An examination of transcapillary water flux in renal inner medulla

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Sanjana, Veeraf M., Paul A. Johnston, Channing R. Robertson, and Rex L. Jamison. An examination of transcapillary water flux in renal inner medulla. Am. J. Physiol. 231(2): 313-318. 1976. - We recently demonstrated that net fluid uptake occurs in the capillary system of the inner medulla. To define the site of fluid uptake, the concentration of protein was determined in plasma from descending vasa recta at the base and tip of the exposed papilla in Munich-Wistar rats. The vasa recta plasma-to-arterial plasma protein concentration ratio (VR/P) was 1.43 ± 0.09 at the base and 1.66 ± 0.09 at the tip. These results, which indicate fluid loss from the descending vasa recta, are difficult to explain on the basis of hydraulic and oncotic forces alone. The osmolality of the contents of descending vasa recta increased between base and tip (Δ = 72 ± 30 mosmol/kg H2O). If the increase in osmolality of plasma in descending vasa recta lags behind that of the adjacent medullary interstitium, a transcapillary osmotic driving force exists favoring water loss from descending vessels. It is concluded that fluid uptake by the inner medullary circulation occurs beyond descending vasa recta in interconnecting capillaries or ascending vasa recta. In our view the most likely interpretation of these results is that fluid movement across vasa recta in the inner medulla is influenced by three forces: those owing to transcapillary differences in osmotic, oncotic, and hydraulic pressures.

METHODS

Young Munich-Wistar rats of either sex ranging in weight from 60 to 130 g were prepared for micropuncture of the renal papilla as described previously (8). This strain of rats possesses relatively long extrarenal papillae, approximately 1–2.5 mm in length. Micropuncture was attempted only in papillae exceeding 1 mm in length. A total of 25 rats were studied. Throughout the experiment the animals were infused with isotonic saline at a rate of 15 μl/min.

In each experiment, descending vasa recta were punctured at two sites in the papilla, as close to the tip and as close to the base as was technically possible. (Base refers to the portion of the exposed papilla opposite to the tip and next to the body of the kidney.) The distance between puncture sites varied from 0.4 to 1.1 mm. Collections of blood were spontaneous. The flow of blood in the vasa recta upstream to the pipet exhibited neither a noticeable acceleration nor deceleration. Samples of vasa recta plasma were analyzed for protein concentration in 18 rats and for osmolality in 15 rats. Femoral arterial blood was obtained for determination of systemic plasma protein concentration. In 3 rats, samples were collected from ascending vasa recta at the base of the papilla as well as from the descending vessels at the base and tip. (In the remaining animals, it proved impossible to obtain samples from all three locations due to capillary hemorrhage after puncture.) Methods for determining protein concentration and osmolality have been described before (7, 18). Data presented are the means ± SE. Paired determinations were tested for significance using the Student t test (19).

RESULTS

In 15 of 18 rats the vasa recta plasma-to-systemic plasma (VR/P) protein concentration ratio was higher in descending vasa recta at the tip than at the base of the papilla (Fig. 1). The mean plasma protein concentration and mean VR/P protein concentration ratio were significantly higher in descending vasa recta at the tip.
than at the base of the papilla, \( P < 0.01 \) (Table 1). The corresponding oncotic pressures, calculated as described previously (18), are presented in Table 1. Shown in Table 2 are individual VR/P ratios in three experiments in each of which plasma protein concentration was determined in descending vasa recta at the base and tip and in ascending vasa recta at the base of the papilla.

In 15 rats, the mean osmolality of plasma from descending vasa recta at the tip was significantly higher than that from descending vasa recta at the base of the papilla, \( P < 0.05 \) (Table 3).

The mean hydraulic pressures in descending vasa recta at base and tip in three rats are shown in Table 4. There was no statistically significant difference between mean hydraulic pressures at the two sites.

**FIG. 1.** Vasa recta-to-systemic plasma protein concentration ratios (VR/P). Prot = protein. Lines connect paired measurements of descending vasa recta (DVR) at base and tip of papilla. Where more than one vessel at a site was sampled in a single rat, results were averaged. DVR ratios are significantly higher at tip than at base, \( P < 0.01 \).

**TABLE 1.** Protein concentrations and oncotic pressures in descending vasa recta

<table>
<thead>
<tr>
<th>Structure</th>
<th>Protein Conc, g/100 ml</th>
<th>Conc Ratio, VR/P</th>
<th>Oncotic Pressure, mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVR (base)</td>
<td>5.6 ± 0.4</td>
<td>1.43 ± 0.09</td>
<td>17.7 ± 1.9</td>
</tr>
<tr>
<td>DVR (tip)</td>
<td>6.4 ± 0.4*</td>
<td>1.66 ± 0.09*</td>
<td>21.8 ± 1.9</td>
</tr>
<tr>
<td>Femoral artery</td>
<td>3.9 ± 0.1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

All values are means ± SE and are based on 18 rats. VR/P, vasa recta to femoral artery (systemic) plasma protein concentration ratio. DVR (base) and DVR (tip) refer to descending vasa recta near the base and tip of the exposed papilla, respectively. * Difference between value for DVR (base) and that for DVR (tip) is statistically significant, \( P < 0.01 \).

**TABLE 2.** VR/P ratios of protein concentration at three sites in countercurrent capillary network

<table>
<thead>
<tr>
<th>Expt No.</th>
<th>DVR (Base)</th>
<th>DVR (tip)</th>
<th>AVR (Base)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.56</td>
<td>1.94</td>
<td>1.32</td>
</tr>
<tr>
<td>2</td>
<td>1.64</td>
<td>1.81</td>
<td>1.12</td>
</tr>
<tr>
<td>3</td>
<td>1.30</td>
<td>1.93</td>
<td>1.41</td>
</tr>
</tbody>
</table>

Abbreviations: VR/P, vasa recta-to-systemic plasma; DVR (base), descending vasa recta at base of exposed papilla; DVR (tip), descending vasa recta at tip of exposed papilla; AVR (base), ascending vasa recta at base of exposed papilla.

DISCUSSION

The purpose of this study, stemming from our previous work (18), was to define more specifically the site of fluid uptake by the capillary network in the inner medulla. Determination of the protein concentration of vasa recta plasma served two functions: as a marker for water movement across the capillary membrane (18) and for calculation of capillary oncotic pressure.

The volume flux across a membrane may be described by the following relationship, obtained from linear nonequilibrium thermodynamics (11):

\[
J_v = L_p (\Delta P - \Sigma \sigma_i \Delta \pi_i)
\]

where

- \( J_v \) = transmural volume flux
- \( L_p \) = membrane hydraulic permeability
- \( \Delta P \) = transmembrane hydraulic pressure difference
- \( \Delta \pi_i \) = transmembrane osmotic pressure difference due to solute i
- \( \sigma_i \) = reflection coefficient of membrane to solute i

Water (volume) movement occurs as the result of a net imbalance between differences in transmural hydraulic pressure and opposing effective osmotic pressure. The effect on water flux of a difference in osmotic pressure due to a given solute depends on the reflection coefficient, \( \sigma \), of the membrane to that solute. By definition, if \( \sigma \) is unity, that solute exerts the full magnitude of its transmembrane osmotic pressure difference on water flux. Solutes with membrane \( \sigma \)'s less than unity exert less than the measured transmembrane osmotic pressure differences.

The Starling equation (20):

\[
J_v = L_p (\Delta P - \Delta \pi_{\text{osm}})
\]

where \( \Delta \pi_{\text{osm}} \) is the transmembrane difference in oncotic pressure (due to protein), is a special case of equation 1 in which \( \sigma_{\text{osm}} \), the reflection coefficient of the membrane to protein, is equal to unity, and \( \sigma_{\text{osm}} \Delta \pi_{\text{osm}} = 0 \), where \( \Delta \pi_{\text{osm}} \) is the osmotic pressure difference across the membrane due to the small solutes and \( \sigma_{\text{osm}} \) is the average effective reflection coefficient of the membrane to small solutes. Equation 2 has been used to describe the flux of water across capillaries in the kidney (4) and elsewhere (12).
based on the observation (16) or assumption (4, 20) that the capillary endothelia in question are virtually impermeable to protein molecules and freely permeable to all small (nonprotein) solutes in the system. With this assumption, integration of equation 2 along the length of the capillary network in the renal cortex (4) revealed a monotonic decline in plasma protein concentration within the capillaries from efferent arteriole to venule.

An earlier series of experiments (18), in which blood was sampled at two points in the countercurrent capillary network of the renal inner medulla, demonstrated a significant decrease in plasma protein concentration between descending vasa recta and ascending vasa recta at the base of the exposed papilla. This finding indicated net fluid reabsorption by the capillary network and was consistent with a model utilizing equation 2 to describe transcapillary water flux. In other words, net water flux into the capillary system was explained on the basis of an excess of an inward oncotic pressure difference (favoring water uptake) over an outward hydraulic pressure difference (favoring water loss). Transcapillary fluid uptake thus may theoretically occur along the entire medullary vasa recta, in analogy with peritubular capillaries in the cortex (4). Comparison of the plasma protein concentration in descending vasa recta at the base with that in descending vasa recta at the tip of the papilla (Fig. 1 and Table 1), however, reveals a higher protein concentration in the latter, suggesting net fluid removal from descending vasa recta.1

Since it was rarely feasible to puncture the same vas rectum at two points along its exposed length in the papilla, it was possible that descending vasa recta samples at the two sites did not belong to the same population. If the hydraulic pressure in descending vasa recta at the tip of the papilla is significantly higher than that in descending vasa recta near the base, overall water loss in descending vasa recta punctured at the base might be less than in those punctured at the tip. This would render a comparison of protein concentrations misleading with regard to water abstractions between the two sites of puncture. To examine this possibility, hydraulic pressures were measured in several descending vasa recta at the base and tip of the papilla in three rats. The results (Table 4) failed to reveal significant differences between hydraulic pressures measured at the two sites in descending vasa recta, implying that the vessels sampled at the base and at the tip are functionally from the same capillary population.

We therefore interpret the findings shown in Fig. 1 as indicating net water extraction along descending vasa recta in agreement with an earlier study of the hamster by Gottschalk, Lassiter, and Mylle (5). These data do not conflict with our previous findings (18), which demonstrated net uptake of water by the vasa recta system as a whole. Rather, the results from the two studies taken together indicate that uptake of fluid occurs beyond descending vasa recta, either in the interconnecting capillary network (15) or in ascending vasa recta, and that the magnitude of the uptake exceeds the magnitude of fluid loss from descending vessels. To confirm this interpretation, plasma protein concentrations were determined in descending and ascending vasa recta at the base of the papilla as well as in descending vasa recta at the tip in three rats. In each case the plasma protein concentration increased in descending vasa recta between base and tip and then decreased between the tip site and ascending vasa recta at the base, and by an amount in excess of—or virtually equal to—the increase in plasma protein concentration along descending vasa recta (Table 2).

The failure of equation 2 to explain the rise in protein concentration along descending vasa recta suggests that either the assumption \( \sigma_{pr} = 1 \) or the assumption \( \sigma_{ss} \Delta \pi_{ss} = 0 \), or both, are incorrect.

If \( \sigma_{pr} < 1 \) and \( \sigma_{ss} \Delta \pi_{ss} = 0 \), equation 2 becomes:

\[
J_v = L_p (\Delta \pi - \sigma_{pr} \Delta \pi_{pr})
\]

As shown in the APPENDIX, however, it is unlikely that the present finding of a rise in protein concentration along descending vasa recta coupled with our previous demonstration of net water uptake by vasa recta in the exposed papilla can be explained solely on the basis of a water flux equation, which assumes that \( \sigma_{ss} \Delta \pi_{ss} = 0 \). In particular it is demonstrated in the APPENDIX that if \( \sigma_{ss} \Delta \pi_{ss} = 0 \), then \( \sigma_{pr,AVR} > \sigma_{pr,DVR} \) and 0.175 < \( \sigma_{pr,DVR} < 0.57 \) (where \( \sigma_{pr,AVR} \) and \( \sigma_{pr,DVR} \) are reflection coefficients for protein of AVR and DVR, respectively). These requirements do not appear to be in accord with the comparative ultrastructure of descending and ascending vasa recta. Longley et al. (13) and more recently M. A. Venkatachalam and co-workers (personal communication) have observed that the ultrastructure of the endothelium of ascending vessels resembles the thin and highly fenestrated endothelium of peritubular capillaries in the renal cortex, the endothelium of descending vasa recta is much thicker, lacks fenestration, and contains infrequent intercellular junctions.

Therefore, it is probably incorrect to assume that \( \sigma_{ss} \Delta \pi_{ss} = 0 \). Equation 1 may therefore be rewritten (for \( \sigma_{pr} = 1 \)):

\[
J_s = L_p [\Delta \pi - (\Delta \pi_{pr} - \sigma_{ss} \Delta \pi_{ss})]
\]

In our view the most probable explanation for fluid removal from descending vasa recta is that those capillaries possess nonzero reflection coefficients for small solutes (\( \sigma_{ss} > 0 \)) and that a significant transcapillary difference in small solute concentration exists across the DVR (\( \Delta \pi_{ss} > 0 \)) so that \( \sigma_{ss} \Delta \pi_{ss} > 0 \). We previously observed that plasma entering the hypertonic inner medulla in descending vasa recta at normal flow rates apparently does not achieve complete osmotic equilibrium with the adjacent interstitium (9), resulting in a significant inward concentration gradient for small solutes from interstitium to capillary lumen (estimated magnitude of the gradient was approximately 75 mosmol/kg H2O (9)). Owing to the design of the present

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1 The mean VR/P protein concentration ratio in descending vasa recta at the base in rats in this study was found to be slightly lower than that in our earlier study (18). Several factors might account for this difference, including papillary interstitial osmolality and distance of puncture site from papillary tip. The difference stresses the importance of making paired comparisons in each animal.
experiments, it was not possible to determine directly if an "osmotic lag" existed between the contents of descending vasa recta and the surrounding medullary interstitium. As in indirect assessment of osmotic lag, however, one would expect to find an axial osmotic gradient within descending vasa recta from base to tip, reflecting inward diffusion of small solutes owing to a transcapillary concentration gradient. Despite some scatter, the data indeed demonstrated an axial osmotic gradient (Table 3).

Some fraction of the transcapillary concentration difference due to osmotic lag may thus serve as an effective driving force for water extraction from the capillary; that fraction is equal to the average reflection coefficient of the membrane for small solutes. For example if \( \sigma_{ss} = 0.1 \) and an average transcapillary osmotic gradient of 20 mosmol/kg H2O exists, there would be a net outward driving force of 2 mosmol/kg H2O for water extraction, which is approximately equivalent to a pressure of 38 mmHg (using van't Hoff's equation). Even if the hydraulic pressure difference across the capillary were zero and the protein concentration in the interstitium were zero (and it is likely that both are greater than zero), the maximum transcapillary oncotic pressure difference favoring water uptake by the descending vasa recta in the present study would be approximately 22 mmHg (Table 1). Therefore, in the example cited, there would exist a minimum net driving force of 16 mmHg favoring water removal from descending vasa recta in the exposed papilla.

Fluid uptake by ascending vasa recta would likewise be governed by the same driving forces as those acting across descending vessels except that the driving force due to small solutes, \( \sigma_{ss}\Delta\sigma_{ps} \), is reversed, favoring fluid uptake by the capillaries, because the concentration of small solutes would be slightly higher in ascending vessels than in the adjacent interstitium, due to osmotic lag. It is not yet possible to compare average driving forces integrated over the length of descending vasa recta with those over the length of ascending vessels. Since the protein and small solute driving forces appear to act in opposition along descending vasa recta, but in concert along ascending vasa recta, however, the magnitude of transmural water flux is probably greater in ascending than in descending vessels.

Finally, it is possible that both \( \sigma_{pr} < 1 \) and \( \sigma_{ss}\Delta\sigma_{ps} > 0 \). In this case the transcapillary driving forces exerted by small solutes would be even more effective in removing water from descending vasa recta than when \( \sigma_{pr} = 1 \) and \( \sigma_{ss}\Delta\sigma_{ps} > 0 \).

In summary, our previous findings (18) demonstrated net water uptake by the capillary network in the exposed papilla. Since the present experiments indicate water removal from descending vasa recta, net water entry into the capillary system must occur beyond descending vasa recta, either in the interconnecting capillary network or ascending vasa recta, and must exceed water extraction from descending vessels. These findings are difficult to explain on the basis of hydraulic and oncotic forces alone and, in our view, suggest that transcapillary fluid movement in the inner medulla is influenced by differences in osmotic (due to small solutes) as well as in oncotic (due to protein) and hydraulic pressures.

**APPENDIX**

To test the possibility that net filtration of plasma water in the DVR and net reabsorption of plasma water in the AVR in excess of that filtered in the DVR result solely from imbalances in oncotic and hydraulic pressures, the contribution of small solutes to transcapillary plasma water movement will be ignored, thus \( \sigma_{ss}\Delta\sigma_{ps} = 0 \). From measurements made at the base of the exposed papilla (18) it was previously established that:

\[
P_{AVR}^{VR} = 9.2 \text{ mmHg}
\]

\[
P_{AVR}^{VR} = 7.8 \text{ mmHg}
\]

\[
(p_{VR})_{APR} = 26 \text{ mmHg}
\]

\[
(p_{VR})_{APR} = 18 \text{ mmHg}
\]

where \( P \) and \( (p_{VR})_{APR} \) refer to the intracapillary hydraulic and oncotic (due to protein, PR) pressures, respectively, and the superscripts designate AVR or DVR. Therefore, at the base of the exposed papilla:

\[
P_{AVR}^{VR} - P_{AVR}^{VR} = 1.4 \text{ mmHg}
\]

and for a constant value of interstitial hydraulic pressure, \( P_{i} \), at the base:

\[
\Delta P_{AVR}^{VR} = \Delta P_{AVR}^{VR} = 1.4 \text{ mmHg}
\]

where \( \Delta P = P_{i} - P_{i} \), Also, at the base of the exposed papilla:

\[
(p_{VR})_{APR} > (p_{VR})_{APR}
\]

and for a constant value of interstitial oncotic pressure, \( (p_{VR})_{APR} \), at the base of the exposed papilla:

\[
(p_{VR})_{APR} > (p_{VR})_{APR}
\]

Since it is not possible from available data to ascertain unequivocally that there is water filtration or reabsorption occurring in either AVR or DVR at the base of the exposed papilla, four possible cases must be examined:

*case 1:* water reabsorption in DVR and water filtration in AVR at base

*case 2:* water reabsorption in DVR and AVR at base

*case 3:* water filtration in DVR and AVR at base

*case 4:* water filtration in DVR and water reabsorption in AVR at base

Given that there is net water filtration by DVR and net water reabsorption by AVR, cases 1–3 require that a reabsorption mode change to a filtration mode at some point along the capillary between DVR and AVR at the base.

Deen et al. (3) have demonstrated for the glomerular capillary when \( \sigma_{pr} = 1 \) and \( \Delta P = \Delta \pi_{pr} \), that \( d(\Delta \pi_{pr})/dx = 0 \), that is, the axial capillary (\( \Delta \pi_{pr} \)) profile must reach an extremum when it intersects the axial \( \Delta P \) profile. Since in the vasa recta, \( \sigma_{pr} \approx 1 \), it is not immediately evident that an analogous extremum property exists for this capillary network. To examine this possibility, the following relationship must be considered.

\[
Q = \frac{m}{C}
\]

where, \( Q \) is the volumetric plasma flow rate and \( m \) and \( C \) are the mass flow rate and concentration of plasma protein, respectively. Since each of these quantities is axially dependent, differentiation of equation 9 gives,

\[
dQ/dx = -(m/C) dC/dx + (1/C) dm/dx
\]

where \( x \) is the axial length coordinate along the vasa recta. When \( \Delta P = (\sigma_{pr})_{APR} \) become equivalent, a transcapillary force for water movement ceases to exist and,

\[
dQ/dx = -dC/dx = dm/dx = 0
\]

Consequently, even when \( \sigma_{pr} = 1 \), \( d(\Delta \pi_{pr})/dx = 0 \) when \( \Delta P = (\sigma_{pr})_{APR} \).
Consider cases 1 and 2, both of which assume that water is reabsorbed in DVR at the base. This requires that $\Delta P_{\text{DVR}} < (\sigma \Delta p)_{\text{DVR}}$ at the base. However, since that inequality must be reversed at some point along the DVR to explain the net water filtration which was observed, equation 11 requires that at this point of equilibration, i.e., where $\Delta P_{\text{DVR}} = (\sigma \Delta p)_{\text{DVR}}$ that:

$$\Delta \pi \frac{d\pi_{\text{G}}}{dx} < d\Delta P/dx < 0 \text{ (at the equilibration point) } (12)$$

Since the point of equilibration will, in general, change location with, e.g., alterations in blood flow rate, it is highly unlikely that equation 12 will be satisfied at all possible sites of equilibration along DVR. A similar argument applies to case 3, wherein water is filtered from AVR at the base. Consequently, although it is possible that any of the combinations of water reabsorption and filtration given by cases 1-3 may indeed occur in DVR and AVR at the base, this is improbable since the reflection coefficients of DVR and AVR protein are required to vary in a very restrictive manner, as evidenced by equation 12.

There still remains case 4 in which water is filtered in DVR and reabsorbed by AVR at the base. Water filtration in DVR at the base requires that:

$$\Delta P_{\text{DVR}} > (\sigma \Delta p)_{\text{DVR}} \text{ (at the base) } (13)$$

and water reabsorption in AVR at the base requires that:

$$(\sigma \Delta p)_{\text{AVR}} > \Delta P_{\text{AVR}} \text{ (at the base) } (14)$$

Since the values of $(\sigma \Delta p)_{\text{DVR}}$ and $(\sigma \Delta p)_{\text{AVR}}$ remain indeterminate, the following three possible situations need to be considered:

- $a) \sigma_{\text{DVR}} = \sigma_{\text{AVR}}$
- $b) \sigma_{\text{DVR}} > \sigma_{\text{AVR}}$
- $c) \sigma_{\text{DVR}} < \sigma_{\text{AVR}}$

To facilitate the comparison among these three possibilities, a plot of $P_i$ versus $(\pi_i)_{\text{inter}}$ is given in Fig. 2. The lines shown in this figure are acquired from equations 13 and 14 together with the experimental values of $P_i$ and $(\pi_i)_{\text{inter}}$ at the base of the papilla listed at the beginning of the Appendix. The heavy line labeled $\sigma_{\text{DVR}} = \sigma_{\text{AVR}} = 0.175$ is obtained using either of the following equations:

$$9.2 - P_i = (0.175) (26 - \pi_i) (13a)$$
$$7.8 - P_i = (0.175) (18 - \pi_i) (14a)$$

and separates the regions $0.175 > \sigma_{\text{DVR}} > \sigma_{\text{AVR}}$ and $\sigma_{\text{DVR}} < \sigma_{\text{AVR}} < 1$ indicated by the respective labels within the rectangles on the figure. The choice $\sigma_{\text{DVR}} < \sigma_{\text{AVR}} = 0.175$ is discussed in the next section. The heavy line labeled $\sigma_{\text{DVR}} = 1$ is derived from the equation:

$$7.8 - P_i = (18 - \pi_i)$$

and separates the region $\sigma_{\text{DVR}} > \sigma_{\text{AVR}} = 1$ and $\sigma_{\text{DVR}} < 1$ indicated by the respective labels within the rectangles on the figure. The light lines shown in the figure are derived from the equation:

$$9.2 - P_i = \sigma_{\text{DVR}} (26 - \pi_i) (13b)$$

where $\sigma_{\text{DVR}}$ assumes the values indicated by the equations on the lines. Consider now each of the three cases individually:

- $a) \sigma_{\text{DVR}} = \sigma_{\text{AVR}}$

In this case, it follows from equations 8, 13, and 14 that:

$$\Delta P_{\text{DVR}} > (\sigma \Delta p)_{\text{DVR}} > (\sigma \Delta p)_{\text{AVR}} > \Delta P_{\text{AVR}}$$

Combining this equation with equation 6 indicates that:

$$\sigma_{\text{DVR}} (\Delta P_{\text{DVR}} - \pi_i - \pi_c + \pi_i)_{\text{inter}} < 1.4 \text{ mmHg} \tag{15}$$

Since $\sigma_{\text{DVR}} < 0.175$, the case that $\sigma_{\text{DVR}} = \sigma_{\text{AVR}}$ and $(\sigma \Delta p)_{\text{AVR}} = 0$ is unlikely.

- $b) \sigma_{\text{DVR}} > \sigma_{\text{AVR}}$

This case corresponds to the region where $0.175 > \sigma_{\text{AVR}}$ and is shown as the stippled area in the upper left-hand portion of Fig. 2. Again, since this is unlikely, the assumption that $\sigma_{\text{DVR}} > \sigma_{\text{AVR}}$ and $\sigma_{\text{DVR}} < 1$ is unlikely, the assumption that $\sigma_{\text{DVR}} > \sigma_{\text{AVR}}$ and $(\sigma \Delta p)_{\text{AVR}} = 0$ is unlikely.

The clear area shown in Fig. 2 corresponds to the region in which the inequality holds and in which $(\sigma \Delta p)_{\text{AVR}} < 1$. This region also encloses reasonable values for $P_i$ and $(\pi_i)_{\text{inter}}$. The lower bound for $\sigma_{\text{DVR}} = 0.175 - 0.175$ and the upper bound is $\sigma_{\text{DVR}} = 0.57$ (at which point $(\sigma \Delta p)_{\text{AVR}} = 1$ and $P_i = 0$). As the physiologically unacceptable lower bound for $\sigma_{\text{DVR}}$ increases (indicated by the light lines), the region of validity decreases. At $\sigma_{\text{DVR}} = 0.57$, $\sigma_{\text{AVR}} = 1$ and for $\sigma_{\text{AVR}} > 0.57$ no region will exist such that $\sigma_{\text{DVR}} < 1$ and $\sigma_{\text{AVR}} < \sigma_{\text{AVR}}$.

It appears likely from these results that $(\sigma \Delta p)_{\text{AVR}} = 0$, that is, small solutes do play a role in the transcapillary exchange of plasma water in the vasa recta. To explain water removal from the DVR solely on the basis of imbalances between oncotic and hydraulic pressures, it becomes necessary to restrict $\sigma_{\text{AVR}}$ such that $I) \sigma_{\text{AVR}} < \sigma_{\text{AVR}}$ and $2) 0.175 < \sigma_{\text{AVR}} < 0.57$. As noted in the discussion, morphological observations suggest that the first restriction is unlikely. However, in order to exclude alternatives and to assess the magnitude of the effective driving forces for water flux due to transcapillary differences in small solute concentrations, $\sigma_{\text{AVR}}$ and $\sigma_{\text{AVR}}$ need to be determined.

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