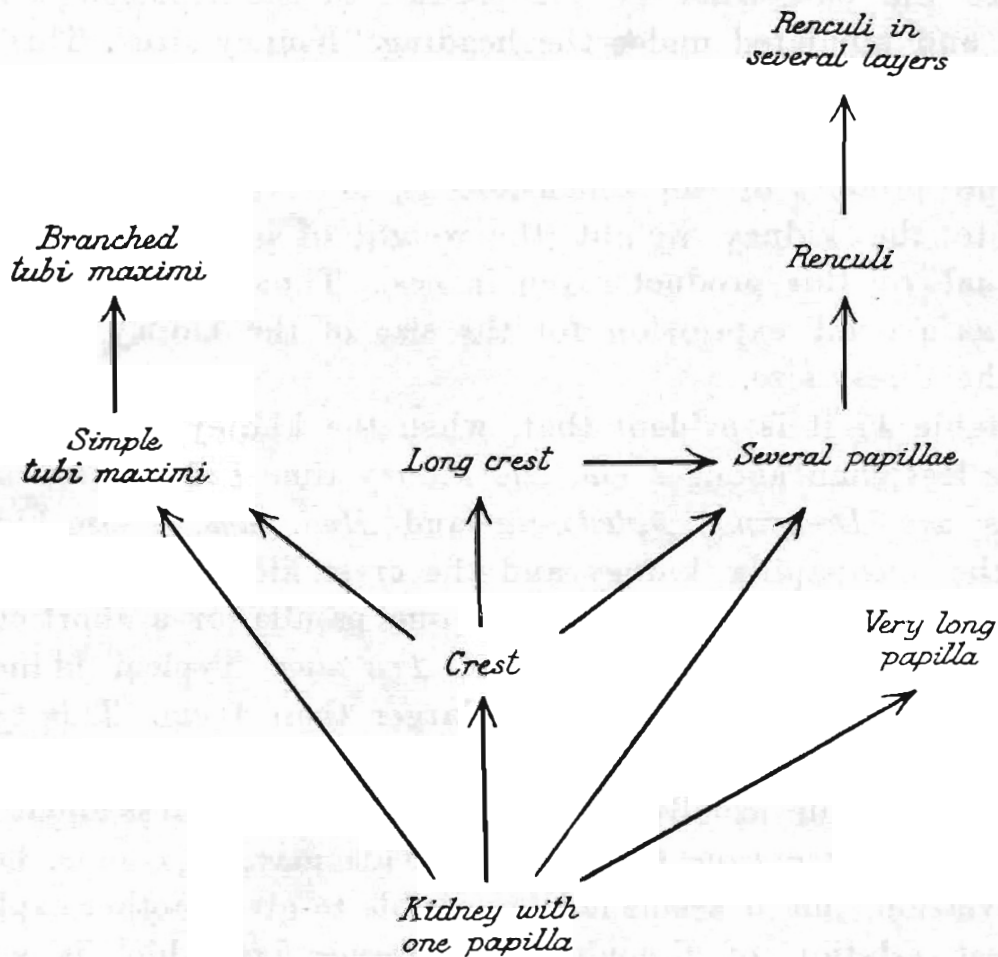

Fig. 27. Scheme of the phylogenetic development of the mammalian kidney types.

renculi is much increased and the renculi are arranged in several layers. The renculi kidney seems to have developed independently in several groups (cf. above).

The derivation of the kidney types is shown in fig. 27.

As is shown by the above the kidney has developed along a large number of parallel lines. This may be considered to be the most outstanding feature in the phylogenetic development of this organ. This makes the kidney little suited for a basis to phylogenetic conclusions, as far as the large groups are concerned. It seems, however, as if the kidney structure might well play a part in the discussion of the phylogeny of certain smaller groups.

The distribution of the kidney types in relation to size.

The distribution of the kidney types is relatively irregular in phylo-genetic respects. The distribution is, however, regular as regards the size of the kidneys. In table 47, p. 415, the dimensions of the kidneys of all species examined by me have been tabulated, together with some measurements from the literature. As a more accurate measure of the kidney size the cube root of the product of the dimensions has been calculated and tabulated under the heading "Kidney size". This measure has been chosen, as the weight of the kidneys is not known either in my own alcohol kidneys or in most data from the literature. In fresh kidneys the product of the dimensions is, however, almost exactly pro-portional to the kidney weight (the weight of both kidneys in gms is nearly equal to this product given in ccs). Thus this product must be regarded as a good expression for the size of the kidney, and its cube root for the linear size.

From table 47 it is evident that, when the kidney size in the *Mono-delphia*[1] is less than about 2 cm, the kidney almost always has a papilla. Exceptions are *Desmana*, *Aplodontia* and *Hydromys*, whose kidneys lie between the one-papilla kidney and the crest kidney. Kidneys with a size between 2 and 3 cm usually have one papilla (or a short crest), but striking exceptions are *Myocastor* and *Tragulus*. Typical kidneys with papilla do not occur among kidneys larger than 4 cm. This type thus occurs only in small animals, and is almost the only kidney type there. The exceptions occur usually in animals with more or less aquatic habits. *Tragulus* is an exception to this rule. This may, of course, be only a chance deviation, but it seems not impossible to give another explanation. The nearest relation of *Tragulus*, i. e. *Hyemoschus*, which is considered more primitive than *Tragulus*, is larger than *Tragulus* and leads a more water-loving life. It seems possible to assume that the ancestors of *Tragulus* have been larger and lived in a more moist habitat than does *Tragulus*. According to this view the kidney form of *Tragulus* could be explained as a character retained from an earlier stage of phylogenetic development.

Kidneys with a short or a moderately long crest are usually about 3—6 cm, but the large *Felidae* are forms with relatively large kidneys with a short crest.

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[1] To make the material more homogenous the *Monotremata* and *Marsupialia* have been excluded from the following discussion of the kidney form, but they seem to agree in essentials with the *Monodelphia,* though the small size range in the former groups makes it difficult to ascertain this.

The large kidneys belong to the remaining types: namely, the kidneys with long crest, with several papillae, with tubi maximi, and the renculi kidneys. Among the very largest (*Cetacea*, *Rhytina*) there are only renculi kidneys with several layers of renculi. The extreme development of the kidney with tubi maximi in *Hippopotamus* and the longest crest kidneys in *Halicore* and *Giraffa* also occur in large animals.

It is evident that the kidney with one papilla occurs almost exclusively in small animals[1] and that the fairly long crest is mainly confined to animals of moderate size. The remaining types occur most often in large animals. There are exceptions, but in these cases the aberrant kidneys usually belong to aquatic animals (*Desmana*, *Hydromys*, *Myocastor*, *Coelogenys*, *Castor*, *Lutra*). Thus, there is a clear relation between kidney form, and size and habits of the animals. The fact that almost all small mammals have simple kidneys, usually with a distinct papilla, very much supports the opinion that this type is primitive. It seems to be generally agreed that the most primitive mammals were small and that, in most orders, there has been a successive increase in size. There is no reason to think that the small mammalian ancestors should not have had simple kidneys, when all mammals of similar size now living show this feature.

The relative thickness of cortex and medulla.

In table 47, p. 415, are given figures expressing the relative thickness of cortex + medulla, medulla, and cortex + outer zone. These figures have been obtained by dividing the absolute thicknesses of these layers (in mm) by the size of the kidney (in cm). If a kidney is enlarged without alteration of its structure the relative thicknesses are unaltered, but any change of the kidney structure affecting the relative thickness of its layers is indicated by these figures. The following summary of the data of table 47 as regards the Monodelphia shows roughly how the relative thicknesses are distributed among the types. The means are bracketed.

In this review the types have been subdivided according to the degree of development of their special characters. Among the crest kidneys are included the transitional forms to this type. It is apparent that the types show different relative thicknesses of the layers. There is, however, great variability within the groups. This is due to the fact that not only the kidney type but also other factors influence the thickness of

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[1] The mean size of the kidney with a long papilla is 6.8 ± 0.72 mm, that of the kidney with a moderate papilla 16.1 ± 1.65 mm. The crest kidney (incl. transitional forms) is 40.4 ± 3.86 mm, the kidney with tubi maximi 50 mm (8 data), the kidney with papillae 68 mm (7 data), the renculi kidney 84 mm (7 data).

Kidney type	Cortex + medulla, rel. thickness	Cortex + out. zone, rel. thickness	Medulla, rel. thickness
Long papilla	7.7—12.3 (10.3)	3.5—5.7 (4.2)	6.2—10.7 (8.3)
Papilla	5.7—8.9 (7.2)	2.4—5.8 (3.8)	3.5—6.8 (5.3)
Crest	4.5—6.4 (5.6)	1.7—5.7 (3.2)	2.6—4.8 (3.8)
Long crest	2.5—3.6		1.9
Tubi	3.8—6.7 (4.97)	2.9—9.6 (4.2)	2.1—3.9 (2.9)
Branched tubi	1.8	1.8	1.0
Papillae	3.7—5.8 (4.5)	2.2—5.8 (4.1)	1.6—3.9 (2.6)
Lobes and few renculi . .	2.4—4.0 (3.15)	1.8—2.4 (2.1)	1.2—3.0 (2.3)
Renculi	0.9—2.7 (1.7)	0.5—1.6 (0.9)	0.7—1.9 (1.3)

the layers. Flattened kidneys show relatively high values (e. g. *Gulo* and *Castor*). The occurrence of very thick cortices (in species with cortical nephrons) and the absence of an inner zone influence the figures. This seems to be the reason why the kidneys with tubi or papillae have high relative cortex thicknesses, as most members of these groups have cortical nephrons. In addition to these factors, the deformation of some kidneys during preservation also adds to the variability. In the groups with tubi and renculi there is undoubtedly a relation between the development of the tubi and the number of the renculi, and the relative layer thickness.

When regard is paid to these factors it is apparent that the simple kidney has high figures. The medulla is especially deep in forms with long papilla. The joint thickness of all layers, and of the inner zone, is decreased relatively in the crest kidney, and this process continues in the kidneys with tubi maximi, papillae and long crest, to reach its maximum in kidneys with numerous renculi. The cortical thickness decreases less regularly, but on the whole in a similar way.

The relation of relative layer thickness and size is shown in fig. 28. In these diagrams animals living in deserts and other arid habitats are marked with crosses, acquatic animals with circles, and the others with dots. Under the arid group have been classed *Macroscelides, Dipodomys, Pedetes, Jaculus, Gerbillus, Meriones, Psammomys, Dolichotis, Ctenodactylus, Camelus, Antilope, Connochaetes, Giraffa, Hyaena, Felis leo.* The inclusion of some of these might be questioned, and some others, for example *Hystrix cristata,* could perhaps be included, but such changes could have little influence upon the general picture.

The relative thickness of the layers diminishes clearly with increasing kidney size. The arid group has high values, especially for the medulla, and the aquatic group has, on the whole, low ones (cf. p. 389).
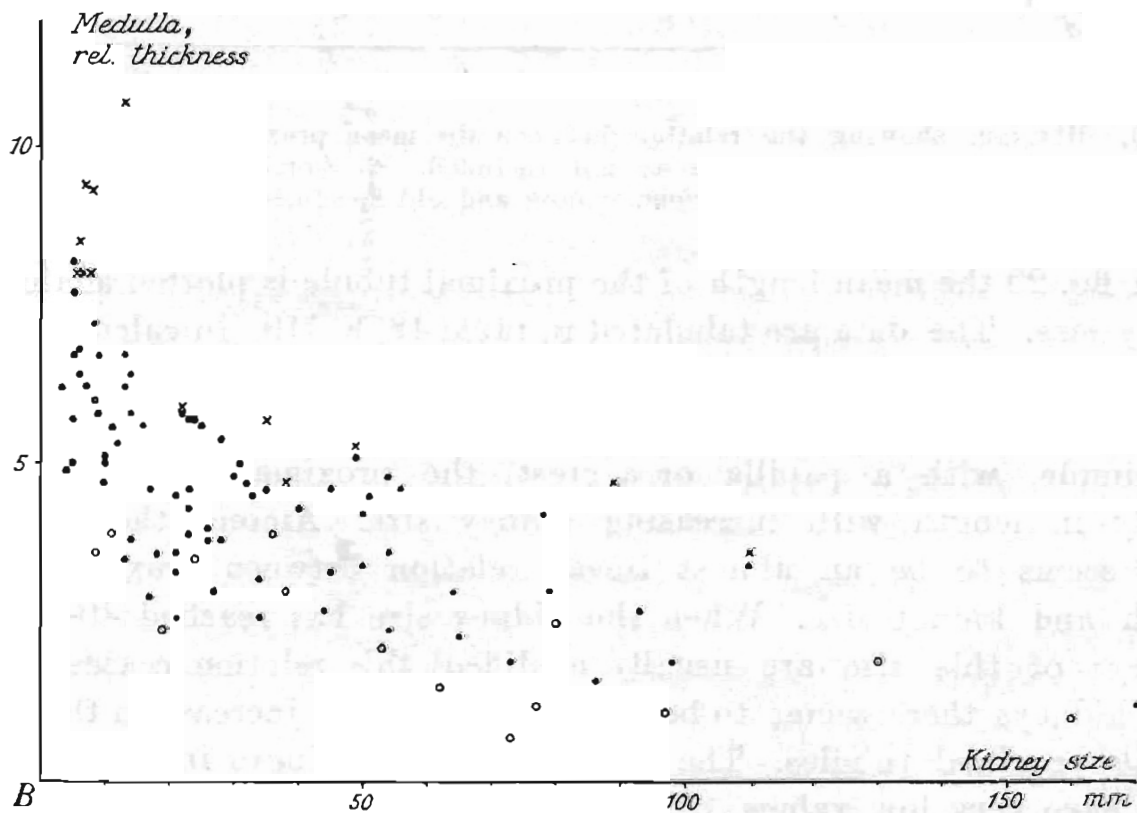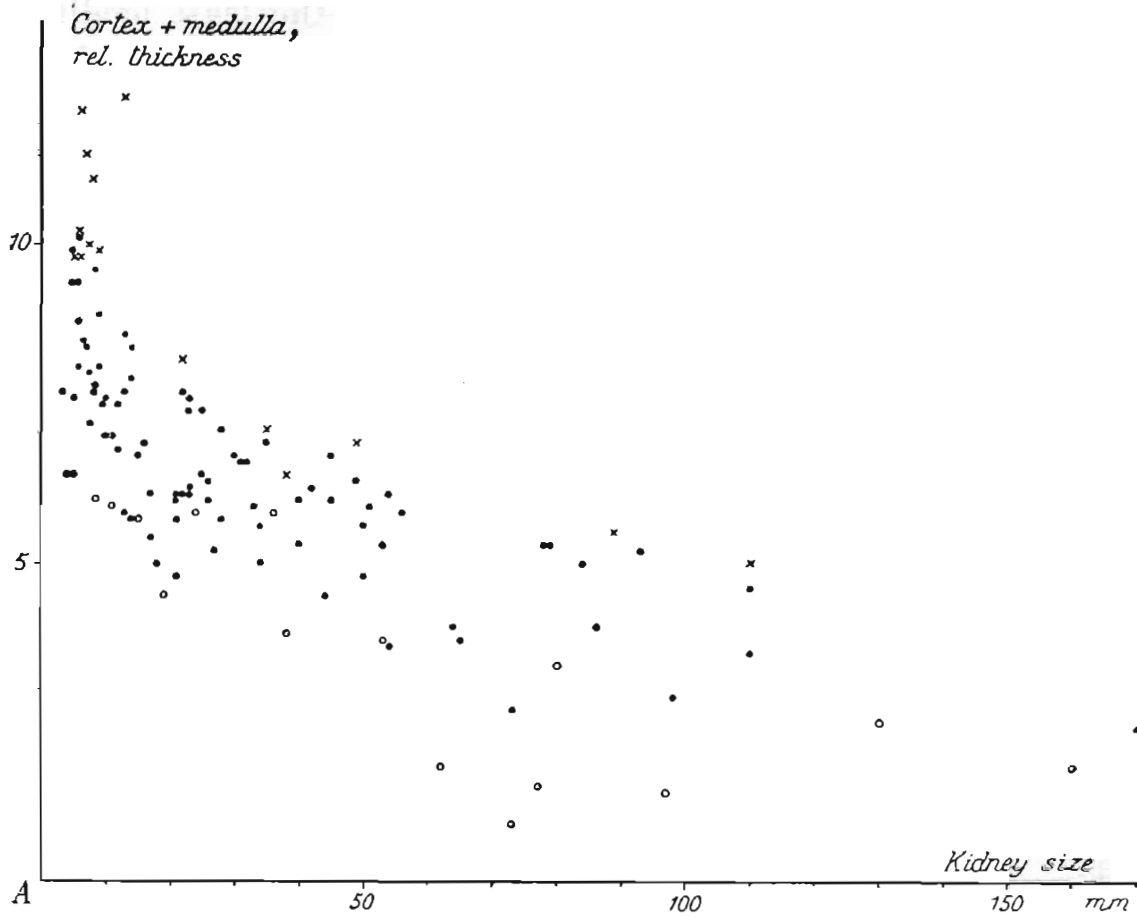
Fig. 28. Diagrams showing the relation between the relative thickness of A cortex+
medulla, B medulla, and the kidney size.

Arid forms designated by crosses, water-loving forms by open circles.

As the relative layer thickness is highest in the least modified kid-
neys, it is easy to understand that the desert forms with their high
medulla thickness have less modified kidneys than most other forms.
The aquatic forms, on the other hand, which have low medulla thickness,
usually have more modified kidneys than other mammals of equal size.

The relation of the length of the proximal tubule and the kidney size.

It has previously been shown that the length of the proximal tubule
is closely related to the thickness of cortex and medulla (p. 377). It is
then natural that this length should show a connection with the kidney
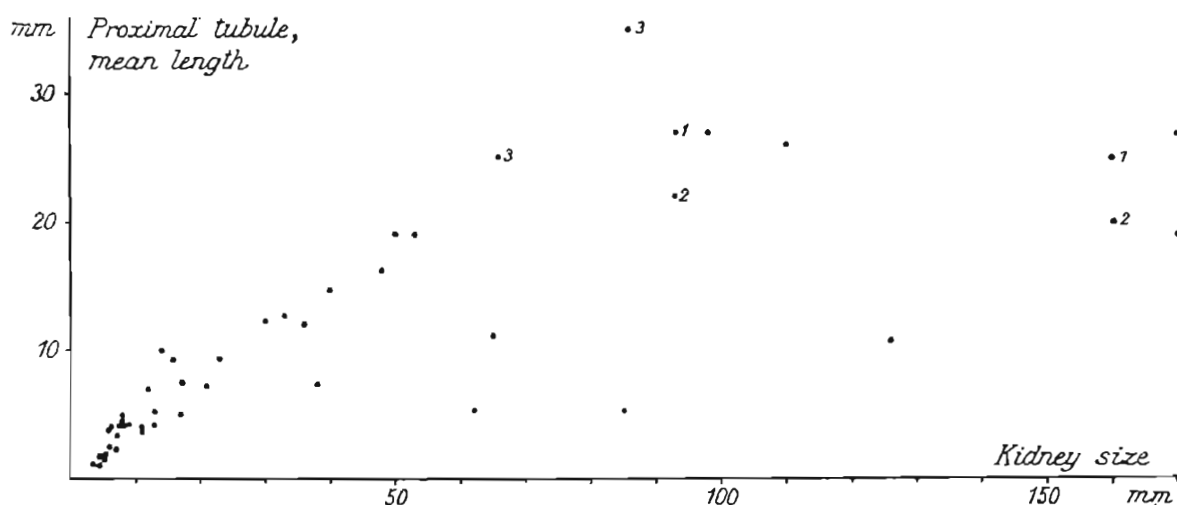size similar to that shown by the layer thickness.

Fig. 29. Diagram showing the relation between the mean proximal tubule length and
the kidney size. 1. Cortical nephrons not included. 2. Cortical nephrons included.
3. *Sus scrofa dom.*, young and old specimen.

In fig. 29 the mean length of the proximal tubule is plotted against the
kidney size. The data are tabulated in table 48, p. 419. In calculating the
mean length the cortical nephrons in large animals have been regarded
(dots marked 2), or disregarded (dots marked 1). In small kidneys (which
are simple, with a papilla or a crest) the proximal tubule increases
rapidly in length with increasing kidney size. Among these kidneys
there seems to be an almost linear relation between proximal tubule
length and kidney size. When the kidney size has reached 40—70 mm
(kidneys of this size are usually modified) this relation ceases, and in
large kidneys there seems to be no or slight further increase in the length
of the proximal tubules. The extreme renculi kidneys in marine carni-
vores have very low values.

Thus, the proximal tubule length shows similar conditions to the
layer thickness. In large kidneys it is sometimes comparatively more
reduced than the thickness of the cortex. This feature is especially

prominent when cortical nephrons are included in the means (dots marked 2). This is due to the fact that the high nephrons are no longer dependent on cortical thickness, as they do not reach the medulla (cf. p. 376).

The general picture is somewhat obscured by the carnivores and insectivores usually having relatively shorter nephrons than the herbivores. As the former are usually small or middle-sized forms (except the marine carnivores) the small kidneys show more varying proximal tubule length than if the herbivores are considered alone. If this is done, the relative shortness of the proximal tubules in the large kidneys is still more striking.

The marine mammals examined show very low proximal tubule lengths, which is connected with the great number of renculi in their kidneys. This may indicate that aquatic carnivores tend to have much shorter proximal tubules than terrestrial forms. *Neomys, Desmana* and *Lutreola* have, however, tubule lengths comparable to those of other carnivores and insectivores. *Lutra*, on the other hand, has comparatively short tubules, and *Latax* and the American *Lutra* (p. 333, foot-note) no doubt have still shorter ones, as they have numerous renculi. Thus, it would seem that all carnivores strongly adapted to water-life have shorter proximal tubules than other mammals of equal size.

Among the herbivores the aquatic forms examined do not seem to have unquestionably shorter proximal tubules than similar terrestrial forms. The *Sirenia* have not been investigated in this respect, but it is not probable that they have especially short tubules (perhaps with the exception of *Rhytina*, which had numerous renculi).

As shown on p. 375 the deepest proximal tubules are much longer than the average in small kidneys, but in the middle-sized kidneys they are not. The longest proximal tubules must, then, become shortened relative to kidney size in comparatively small kidneys, where the mean proximal tubule length is still directly proportional to kidney size.

Discussion of factors limiting the tubule length.

The facts given above show that there is a connection between the proximal tubule length and the form of the kidney. The length of the nephrons seems to be limited. It might be supposed that this limitation of the tubule length is only a consequence of the modification of the kidney form, which is determined by other factors. It seems, however, difficult to find such other factors. The surface of the kidney is certainly not essential in this respect (cf. p. 395). The frequent superficial fusion of the renculi and lobes (*Pinnipedia, Bos, Elephas, Homo*) con-

tradicts this explanation, as well as the assumption that large, undivided kidney masses are in themselves unsuitable in some respect. The kidneys of the elephant or the seal are very compact structures, despite their composition of renculi. The very thick cortices in forms with numerous cortical nephrons show that the thickness of the cortex is probably not essential.

On the other hand, not only the limitation of the proximal tubule mean length indicates that tubule length is of importance in itself. The longest nephrons in the small kidneys, namely the deepest ones, are relatively most shortened, and this shortening begins before any shortening of the higher nephrons is evident. In large kidneys the high proximal tubules are the longest ones. In several large herbivores these are considerably shortened by the formation of numerous cortical nephrons, which is especially noteworthy as the plan of the kidney structure is thereby upset (cf. p. 373).

If, thus, the nephron length itself is limited, it seems most probable that the limiting factor is of a physical nature. Chemical processes cannot well be directly influenced by the tubule length.

In the capsule of Bowman an ultra-filtrate of the blood is formed. The driving force of this process is the blood-pressure, opposed by the colloid-osmotic pressure of the blood and the pressure in the capsule (cf. SMITH 1937 and SMITH, CHASIS, GOLDRING & RANGES 1940). The filtration is considered to result in an equilibrium between these forces, as the blood-pressure falls and the colloid-osmotic pressure rises towards the vas efferens. The pressure in the capsule is the one required to force the fluid through the tubules into the pelvis (when the pressure in the pelvis is assumed to be zero). This pressure follows Poiseuille's law. According to this law, in this case, the pressure is proportional to the volume of the fluid passing a tubule in the time unit and to the length of the tubule. The pressure is also inversely proportional to the fourth potence of the radius of the lumen.

If the lumen radius is not altered and the nephron length is increased, the volume of fluid flowing through it must be increased in the same proportion if the efficiency of the nephron is not to be diminished. Thus, the pressure in the capsule is increased proportionately to the square of the length of the nephron.

It has previously been shown that the diameter of the proximal tubule, the thick segment and the distal tubule, increases with increasing nephron length in short nephrons. This may be ascribed to the necessity of increasing the lumen width, as otherwise the pressure in the nephrons must rise rapidly. This increase in tubule diameter is, however, almost absent in longer nephrons (cf. p. 381), and in these it may be correct to

assume that the lumen width of the nephrons is constant, or at least increases very little with nephron length. Thus, in large kidneys, an increase in the nephron length must cause a rapid rise in the intracapsular pressure. If there is a considerable pressure within the capsule this must markedly diminish the filtration rate and the fraction of the plasma which is filtered. If the latter is diminished the blood flow through the glomeruli must increase, or the volume of the filtrate decreases too.

It is clear that the intracapsular pressure must be of a certain magnitude to have an appreciable effect on the filtration. If this pressure is very low the increase in it due to a moderate lengthening of the tubule can have very little importance.

The intracapsular pressure in mammals has not been measured. BRODIE (1914) has given reasons for thinking that this pressure is relatively high, especially during diuresis. He has also calculated the pressure in the dog, but his calculations are no doubt erroneous (both number and diameter of the nephrons are underestimated). SMITH, CHASIS, GOLDRING and RANGES (1940, p. 756) have estimated the intracapsular pressure at about 15 mm Hg, but the basis for this estimation seems uncertain. WALKER and OLIVER (1941) have made direct observations of the intratubular pressure in rat and guinea-pig. They have not measured it, but state that the intratubular pressure (in the proximal tubule) was "very high", "which was particularly prominent during the infusion of hypertonic sucrose solutions" (op. cit. p. 569). On the other hand the intratubular pressure was low within the distal tubule.

It may thus be concluded that there is in the capsules of the mammals a considerable pressure that can be an important factor diminishing the filtration. If the tubule diameter is constant and the nephron length increases, the intracapsular pressure increases rapidly. If the nephrons in large kidneys were much longer than they are, the pressure in the capsules would be considerably higher. There can be little doubt that such an increase of the intracapsular pressure would reduce the efficiency of the kidneys.

It may thus be assumed that the factor limiting nephron length in large mammals is the pressure required to force the fluid through the nephrons.

The relative shortening of the nephron length in large mammals is effected either by the occurrence of cortical nephrons or by the modification of the kidney form, or by both these means.

The occurrence of the modified kidney types in freshwater forms seems, on the other hand, mainly to be due to the diminished thickness of the medulla (cf. p. 404). It is, however, probable that the volume of the fluid passing through the nephrons (at least their distal parts) is larger

in aquatic forms than in terrestrial ones. This would tend to rise the pressure in the capsule and thus to limit the nephron length.

As pointed out above, the examined *Cetacea, Pinnipedia* and *Lutrinae* have very short nephrons. The marine mammals apparently do not excrete particularly large volumes of water (IRVING, FISHER & McINTOSH 1935, SMITH 1936). That their kidneys are strongly modified is natural, as they are large animals, but the fact that the nephrons are much shorter than in other mammals of equal size would seem to require a special explanation. It may, of course, be only coincidence that these aquatic carnivores are similar in this respect, but this does not seem very probable. There seem, however, to be some special features in the physiology of diving animals worthy of mention in this connection. In the seal very little urine is formed when the animal has not eaten for some time, but both volume and concentration are much increased after a meal (SMITH 1936). The urine volume is thus relatively higher at some periods than it would be with a more uniform flow of urine. Further, during diving the blood flow to most of the organs of the seal is assumed to stop to a great extent (IRVING, SOLANDT, SOLANDT & FISHER 1935, IRVING 1939). This must also tend to increase the urine volume during the periods of renal activity. The blood-pressure changes rhythmically in the seal, also when not diving. It seems possible that the rhythm of blood-pressure is accompanied by a similar rythm in kidney function, and this further increases the filtration rate and the urine volume necessary at top activity of the kidney. This concentration of the kidney activity to certain periods may have some connection with the high relative kidney weight in the marine mammals (DENZER 1935). It is, ofcourse, difficult to say definitely what influence this increased top activity of the kidney in the diving mammals will have upon the filtration in the capsule. It would, however, seem that the blood flow to the kidneys during certain periods should be relatively larger in the diving animals than in other mammals, where it already constitutes a large part of the total blood flow. It would then be more necessary to avoid any interference with the filtration process — especially with regard to the magnitude of the filtered plasma fraction — and thus to have short nephrons. It is of course also possible that other factors are at work, such as diminished tubule diameter, or increased volume of filtrate, but to my knowledge there are no data available which indicate such circumstances.

The evolutionary mechanism of the phylogenetic development of the mammalian kidney types.

In the above account attention has repeatedly been drawn to cases of parallel phylogenetic development. Such cases are the strong development of arcades in herbivores, the composition of the nephrons in herbivores and carnivores, the occurrence of cortical nephrons and the absence of long loops in several herbivores, and especially the macroscopic structure of the kidney. From the simple kidney several types have developed, each of them independently in several groups. The author has attempted to explain this mainly on the assumption that it is advantageous to have relatively short nephrons, as otherwise the pressure needed to force the fluid through the nephrons would be too high. An attempt will be made below to examine which evolutionary mechanism may be responsible for the development of the mammalian kidney types.

It seems clear from the distribution of the derived kidney types, if we regard the size and habits of the forms showing them, that they must be considered as adaptations. Most of them are, however, adaptations not to environment in the usual sense, but to the size of the animal. Some of the cases seem to be adaptations to environment, as in the aquatic types. The view of the derived kidney types as adaptations is of course strengthened by the explanation of their occurrence given above, but is by no means solely dependent on the correctness of this explanation.

It seems to me quite impossible to explain the development of these adaptations along Lamarckian lines of thought. It is clear that the relative shortening of the nephrons of a kidney must be connected with an increase in the number of the nephrons, which is obviously what occurs in the phylogenetic development. In the individual postnatal development, increased demands on the kidney are met with a lengthening of the nephrons. This is shown to be the case after unilateral nephrectomy (cf. e.g. PETERS 1928) and is also the case in the individual development. Thus, there is no response in the individual comparable to the changes occurring in the phylogenetic development. It is also difficult to imagine how this could come about. The kidney of mature mammals cannot form new nephrons, and this is essential if the nephron length is not to increase with the size of the kidney. Thus, even if the possibility of splitting a kidney into parts in the mature state were admitted, it would not be possible to explain the phylogenetic development of the mammalian kidney by the inheritance of, acquired characters. If the connection between the pressure in the capsule of the nephrons and the kidney form is accepted as true, it would seem so indirect that the as-

sumption of this need directly causing this change must involve the action of a regulating intellect, and thus falls entirely outside the limits of science.

It would perhaps seem possible to explain the development of the different kidney types on an orthogenetic basis. Each of them could arise through a series of mutations occurring in all members of a given species or group. This explanation, however, stands in opposition to the above opinion that the kidney types are adaptations. And even if this opinion is not accepted the main fact supporting it, namely the distribution of the kidney types, opposes the orthogenetic explanation. If the derived kidney types have developed by orthogenetic processes it does not seem possible to explain why they are predominant among mammals of large size, and especially why they do not occur among the numerous small forms (except in more or less aquatic types). This fact is all the more impossible to explain as the derived type is not uniform; were it so, it might perhaps be possible to think of it as a purely consequential phenomenon, following the increase in size more or less as a matter of course. This view seems untenable if due regard is paid to the fact that there are at least three fundamentally different types, each with a similar distribution.

It seems clear that the observed facts cannot well be interpreted on either a Lamarckian or an orthogenetic basis. On the other hand, they easily fall in with a selectionist interpretation. The distribution of the derived kidney types is quite natural if it is assumed that they are all advantageous in forms with heavy bulk or with aquatic habits. Which of the derived types has developed in a certain form must be attributed on the whole to chance. At any rate in their first stages, they seem to be similar in respect of the advantage they can offer, and as far as suitable mutations occur, are thus equivalent with regard to selection. Of course it is possible that some structural features in the ancestral type may dispose it to develop into a certain one of the secondary types, but there is no indication of this. In some orders all forms show the same kidney type, as in *Pinnipedia* and *Cetacea*; in others there are more than one of the secondary kidney types, as in *Sirenia*, *Artiodactyla*, *Perissodactyla*, *Primates*.

Finally, it is obvious that the almost complete absence of the secondary kidney types in small mammals is in conformity with the selectionist view. In this respect two views are possible. Either the simple kidney type with a papilla is the most advantageous one in small mammals, and would thus be maintained even against some mutation pressure, or it is only the absence of a sufficient advantage in the other types that has preserved the original type in small animals.