THE EXCRETION OF SULFATES BY THE DOG

ARNOLDUS GOUDSMIT, JR., MARSCHELLE II. POWER AND JESSE L. BOLLMAN

From the Division of Biochemistry and Division of Experimental Medicine, The Mayo Foundation, Rochester, Minnesota

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Among the first studies inspired by Cushny's theory of renal function was the one undertaken by Mayrs, who investigated the excretion of sulfates as compared with the elimination of a number of other substances. He injected sodium sulfate intravenously into rabbits in order to raise the concentration of sulfate in the plasma to allow its determination with a sufficient degree of accuracy and found that sulfates were concentrated approximately twice as much as urea (maximum: 2.75, minimum: 1.50). In a subsequent series of experiments the degree of concentration of sulfates ("concentration ratios") was compared with that of phosphates and of creatinine and all these values were found to be approximately the same.

White could not find as satisfactory agreement between ratios of concentration of different substances as compared with the concentration ratio of sulfates and concluded that "no fixed rule such as Cushny sought to apply in his 'modern theory' can be assigned to the process of sulphate elimination." The same investigator, in collaboration with Monaghan, in a subsequent study of phlorhizinized dogs was led to recognize the important fact that "the sulphate clearances are always greater with high plasma sulphate levels than with normal, with rough proportionality."

In man the endogenous sulfate clearances were studied by Macy, who reported that they were 10 to 50 per cent less than those of urea. Cope found essentially analogous clearance ratios. He could not discover any influence of moderately increased sulfate levels as obtainable by the oral administration of sodium sulfate on sulfate clearance. Hayman, on the other hand, recognized a very definite tendency of the concentration ratio of sulfates to approach that of creatinine after the intravenous administration of the former.

In the last few years, thanks to the work of Richards, Smith and Shannon, and Van Slyke and co-workers along the lines of Cushny's theory, the equality of the clearances of creatinine, inulin and ferrocyanide in dogs has been firmly established. Apparently the magnitude of these clearances at the same time indicates the extent of glomerular filtration. Generalizing, it can be said that in the dog a rate of excretion in excess of simul-
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simultaneously determined creatinine, inulin or ferrocyanide clearances is considered very widely as strongly suggestive evidence of active secretion by the tubules, whereas rates of excretion below the clearance of one such standard test substance would be indicative of tubular reabsorption.

In the study which is to follow, the excretion of sulfate has been studied in the dog under a variety of conditions and has been compared with the simultaneous excretion of injected creatinine.

PHYSIOLOGIC PROCEDURE. All dogs were between 10 and 15 kgm. in weight and they all received a standard diet consisting of 38 per cent horse meat, 35 per cent cracker meal, 15 per cent cooked tomatoes, 8 per cent lard and 4 per cent bone ash. This diet was fed in amounts calculated to be the equivalent of twice the basal caloric requirement for the individual animal. Until the beginning of each experiment water was allowed ad libitum. Food was withheld for periods of from seventeen to twenty-four hours preceding the experiment.

In most experiments in order to obtain a desirable volume of urine, 200 to 500 cc. of tap water were introduced by stomach tube before the beginning of the clearance periods; also, 400 to 800 cc. of a 0.64 to 0.72 per cent solution of sodium chloride was given intravenously. The beginning of the clearance periods was preceded by the intravenous injection of 1 cc. of a 10 per cent solution of creatinine per kilogram body weight. Immediately after this, administration of additional creatinine was started in order to maintain its level in the plasma. This was accomplished by the intravenous injection at a constant rate (by means of a Woodyatt pump) of approximately 200 cc. per hour of a solution containing 0.3 per cent creatinine and 5 per cent d-glucose ("creatinine maintenance solution"), the d-glucose serving the purpose of making the solution approximately isotonic to the blood.

Twenty to thirty minutes after the beginning of the injection of the "creatinine maintenance solution" the bladder was emptied. Usually twenty-five minutes was allowed for each clearance period, in the middle of which blood was drawn.

In those experiments in which the rate of excretion of sulfate was investigated at plasma concentrations higher than normal, the increased plasma level was obtained by the intravenous administration of sodium sulfate in a 10 per cent solution. When larger amounts were being given the rate of injection amounted to 5 cc. per minute. A rise of approximately 20 mgm. of sulfate (expressed as SO₄) per 100 cc. of plasma was found to result from the introduction of 100 mgm. of sodium sulfate per kilogram body weight. Maintenance of the concentration of sulfate in the plasma so reached was attained by the addition of suitable amounts of sodium sulfate to the "creatinine maintenance solution."

CHEMICAL PROCEDURES. The blood after it was drawn was mixed with
heparin in a 15 cc. graduated centrifuge tube. In those instances in which the hematocrit value was determined, the total amount of blood in the sample was noted and the volume of the packed erythrocytes was determined after centrifugation for two hours at a speed of 2,800 revolutions per minute and a temperature of 1.5°C.

Sulfates in plasma and urine were determined volumetrically on trichloracetic acid filtrates after precipitation with benzidine according to the method of Power and Wakefield.

Creatinine in the plasma was determined in tungstic acid filtrates; the color was developed essentially according to the method of Folin and Wu, using an alkaline picrate solution. The resulting colors were compared with those developed in two standard solutions, using the Goudsmit-Summerson variable layer photoelectric comparison photometer as a measuring instrument.

Creatinine in the urine was determined on portions containing approximately 1 mgm., essentially according to the method of Folin, and in the manner described for the determination in the blood.

Calculation. "Clearances" throughout this study have been calculated as: concentration of substance in the urine \times \text{volume of urine in cubic centimeters per minute.} In all instances the "clearance ratio," viz., sulfate clearance/creatinine clearance, has been calculated and used in preference to the sulfate clearance itself. Creatinine clearances have been calculated without correction for "endogenous" creatinine values, since Goudsmit has shown that the "endogenous" creatinine disappears from the blood flowing through the kidney at a rate rather similar to the one ("extraction percentage") which Van Slyke, Hiller and Miller determined for exogenous creatinine. Thus the clearance of the "endogenous plus exogenous" creatinine equals that of "exogenous" creatinine alone.

Clearance ratios have been calculated to three decimal places (e.g., 0.103) because we believe that two would not do full justice to the consistency of our findings. It is realized that the third decimal place cannot be relied on to the full extent of its value. Equally the value 1.063 has its third decimal place included only for the sake of uniformity; in itself, 1.06 covers all the accuracy that can be claimed.

Results. Since a substance in order to be available for glomerular filtration should be present in the plasma in a freely diffusible state, ultrafiltration studies were carried out on three different samples of serum. After having been placed in collodion sacks, the samples were subjected to a pressure not exceeding 30 cm. of mercury. The results, seen in table 1, clearly indicate that most of the sulfate present in dog's serum, if not all, is ultrafiltrable through a collodion membrane. This is in agreement
with the observations of Hayman on human blood serum and, together with the observation that sucrose and sulfate, after their intravenous injection, are distributed in the same fashion throughout the fluids in the body, (12, 15) meet, in great part at least, the statement of Peters: "Until the permeability of vascular and cellular membranes to sulfates has been determined, it is futile to attempt an analysis of the mode of excretion of this ion."

**Sulfate clearance at normal (endogenous) concentrations of sulfate in the plasma.** A total of twenty-nine clearance periods have been available for analysis. They were obtained on six dogs, to none of which sulfate had been administered in any form (except for whatever small amount was contained in their diet) for a period of at least two weeks preceding the experiment.

The normal concentration of sulfate in the plasma of dogs was found to vary between 11.5 and 18 mgm. of SO$_4$ per 100 cc. of plasma, most of the values falling between 12 and 15 mgm. In one instance after the administration of 1,500 cc. of water partly by the oral and partly by the intravenous route, values as low as 10.4 mgm. were recorded.

In figure 1 the clearance ratios obtained at normal plasma levels have been plotted against urine volume. As can be seen, the scattering is fairly large; still the general shape strongly suggests an increase of the clearance ratio as the extent of diuresis rises. In other words, no "aug-
mentation limit" can be demonstrated to enter into the mechanism of elimination of sulfates in the dog. A similar situation might well exist with regard to the excretion of sulfates in man, although Hayman did not choose to interpret the clearances plotted in his graphs in this manner. In this connection it seems worthy of note that Shannon found in dogs a progressive increase of the ratio of urea clearance to creatinine clearance with increased urinary volume without its ever reaching a point which could be termed an augmentation limit. Recently figures have been presented indicating that in man, too, "there is a progressive increase in the urea clearance as the urine flow increases from low to high values" (4).

![Diagram of sulfate:creatinine clearance ratios at increased concentration of sulfate in the plasma.](http://ajplegacy.physiology.org/)

**Fig. 2.** Sulfate: creatinine clearance ratios at increased concentration of sulfate in the plasma.

*Sulfate clearance at increased concentrations of sulfate in the plasma.* In figure 2 fifty-six individually observed ratios of sulfate clearance to creatinine clearance obtained in eight different experiments on three different dogs have been plotted against the concentration of sulfates in the plasma. Details about an illustrative individual experiment and the actual results on the analytic data obtained, as well as clearance ratios calculated from those data, are recorded in tables 2 and 3. As can be seen, SO₄ concentrations as high as 259 mgm. per 100 cc. of plasma have been reached and a total of six clearance periods at levels of over 215 mgm. have been included. At these high levels sulfate clearance ranges between 89 and 95 per cent of the creatinine clearance. At lower plasma levels the ratio becomes slightly smaller; however, at levels between 30 and 40 mgm. of SO₄ per
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100 cc. of plasma the clearance ratio ranges between 56 and 76 per cent, the average being very close to 70 per cent. It is apparent that between the concentrations of \( \text{SO}_4 \) in the plasma of 30 and 259 mgm. per 100 cc.

### TABLE 1

Concentrations of sulfate in dog’s serum and in its ultrafiltrate

<table>
<thead>
<tr>
<th>EXPERIMENT</th>
<th>SULFATE, MGM. PER 100 CC.</th>
<th>CHLORIDE, MGM. PER 100 CC.</th>
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<td>Ultrafiltrate</td>
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<tr>
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</tr>
<tr>
<td></td>
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</tr>
<tr>
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<tr>
<td></td>
<td>14.7</td>
<td>12.7</td>
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</tbody>
</table>

### TABLE 2

Illustrative protocol

Experiment 2. Dog T359, \( \sigma \), weight 12.4 kgm. Date 1/24/38

- 10:25 a.m. 500 cc. 0.8 per cent solution of NaCl by stomach tube.
- 10:39 Intravenous administration of solution A (see below) started at a rate of 200 cc. per hour.
- 10:51-10:53 12.4 cc. 10 per cent solution of creatinine intravenously.
- 11:15 a.m.-12:55 p.m. Clearance periods 1 to 4 inclusive.
- 1 to 3 Solution B substituted for solution A; intravenous infusion continued at same rate.
- 1:10 to 1:35 Intravenous administration of 125 cc. of 10 per cent solution of \( \text{Na}_2\text{SO}_4 \) (in addition to continuous injection of solution B).
- 1:23 Dog vomited approximately 100 cc. of greenish-yellow fluid.
- 1:46 to 3 Clearance periods 5 to 7 inclusive.
- 3 Intravenous administration of solution A substituted for that of solution B.
- 3 to 5:05 Clearance periods 8 to 12 inclusive.

**Solution A**

(“Creatinine maintenance solution”)

- Glucose .................. 50 gm.
- Creatinine ............... 3 gm.
- Distilled water to make 1000 cc.

**Solution B**

- Glucose .................. 25 gm.
- Creatinine ............... 1.5 gm.
- Sodium sulfate .......... 18 gm.
- Distilled water to make 500 cc.

of plasma no consistent differences are seen between clearance ratios obtained at rising and those obtained at falling concentrations of sulfate in the plasma (indicated by different symbols).

The question could be raised here whether the fact that sodium sulfate
acts as a diuretic is not responsible for these high clearance ratios. However, at normal concentrations of sulfate in the plasma, even higher urinary volumes were observed without the clearance ratio rising to more than a fourth the ratios obtained at high plasma levels. In addition, in no instance did we find a significant change of creatinine clearance attributable to the injection of these large amounts of sodium sulfate. Finally, bringing out the point that this increase of clearance with concentration is not a generally accepted pattern of excretion of end products of metabolism: an increase in the concentration of urea in the blood does not increase its clearance to any appreciable extent, no greater certainly than could be

<table>
<thead>
<tr>
<th>PERIOD</th>
<th>BLOOD</th>
<th>URINE</th>
<th>CLEARANCES</th>
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<td>Cl</td>
</tr>
<tr>
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<td>mgm. per min.</td>
<td>mgm. per min.</td>
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<td>9</td>
<td>25</td>
<td>1.56</td>
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</tr>
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* Interpolated.

attributed to the increased urinary volume (cf. also Addis and Drury; Drury).

*Retardation of readjustment of clearance of sulfate after its intravenous administration.* From 30 mgm. of SO₄ per 100 cc. of plasma on downward there is a sharp drop of the ratio of sulfate clearance to creatinine clearance down to the range recorded as normal. However, a complicating factor here enters the picture, viz., that—in contradistinction to what happens at higher concentrations, as previously mentioned—the sulfate clearance ratio with falling plasma concentrations tends to be higher than that observed at rising concentrations (the actual concentration being the same in both cases).
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This point was investigated further in two dogs in which the ratios of sulfate clearance to creatinine clearance were determined before and after the injection of sufficient sodium sulfate to raise the plasma level to approximately 30 mgm. per 100 cc. and the clearance ratios to approximately 0.70. The results of these experiments are shown in figure 3 and appear to indicate 1, that the ratio of sulfate clearance to creatinine clearance (the creatinine clearance remained essentially constant) does not return to the control level as promptly as does the plasma sulfate, and 2, that the ratio of sulfate clearance to creatinine clearance may be even lower than the control levels when examined after a greater lapse of time after discontinuance of the sulfate injection (twenty-two hours).

**Effect of extra sulfate in the diet on renal clearance.** One animal was given 5 gram doses of sodium sulfate daily in his food. No influence on the concentration of sulfates in the serum was found after prolonged adminis-
Figure 1 includes the results of the study of this dietary factor on the rate of excretion of sulfates. As can be seen, all three periods examined reveal a ratio of sulfate clearance to creatinine clearance exceeding any others obtained at comparable rates of urinary flow either in the same or in any other animal. Thus it would seem justifiable to conclude that a real increase was obtained. After discontinuing the extra sulfate in the diet the clearance ratio dropped back to normal.

Results of attempts to obtain concentrations of sulfate higher than 260 mgm. per 100 cc. of plasma. In view of our experiences with sulfate clearances at concentrations up to 260 mgm. per 100 cc. of plasma it seemed worth while to try to examine the excretion at still higher levels. This seemed justifiable since two animals had been able to stand concentrations of between 230 and 260 mgm. per 100 cc. quite well except for the vomiting which both of them had shown during the period of rising levels of sulfate in the blood. Thus, in a dog of 13.9 kgm., after ample fluids had been administered orally as well as by vein, three clearance periods were studied under standard conditions. An average creatinine clearance of 64.6 cc. per minute was observed; the average urinary volume amounted to 10.7 cc. per minute. Next the animal received intravenously 225 cc. of a solution of 5 per cent Na₂SO₄ and, in addition to that, was given at a constant rate of 300 cc. per hour, a solution containing 74.2 grams of Na₂SO₄, 33 grams of d-glucose, and 2 grams of creatinine per liter. A very abundant diuresis ensued.

After one and a half hours the animal appeared to be in a poor condition so that the injection had to be discontinued; 500 cc. of 5 per cent solution of d-glucose were administered during the following twenty minutes. After this the dog seemed to have recovered to some extent and the constant injection was re instituted. Two consecutive clearance periods of ten minutes each were obtained at this stage with the following results: plasma SO₄ 325 and 353 mgm. per 100 cc. respectively; sulfate clearance 67.4 and 50.9 cc. per minute and creatinine clearance 63.4 and 49.2 cc. per minute. The flow of urine amounted to 31.2 and 22.5 cc. per minute. Ratios of sulfate clearance to creatinine clearance calculated from these data amounted to 1.063 and 1.035 respectively. It is felt that this indicates very close approximation of both clearances at this level of sulfates in the plasma such as might be expected in view of the general trend of this ratio as indicated earlier in this paper and as illustrated in figure 2. It would seem erroneous, however, to assign too much value to the fact that the ratio is greater than unity, since the circumstances under which this part of the experiment was conducted were not as favorable as is considered necessary to form the basis of more far-reaching conclusions.

Five minutes after the last clearance period was concluded the animal died. Anatomically no apparent cause of death could be found. The
kidneys, which together weighed 90 grams, did not show any gross abnormalities. Microscopic study revealed a rather wide space between the capillaries of the glomeruli and Bowman's capsule. A slight degree of degeneration was visible in the tubular cells.

Chemical analysis of the blood taken twenty and ten minutes before death showed chlorides to be 314 and 315 mgm. per 100 cc. respectively (before sulfate administration, between 367 and 373 mgm.). Thus, judged by the sum total of sulfates and chlorides, the electrolyte concentration had been increased from 106.5 to 161.5 m. eq. per liter. One cannot help feeling that this upset of ionic concentration was one, possibly a very important, cause of rapid failing of the animal.

A similar experiment on another dog was equally unsuccessful in maintaining the life of the animal. One hour and fifteen minutes after the beginning of the injection of sodium sulfate (i.e., after the animal, which weighed 10.2 kgm., had received approximately 37.5 grams of Na₂SO₄) the blood contained 372 mgm. of SO₄ per 100 cc. and the chlorides had dropped to 298 mgm. Very shortly afterward, after muscular twitchings had been noted, the animal was seized by violent convulsions. It died approximately one and a half hour after the administration of sulfates had been discontinued. The blood removed at the height of the concentration of sulfate contained 56.5 more m. eq. of sulfate plus chloride per liter of plasma than at the outset of the experiment. Interestingly enough, the increase in sodium amounted to 130 mgm. per liter (equaling 56.5 m. eq.). A careful check of the fluid balance during the experiment had obviated dehydration as a factor in the fatal outcome (total intake 2,300 cc.; output of urine plus vomitus 1,400 cc.).

Since these experiments were concluded we noticed the very recent publication of Amberson, Nash, Mulder and Binns, who found that the cat, through diuresis induced with "sulfate-Ringer" solution, never gives up more than 25 per cent of its plasma chloride. Judged by the results of our experiments, the cats, if their mechanism of excretion of sulfates is similar to that of dogs, should have had little difficulty in excreting the sulfate at the same rate as it was being administered, thus obviating the necessity of excreting additional chlorides. By the use of total plasmapheresis, however, these investigators were able to reduce plasma chlorides to 7 millimols per liter. Since their artificial serum contained 106.9 millimols of sulfate the assumption seems justifiable that the concentration of sulfate reached in their experiments approached 100 millimols per liter of plasma or 960 mgm. per 100 cc. Some of their animals, at this stage, were still in comparatively good shape. Thus it would seem that in our experiments one reason for the failure to push the concentration of sulfate higher than 350 mgm. per 100 cc. of plasma is related to the failure of the body (kidney) to excrete chlorides as more sulfate is being administered.
One pertinent question regarding the significance of sulfate clearances in dogs should be raised here: viz., to what extent does sulfate clearance define kidney function? A tentative answer may be obtained from a consideration of table 4, in which the results of two different experiments, two weeks apart, on the same dog are recorded. The sulfate clearances at normal concentrations of sulfate in the plasma were practically the same on both days (the average volume of urine per minute was nearly identical). On January 31, 1938, after the administration of an appropriate amount of sodium sulfate, a sulfate clearance of 43.8 cc. per minute was observed at a concentration of sulfates in the plasma of 225 mgm. per 100 cc. and two weeks later at a concentration in the plasma of 28.9 mgm. per 100 cc. the sulfate clearance amounted to 51.0 cc. per minute (all values are averages; the statistical spread is insignificant). Since the sulfate clearances in the control periods were practically the same on both days the conclusion would seem justifiable that at moderately elevated concentrations (region of 28.9 mgm. per 100 cc. of plasma) the clearance is 16.5 per cent higher than at much higher concentrations of sulfate in the plasma. Thus, all that one would have gained from these data, statistically significant by themselves, is confusion. However, once the proper emphasis is given to the creatinine clearances in the period under observation it becomes evident that the condition of the kidney in the “control” periods was not the same even though this was not revealed by a difference in “endogenous” sulfate clearance. And, after they have been properly related to the creatinine clearances, the seemingly contradictory sulfate clearances at increased plasma levels can be fitted easily within a comprehensible picture of the excretion of sulfates.

COMMENT. White, in 1923, summarized his studies of the excretion of sulfate in the dog as follows: “The elimination of sulphate in the urine is regulated by factors which are as yet quite obscure.” We believe that the present study brings out the importance of a number of definite factors.
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which are operative in the elimination of sulfates and which in terms of the filtration-reabsorption theory may be described as follows:

Sulfate is present in the glomerular filtrate in the same concentration as in the plasma. Although direct proof is lacking this seems a logical deduction from our knowledge of the distribution of sulfate over the fluids of the body as well as from the ultrafiltration studies reported in this paper and those of Hayman.

Approximately 90 per cent of the endogenous sulfate is reabsorbed by the tubules. Among factors operative in adjusting the exact extent of reabsorption, nonspecific ones might be contrasted to specific ones. The former category, so far as this investigation has been able to uncover, reveals only urinary volume (extent of diuresis) as a definite factor. Further investigation may reveal other important factors. Since reabsorptive processes apparently play so much more predominant a role in determining the extent of elimination of endogenous sulfate than the process of filtration, the possibility seems to exist that a better insight into the functional role of the tubules might be gained from the study of sulfate excretion in conjunction with the determination of the rate of excretion of substances which measure glomerular filtration.

As far as sulfate as a factor influencing sulfate clearance is concerned (the “specific” factor), the most outstanding feature is the great increase which sulfate clearance undergoes after introduction of extra sulfate into the blood stream. Judged by the general slope of the curve (fig. 3) the ratio of sulfate clearance to creatinine clearance appears to approach unity at increasing concentrations of sulfate in the plasma. Its shape becomes readily understandable if it is assumed that a rather definite amount of sulfate is always being reabsorbed regardless of the absolute concentration in the plasma. If the equivalent of approximately 12 mgm. of SO₄ per 100 cc. is being reabsorbed by the tubules (actually 12/100 × F where F represents creatinine clearance [glomerular filtrate] in cubic centimeter per minute) then at a “normal” concentration of approximately 13 mgm. per 100 cc. of plasma roughly 92 per cent is being reabsorbed. At a plasma level of 24 mgm. of SO₄ per 100 cc. this fraction is reduced to 50 per cent, at 36 mgm. per 100 cc. it amounts to 33.3 per cent, and at concentrations of 240 mgm. SO₄ in the plasma the reabsorption would amount to only 5 per cent of the amount filtered. The ratios of sulfate clearance to creatinine clearance at the respective levels would amount to 0.077, 0.500, 0.667, and 0.950 respectively figures which fit well into the picture of figure 2.

It would seem that the mechanism of excretion described above simply represents a closer picture of what happens in the excretion of many of the so-called “threshold substances.” The threshold, however, is not a rigid one: in the case of sulfate it was found to be lowered after the intravenous
administration of sodium sulfate (i.e., there was less reabsorption for a
time), even after enough time had elapsed to allow the concentration in the
blood to come back to normal. Somewhat later (twenty-four hours) the
threshold had become raised (reabsorption taking place in amounts larger
than normal) and finally it returned to normal.

Another striking example of the ease with which "thresholds" adapt
themselves to changing circumstances is given by the behavior of the
chlorides in the case of the experiment summarized in table 3. During
the time that the chlorides in the plasma are lowest—which, incidentally,
is the period when the concentration of sulfates is highest—their excretion
with the urine is highest and with every step of increase of concentration
of chlorides in the plasma (and decrease in concentration of sulfates) a
decrease of the amount of chloride excreted is noted. In this connection
we might recall the experiment where the failure to get rid of a sufficiently
large fraction of the chlorides was considered a prominent factor in the
causation of death of the animals receiving large doses of sulfate. Thus,
this threshold-mechanism might not at all times be operating to the ad-
vantage of the individual.

As far as dietary factors are concerned, our limited data certainly sug-
gest that feeding of extra sulfate with the diet causes a rise in sulfate
clearance without affecting the creatinine clearance and without increasing
the concentration of sulfate in the blood.

The sulfates present in the urine are derived mainly from the sulfur com-
bined in the proteins of the food and tissues and, under normal metabolic
conditions in man and dog, amount to 80 to 90 per cent of the total sulfur
excreted. Thus, on a comparable intake of protein different individuals
should excrete a comparable amount of sulfate. From the standpoint of
renal physiology two ways are open to bring about this elimination: 1,
if the level in the blood is relatively low, not too much is reabsorbed by the
tubules from the total amount present in the glomerular filtrate; i.e., the
clearance is relatively high; 2, if the concentration in the blood is rather
high, much reabsorption can take place and still sulfur intake and output
may be balanced; i.e., the clearance is low. Interestingly enough, man,
with a sulfate concentration in the blood of approximately 3.5 mgm. per
100 cc. and a clearance of approximately 30 per cent of the sucrose clear-
ance (Keith, Power and Peterson), belongs in the former group, whereas
the dog, with 13 mgm. of SO₄ per 100 cc. of plasma and a clearance of only
8 to 10 per cent of the creatinine clearance, represents an example of the
mechanism discussed under (2). As can be readily seen, the actual amount
excreted relative to the extent of glomerular filtration is practically the
same in both species. We do not believe that facts are available at present
which would explain why species differ in this respect.

As mentioned in the beginning of the article, all results have been ob-
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The excretion of sulfate has been studied in dogs. Clearances at the naturally occurring concentrations of sulfate in the plasma amount to approximately 8 per cent of the creatinine clearance. Extent of diuresis (urinary volume per unit of time) has a definite influence on the sulfate clearance.

All, or nearly all, of the sulfate in the serum of dogs can be considered filtrable through collodion membranes.

After the intravenous injection of sulfate its clearance rises markedly and at very high concentrations of sulfate in the plasma it approaches that of creatinine.

The significance of these findings is discussed in terms of the filtration-reabsorption theory and the physiologic implications of this mechanism of a “threshold” are commented on.

The importance of measuring “glomerular filtration” during the periods in which sulfate excretion is studied is stressed.

In view of the great influence of tubular reabsorption in determining the exact extent of the excretion of sulfates at normal concentrations in the plasma—particularly in the dog—it is suggested that more extensive investigation of the elimination of sulfates in connection with studies of renal physiology might prove to be a definite aid in appraising relative tubular activity.

REFERENCES