

## EDITORIAL

# ON THE EXISTENCE OF RENAL MEDULLARY LYMPHATICS

One of the earliest maxims learned by biological scientists is that studies, appearing to be definitive at first glance, are rarely so. As each article, which purports to lay a controversial matter to rest, enters the literature — so must we expect it to be followed shortly by another that calls the issue in question and thus reopens it to even greater argument. This now familiar scene has been enacted on the subject of lymphatic vessels in the kidney. The most intriguing question of this topic is whether or not such vessels exist within the renal medulla and if so what might their function be. Of special interest is whether medullary lymph, if indeed such exists, contributes to the concentrating mechanism of the kidney. An article (Cuttino et al) which appears in the current issue of *LYMPHOLOGY* reawakens with startling clarity the possibility that lymphatic vessels are to be found in the medulla. The topic is made all the more intriguing by the appearance of an article by Eliska (1) in the previous issue of *LYMPHOLOGY*, on the topography of intrarenal lymphatics. Although Eliska's study pertains primarily to lymphatics of the cortex, it is of particular significance that he states "In accordance with previous investigators we were unable to detect lymphatics in the renal medulla."

To those who have searched and failed to find medullary lymphatics, Eliska's article is reassuring in that it adds another study to the growing number that point to the medulla as an lymphatic structure. Yet, as has been stressed repeatedly, failure to find a structure is not acceptable as proof that it does not exist: repeated failures on the

other hand provide circumstantial evidence of growing magnitude. Cuttino et al's study would now appear to bring us back full circle and renew the challenge to lymphologists to prove or disprove the existence of lymphatics in the medulla.

Recent — if forty years can be so described — literature on the subject may be said to start with the detailed and careful study by Peirce in 1944 (2). While it may seem arbitrary to dismiss studies before 1944, space does not permit an analysis of the contradictory findings and trouble-prone techniques that preceded Peirce's study. He, however, used especially rigorous criteria to identify lymphatics in his injection preparations and failed to find such vessels in the medulla. Perhaps that is where the issue might have rested had it not been for the case report by Rawson in 1949 (3). He described in considerable detail a pattern of lymphatics, including medullary vessels, present in a human kidney invaded by metastatic spread from carcinoma of the stomach. These medullary lymph vessels seemingly began as blind-ending vessels in the papilla and ascended through inner and outer medulla to reach the collecting vessels in the arcuate region. This description and the diagram depicting it have been cited and reproduced in numerous texts since then and thus have been accorded greater prominence than might be justified by a single specimen. Major doubts pertaining to his work, question whether the thin-walled structures that he saw containing tumor cells were really lymphatic vessels, and if so were they intrinsic features of the kidney or did they develop

only as a result of the disease. Increasingly, as subsequent studies failed to confirm his findings, these doubts have grown and it has seemed more probable that, despite Rawson's findings, the renal medulla is normally devoid of lymphatics.

It is superfluous to list the appropriate publications here since Cuttino et al in this issue and Eliska in the previous issue of *LYMPHOLOGY* cite a comprehensive bibliography. An objective analysis of this literature, however, must lead the reader to conclude that medullary lymphatics, if they do exist, are so few and far between that their structural and functional significance is minimal. It seems almost inconceivable that lymph vessels, which can be found and traced so readily within the renal cortex, can be a true component of the medulla when they so effectively conceal their presence there. This at least would seem to be the trend of thought among nephrologists, until now when interest must be reawakened by the article of Cuttino et al.

Their study reveals tracer-filled vessels, which both by light and electron microscopy appear to be lymphatics in the medulla of the pig. Once more, then, we are faced with those three standard questions raised by so many studies on lymphatic vessels in the past. Is the technique acceptable? Are the vessels indeed lymphatic vessels? Is there the possibility of significant species differences? A brief comment on each of these questions is appropriate here, because they are critical to the analysis of any structural study on lymphatics regardless of body site.

Injection techniques — the classical method of study — are notoriously prone to misinterpretation, either because some lymph vessels are not filled with tracer and so an incomplete picture is derived; or because tissue spaces and blood vessels, filled with tracer as a result of the high pressures used, are falsely labelled as lymphatics. The method used by Cuttino et al must be regarded as a variation of the injection technique and therefore subject to the same potential problems. They instilled

radiocontrast tracer at high pressure (100-150 mm Hg) up the ureter such that the tracer escaped from ruptured elements of the nephric system into the interstitium of the kidney and thence apparently to the lymphatics. Not only is incomplete filling of the lymphatic system probable with this technique but more importantly the presence of tracer in non-lymphatic components of the kidney is inevitable. Eliska on the other hand retrogradely injected capsular lymphatics that were visible on the surface of the kidney. His technique may be expected, in successful instances, to portray lymphatics in the renal cortex because the dye can enter through connections between the capsular and hilar systems. Dye injected by this route, however, would not be expected to enter medullary lymphatics because the easier path of exit would be through vessels leaving the kidney in the hilar system rather than retrogradely into vessels arising in the papilla. Thus Eliska's failure to find medullary lymphatics could easily be technical in nature.

To answer the second question posed above, Cuttino et al correctly used electron-microscopy to identify the structures filled with contrast medium and applied conventional criteria for the recognition of lymphatics. Without such ultrastructural confirmation, vessels in tissue sections cannot be accepted as lymphatics with any reasonable degree of certainty. Thus Cuttino et al appear to have provided convincing evidence that some lymphatics at least, exist within the outer medulla of the pig's kidney. Unfortunately their study does not provide information on the extent of the lymphatic system. The radiographs suggest a relative paucity of these medullary lymphatics but as with all injection studies it must be asked if this is real or does it stem from a short-coming of the method.

The third question to be asked is does the pig differ from other mammalian species? Clearly the answer must await additional studies. Rawson's description of medullary lymphatics was taken from the human kidney. Most of the negative studies, on the other hand, have been per-

formed on common laboratory animals such as the dog and rat. Even meticulous searches for lymphatics in the canine kidney have failed to reveal more than an occasional vessel in the outer medulla close to the arcuate complex (4). It is well known that some species differences pertain to the mammalian lymphatic system, especially on the thickness of their walls: collecting vessels in dogs have much thinner walls than those in rats, for instance. Recently we have found significant quantitative differences in the density of the renal cortical lymphatic system among dogs, rats, rabbits and hamsters (to be published). The system in the rabbit is particularly sparse and stands in contrast to that of the hamster, which has a rich lymphatic system in the cortex: those in the dog and rat are intermediate between the other two. This finding raises an immediate and intriguing speculation that the density of the system may in some way be related to urinary concentration ability — but as yet no evidence exists to this effect.

The interesting, or some would say frustrating, conclusion to be drawn is that we still lack a ready and accurate method for identifying and depicting the pattern of

lymphatic vessels in such organs as the kidney. Injection methods are too prone to misinterpretation to be regarded as reliable. The more recent and reliable methods using serial sections with ultrastructural confirmation is unfortunately somewhat tedious and time consuming. Perhaps, until a foolproof method is developed we must continue to question the existence of lymphatic vessels in the medulla of the kidney.

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#### REFERENCES

1. Eliska, O: Topography of intrarenal lymphatics. *Lymphology* 17 (1984), 135-141.
2. Peirce, EC: Renal lymphatics. *Anat. Rec.* 90 (1944), 315-335.
3. Rawson, AJ: Distribution of the lymphatics of the human kidney as shown in a case of carcinomatous permeation. *A.M.A. Arch. Pathol.* 47 (1949), 283-292.
4. Albertine, KH, CC O'Morchoe: An integrated light and electron microscopic study on the existence of intramedullary lymphatics in the dog kidney. *Lymphology* 13 (1980), 100-106.