The Salt-Secreting Gland of Marine Birds

By Knut Schmidt-Nielsen, Ph.D.

Marine birds possess salt-secreting nasal glands which produce hypertonic solutions of sodium chloride in response to osmotic loads such as ingestion of sea water. The concentration of the secreted fluid is always high, several times as high as the maximum urine concentration in birds. The presence of this gland must be considered a necessary adaptation to marine life in animals whose kidney cannot excrete high salt concentrations. The structure and blood supply to the gland indicate a countercurrent flow, but at the moment it is not possible to explain the high concentrations of the secreted fluid as the result of a countercurrent multiplier system. The gland is under parasympathetic nerve control; its secretory function is blocked by anesthesia and certain drugs, including carbonic anhydrase inhibitors.

The Comparative Viewpoint

THE SUBJECT which I am going to deal with can, I think, be referred to as comparative physiology. Renal physiologists have more sophistication in comparative physiology than most other physiologists. They are used to discussing animals such as alligators and frogs and the very interesting and unique aglomerular fish, which has a kidney but no glomeruli. Names such as Marshall, Smith, Forster and others testify to the value of a comparative approach in renal physiology.

This leads me to say, without hesitation, something which might have seemed startling a few years ago, but, I am sure, will not be very surprising to most of this audience; that is, that the kidney is not always the most important organ of excretion, and, in fact, that the mammals constitute the only class of vertebrates in which the kidney is always the major organ of osmoregulation.

To explain this statement, it is helpful to review briefly the physiologic conditions for life in the sea and in fresh water. Earlier in this symposium Dr. Fishman quoted from Thales of Miletus that "Water is best," but he made the comment that salt is also good. To be specific, this is a matter of concentration. As you know, the ocean contains over 3 per cent salt, and the body fluids of all vertebrates contain around 1 per cent.* This poses serious physiologic problems of osmotic loss of water, as well as influx of salt from the more concentrated medium. In fresh water, the problems are reversed. Since the water contains very little salt, the fresh-water vertebrates face a steady influx of water and a loss of salt to the dilute surrounding medium.

Dr. Wald suggested yesterday evening that the vertebrates have evolved in fresh water. That may or may not be so. At this time I don't think we know, but it is convenient to start our discussion with fresh-water vertebrates. In fresh-water fish and Amphibia, the kidney is important because it eliminates, as a very dilute urine, the water which enters the body due to osmotic inflow. However, one could say that their major organ of osmotic regulation is not the kidney, for the fresh-water fish makes up for the loss of salts through active uptake of ions in the gill, and the amphibian has a similar mechanism in the skin. In fact, the frog skin has become a classical object of study because it is so eminently suited for experimental work on ionic transport mechanisms, and has permitted the

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*The most primitive vertebrates, the cyclostomes, are exceptions; they are in osmotic equilibrium with and have salt concentrations similar to sea water. The elasmobranchs are in osmotic equilibrium with sea water, but a major part of the solutes in their body fluids is urea and trimethylamine oxide, and the salt concentration of their body fluids is similar to that of other vertebrates.
development of Ussing's ingenious method of measuring the ion flux by means of the short-circuit current.

Salt-water fish have an osmotic loss of water to the concentrated surrounding medium and compensate by drinking sea water. The excess salt is eliminated by the pump in the gill, which, compared to the fresh-water fish, has been turned around. Again, we have a case in which the kidney is not the major organ of osmoregulation. No amphibian has been reliably reported to live in salt water, and it seems that the amphibians as a group are unable to solve the physiologic problems of adaptation to life in salt water.

Other vertebrates, reptiles, birds and mammals are, of course, mostly terrestrial. In these the kidney is the major organ of excretion, and, as such, a very efficient organ. The mammals, in particular, have evolved a kidney with a high concentrating ability, which, as Marshall pointed out, undoubtedly is related to the presence of the loop of Henle. More recently, the role of the loop structure has become clear with the understanding of how it functions as a countercurrent multiplier system.

Some mammals, birds and reptiles have evolved a secondary adaptation to a marine habitat. Seals and whales can handle the problem of life in salt water because their kidney can produce a highly concentrated urine. Elimination of the salts from sea water is well within the capacity of the mammalian kidney. Desert rodents, such as kangaroo rats and jerboas, which have to conserve water, have kidneys that can excrete urine more than twice as concentrated as sea water. The reason that sea water is toxic to man is primarily that his kidney is not very efficient in comparison to other mammalian kidneys.

The kidneys of birds and reptiles have a concentrating ability which is considerably less than that of the mammalian kidney, apparently because they contain no typical loops of Henle. Birds, which can excrete a urine which is about twice as concentrated as the plasma, have some looped nephrons, but these are not as highly developed as in mammals. Reptiles have no loops in their kidneys, there is no countercurrent multiplier system, and their urine cannot be concentrated above the plasma concentration. As a consequence, marine birds and reptiles cannot rely on the kidney for osmoregulation, and they appear to have a choice between avoiding the drinking of sea water and acquiring some means for salt excretion more efficient than their kidneys.

Marine Birds

Many birds and a few reptiles have adapted to marine life. Some birds come to land only to breed, and spend most of the year on the ocean; others, such as the penguins, have become excellent swimmers and have lost the power of flight. The emperor penguin is said never to come on land, not even to breed, but this statement is merely a play on words, for the emperor penguin hatches its eggs standing on the antarctic ice during the cold polar winter. Many marine birds eat fish, which contain much water; this circumstance reduces their problem of salt excretion. In fact, on a diet of fresh fish, cormorants have plenty of water to spare and do not need to drink at all.1 But other birds eat invertebrates which are in osmotic equilibrium with sea water; gulls eat mussels, sea urchins and crabs, eider ducks filter small organisms out of the water, some penguins eat large quantities of krill, and so on. How do these birds, with their inefficient kidney, eliminate the salt that is present in their food and in the water they may drink? The answer is that they possess an accessory organ, a gland in the head, which produces a concentrated salt solution that drips off from the tip of the beak.

This salt-secreting gland is highly developed in all marine birds, as opposed to terrestrial birds. The gland has long been known to anatomists as the nasal gland; it is present in all birds, but in terrestrial species it is very small.2 The size of the gland in marine birds is 10 to 100 times as large, a striking difference that was noticed long ago.

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usual interpretation has been that the function of the gland should be to rinse away the irritating and harmful effects of sea water that might penetrate into the nasal cavity. However, in all the marine birds that we have examined, the gland secretes a solution of sodium chloride which is more concentrated than sea water, and the exclusive function of the gland seems to be that of osmoregulation. The species which we have examined, which include gulls, terns, auks, penguins, albatrosses, petrels, cormorants, pelicans, gannets, herons and ducks, represent all the major orders of marine birds; it seems logical, therefore, to conclude that the salt-secreting gland is present in all marine birds.

It is interesting that the gland not only is large in marine birds, but that, to some extent, its size varies with the exposure to salt loads. Long before the function of the gland was known, Schildmacher found that ducks brought up with access to a 3 per cent salt solution instead of fresh water developed an enlarged gland. However, after a careful discussion of the apparently causal connection between the size of the gland and salt water, Schildmacher repeated the mistake of the old interpretation, stating that the only possible explanation is that the gland protects the nasal mucosa against irritation.

The change in the size of the gland with the degree of exposure to salt was observed earlier by the Heinroths, who found that eider ducks which were reared in fresh water in the Berlin Zoo had smaller gland impressions on their skulls than individuals of the same species collected in the wild. However, the relative ease with which the gland hypertrophies with use and atrophies with disuse should not be taken to mean that terrestrial birds can develop a functional salt gland from their nasal gland. This does not seem to be the case; only those birds that have an evolutionary history of adaptation to a marine habitat seem to have evolved a gland of significant size, and seem to be capable of secreting hypertonic solutions.

With the apparently universal existence of the salt gland in living marine birds, its presence in fossil forms can safely be taken as an indication of a marine habitat. Some fossil birds, such as Ichthyornis and Hesperornis from the Cretaceous period, have clear impressions on the skull where a large gland has been located. These birds were fish eaters, and supposedly marine, and the presence of the large gland in the same location as the salt gland of living birds is a satisfactory confirmation of their marine life.

Marine Reptiles

Only a few reptiles live in the sea; they represent 4 orders: turtles, snakes, lizards and crocodiles. The great sea turtles eat fish or seaweed, and go on land only to lay their eggs on sandy beaches. They are known to shed tears as the eggs are deposited, evidently a sign of osmoregulation, rather than pain. The sea snakes (Hydrophidae) of the Indian Ocean are truly marine; the more primitive lay their eggs on land, but the most specialized bear living young and remain at sea throughout life. They are reputed to be the most poisonous of snakes, and their osmoregulation has never been studied. A single lizard, the Galápagos lizard (Amblyrhynchus cristatus) is marine; it lives on the beaches of the Galápagos Islands where it eats seaweeds and occasionally blows a spray of droplets out through its nostrils, reminiscent of a puff of smoke from a fiery dragon. This harmless creature is easily handled in the laboratory, and it proves to have an osmoregulatory nasal gland that produces the salty fluid which is ejected from the nose. The marine crocodile (Crocodylus porosus) has been found far out at sea, but normally it lives in estuarine swamps. A single specimen which I had in the laboratory did not respond to osmotic loads, and crocodile tears must still be classed as one of the mysteries of biology.

Terminology

The presence, but not the function, of the salt-secreting gland has been known for centuries and received considerable attention early in the last century. It has been called...
the nasal gland (glandula nasalis), although it is not always found in what one would call the nose. In most marine birds it is located on top of the head, above the orbit of the eye, and has therefore also been called the supra-orbital gland, or glandula nasalis supraorbitalis. In the marine turtles the salt-secreting gland is seemingly of a different embryologic origin. It is located in the posterior part of the orbit of the eye, and its duct opens in the posterior corner of the eyelids. This gland in the turtle should, therefore, probably be regarded as a modified lacrimal gland. It is interesting that the gland of the turtle, in spite of its different origin, has the same histologic structure as the gland of the bird.

Since these glands, which anatomically are not homologous, have the same function, the need arises for a convenient terminology. We have therefore decided to call them salt-secreting glands, or simply salt glands; this designation, then, denotes any gland in the head region of marine birds and reptiles which, irrespective of anatomic origin, has an osmoregulatory function and secretes highly hypertonic sodium chloride solutions.

Response to a Salt Load

The effect of a considerable salt load in a black-backed gull (Larus marinus) is shown in table 1. In this case the bird, which weighed 1,420 Gm., was given almost one-tenth of its body weight of sea water by stomach tube. After about 3 hours the total volume of the excreta equaled the infused amount, and all the ingested salt had been eliminated. In other words, a gull handles quite easily a salt load which could not possibly be tolerated by man.

Some details of the relative importance of the kidney and the salt gland are given in table 2. The total amount of fluid excreted from the salt gland was 56 ml., while in the same 3-hour period 75 ml. was eliminated from the cloaca, most of this latter being urine. The concentration of sodium was uniformly high in the nasal fluid, while it was low in the cloacal fluid. Thus, the total amount of salt eliminated by the salt gland was about 10 times as high as the total cloacal excretion. In other words, in this particular experiment, the extrarenal excretion of salt was 10 times as important as the renal excretion. In spite of the salt load, the concentration of sodium in the urine was low and tended to decrease further during the experiment, although the kidney has the capacity to excrete concentrations of sodium up to about 300 mEq./L. This drop in the concentration of sodium in the urine after a salt load has frequently been observed in gulls, but in other species of birds about which we have similarly complete records of the effects of a salt load, the concentrations of sodium in the urine have tended to rise toward the concentration ceiling (about 300 mEq./L.).

Composition of the Nasal Secretion

The fluid secreted from the salt gland is very simple. Except for epithelial cells and other debris in samples collected immediately after the start of secretion, the almost neutral, watery liquid is clear and colorless. The dominating solutes are sodium and chloride in approximately equivalent amounts (table 3). There is a relatively small amount of potassium, some bicarbonate, and almost nothing else. Magnesium and sulfate, which are present in sea water in rather high concentrations, are virtually absent from the nasal fluid. The amount of organic material, including urea, is very small. Phenol red, which apparently is excreted by all kidneys, is not secreted by the nasal gland and does not appear in the fluid.

Concentration of the Fluid

The activity of the salt gland is an all-or-none phenomenon. If there is an osmotic load, the gland secretes; in the absence of an osmotic load, the gland is at complete rest. In this intermittency, the gland differs from the kidney which produces urine continuously. The concentration of salt in the nasal secretion is always very high, and remains fairly constant for each species (table 4). There seems to be a clear connection between the concentrating ability of the salt gland and
THE SALT-SECRETING GLAND OF MARINE BIRDS

Table 1

The Total Excretion of Water and Salt in a Black-Backed Gull After a Load of Sea Water by Stomach Tube

<table>
<thead>
<tr>
<th></th>
<th>Body weight</th>
<th>Total volume in Excreta, ml</th>
<th>Sodium ingested, mEq.</th>
<th>Sodium excreted in 3 hrs., mEq.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1,420 Gm.</td>
<td>134</td>
<td>94</td>
<td>48</td>
</tr>
</tbody>
</table>

Table 2

Nasal and Cloacal Excretion by a Black-Backed Gull During the 175 Minutes Following the Ingestion of Sea Water (see Table 1)

<table>
<thead>
<tr>
<th>Time, min.</th>
<th>Vol., ml.</th>
<th>Sodium conc., mN</th>
<th>Sodium amount, mEq.</th>
<th>Cloacal excretion</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>2.2</td>
<td>798</td>
<td>1.7</td>
<td>5.8</td>
</tr>
<tr>
<td>40</td>
<td>10.9</td>
<td>756</td>
<td>8.2</td>
<td>14.6</td>
</tr>
<tr>
<td>70</td>
<td>14.2</td>
<td>780</td>
<td>11.1</td>
<td>25.0</td>
</tr>
<tr>
<td>100</td>
<td>16.1</td>
<td>776</td>
<td>12.5</td>
<td>12.5</td>
</tr>
<tr>
<td>130</td>
<td>6.8</td>
<td>799</td>
<td>5.4</td>
<td>6.2</td>
</tr>
<tr>
<td>160</td>
<td>4.1</td>
<td>800</td>
<td>3.3</td>
<td>7.3</td>
</tr>
<tr>
<td>175</td>
<td>2.0</td>
<td>780</td>
<td>1.5</td>
<td>3.8</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>56.3</td>
<td>43.7</td>
<td>75.2</td>
</tr>
</tbody>
</table>

Table 3

Typical Composition of the Fluid from the Salt-Secreting Gland of Herring Gulls

<table>
<thead>
<tr>
<th></th>
<th>Na+ mEq./L.</th>
<th>Cl- mEq./L.</th>
<th>K+ mEq./L.</th>
<th>HCO3- mEq./L.</th>
<th>Ca++ + Mg++ mEq./L.</th>
<th>SO4- mEq./L.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>718</td>
<td>720</td>
<td>24</td>
<td>13</td>
<td>2.0</td>
<td>0.68</td>
</tr>
</tbody>
</table>

*Dr. Maren has kindly permitted me to quote average figures obtained in his laboratory. For nasal secretion these are: HCO3-=9.1 mEq./L., pH=7.03; and for plasma: HCO3-=21.7 mEq./L., pH=7.48.

Table 4

Usual Concentration of Sodium in the Nasal Secretion of Different Species of Birds

<table>
<thead>
<tr>
<th>Species</th>
<th>Concentration of sodium, mEq./L.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cormorant, double-crested</td>
<td>500-600</td>
</tr>
<tr>
<td>Duck, mallard</td>
<td>(550)</td>
</tr>
<tr>
<td>Skimmer, black</td>
<td>550-700</td>
</tr>
<tr>
<td>Eider duck, common</td>
<td>(625)</td>
</tr>
<tr>
<td>Pelican, brown</td>
<td>600-750</td>
</tr>
<tr>
<td>Gull, herring</td>
<td>600-800</td>
</tr>
<tr>
<td>Gull, black-backed</td>
<td>700-900</td>
</tr>
<tr>
<td>Penguin, Humboldt's</td>
<td>725-850</td>
</tr>
<tr>
<td>Guilemote</td>
<td>750-850</td>
</tr>
<tr>
<td>Albatross, blackfooted</td>
<td>800-900</td>
</tr>
<tr>
<td>Petrel, Leach's</td>
<td>900-1,100</td>
</tr>
</tbody>
</table>

Some samples fall outside these limits, which represent only the usual range. Numbers in parentheses represent species in which samples have been too few to establish a normal range.

The feeding habits of the bird. For example, in the cormorant, which eats fish that is relatively low in salt content, the concentration in the secretion from the gland is about 500 to 550 mEq./L. and rarely exceeds 600 mEq./L. In the herring gull, which consumes more invertebrate food, and consequently more salt, the concentration is usually between 600 and 800 mEq./L.; the great black-backed gull which is more marine in its habits, has concentrations between 700 and 900 mEq./L. The petrel is a bird with pronounced oceanic habits. It spends most of its life at sea and comes to land only to breed. It lives on planktonic organisms, mostly crustaceans, which it picks off the surface of the ocean as it flies by. The planktonic organisms, being invertebrates, have the same osmotic concentration as sea water and therefore impose a considerable salt load. It is no surprise, therefore, that in the petrel the salt concentration of the nasal fluid is higher than in any other bird we have examined, up to 1,100 or 1,200 mEq./L.

No other gland in higher vertebrates, except the mammalian kidney, can produce fluids which are concentrated to this degree. The concentration limit for electrolytes in the kidney of man is about 400 mEq./L., in the rat 600 mEq./L., in the kangaroo rat, 1,500 mEq./L., and in the champion concentrator, the North African rodent Psammomys, 1,900 mEq./L. Thus, the salt gland compares favorably to the kidney in its concentrating ability. In other respects the salt gland is quite different from the kidney; it secretes only sodium chloride, it always produces a liquid which is highly hypertonic to the blood, and it works as an all-or-none system, becoming active only after an osmotic load.
Table 5

A Comparison Between the Rate of Secretion from the Salt Gland of the Gull and the Volume of Urine During Water Diuresis in Man

<table>
<thead>
<tr>
<th>Flow per Kg. body weight:</th>
<th>Salt gland, herring gull</th>
<th>0.5 ml./min.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Kidney, water diuresis, man</td>
<td>0.24 ml./min.</td>
</tr>
<tr>
<td></td>
<td>Kidney, GFR, man</td>
<td>1.8 ml./min.</td>
</tr>
</tbody>
</table>

Flow per Gm. gland:
- Salt gland, herring gull | 0.6 ml./min.
- Kidney, water diuresis, man | 0.03 ml./min.
- Kidney, GFR, man | 0.2 ml./min.

Volume of Flow

Although the concentration of the nasal secretion is relatively constant, its volume is not. The rate of flow can change from zero to a maximum which varies with the species and, to some extent, between individuals within the species. After a salt load is given to a bird, the rate of flow rapidly increases, and remains rather high for a period that depends on the degree of the load. It then tapers off and diminishes as the salt is eliminated (table 2). However, the rate can remain at near-maximal levels for hours. That this rate is quite high becomes clear when the flow from the gland in the gull is compared with the flow of urine during water diuresis in man. In table 5 flows are calculated per kilogram of body weight. It may be seen that although the osmotic concentration of the nasal secretion is high, the production of nasal fluid is more than twice the maximum water diuresis in man.

Size of the Gland and Flow Rate

What is the size of a gland which has this amazingly high excretory capacity? Its size is not very impressive compared to the kidney; in the gull, which has a relatively large salt gland, it is about 0.1 per cent of the body weight, while the kidney of mammals approaches about 1 per cent of the body weight. Thus, if we relate the volume of secretion to the weight of the gland rather than to body weight, the capacity of the salt gland becomes even more striking. The gland of the gull can produce about 0.5 ml. of fluid per Gm. of gland per minute. The glomerular filtration rate in man is about 0.2 ml. per Gm. of kidney per minute and in the rat, I believe, about 0.5 ml. per Gm. of kidney per minute. In other words, despite the considerable osmotic work necessary to produce the concentrated fluid, the salt gland can secrete at a rate which is as high as, or higher than, the glomerular filtration rate in the mammalian kidney.

Structure of the Gland

What is the structure of this unusual gland which produces fluid as fast as the kidney filters the plasma? Figure 1 shows the location of the gland in the gull. On top of the skull there are 2 crescent-shaped, flat glands, which are located in shallow depressions in the bone. Actually, each gland consists of 2 parts which are so similar in structure and are so closely joined that they can be considered as one functional unit, i.e., as one gland.11 Two ducts run from each side down to the nose where they open at the vestibular concha. From the anterior nasal cavity the secretion flows out through the nares and drips off from the tip of the beak. A few marine birds have closed and nonfunctional external nares; characteristically these birds, e.g., gannets and cormorants, are good divers and enter the water after a fast dive from some height. The closed nares probably are a protection against the penetration of water at the time of impact with the surface. In these birds the nasal secretion flows through the internal nares along the roof of the mouth, forward to the tip of the beak.

The glands consist of longitudinal lobes, which in cross section show tubular glands radiating from a central canal (fig. 2). Except for the most distal portion where the cells are somewhat smaller but of the same general
type (fig. 3), the branching, tubular glands have a rather uniform structure throughout their length. The tubules are closed in the distal end, and there is no structure reminiscent of the glomerulus of the kidney. The structure is characteristic of a tubular gland, which indicates that the secreted fluid is elaborated only by simple glandular secretion, and that there is no ultrafiltration of fluid comparable to that in the kidney. This conclusion is supported by the fact that inulin does not appear in the secretion.

A retrograde injection of India ink into the gland through its duct shows that the ink penetrates all the way into the cells, giving the appearance of intracellular canaliculi which probably have a secretory function. Electron micrographs made by Dr. W. L. Doyle at the University of Chicago, as well as by other investigators, show that there are deep infoldings both in the apical and the basal parts of the secreting cell, which has some similarity to the tubular cell of the nephron. It must be assumed that the deep infoldings are intimately related to the function of the cells, and it could be suggested that the elaboration and transport of fluid does not necessarily take place as a trans-tubular process. If the infoldings prove to be similar to the interdigitations of the renal tubular cells as reconstructed by Rhodin, the transport process might indeed take place in the intercellular spaces of interdigitating cells, rather than across the cell body. These studies are being continued by Dr. Doyle and will be published elsewhere.

**Blood Supply to the Gland**

The gland receives its main arterial blood supply from the arteria ophthalmica interna. In the gull, several blood vessels penetrate the bony wall of the orbit and enter the gland from below. This makes the blood vessels difficult to reach, and attempts at perfusion of the gland are likely to meet with immense technical difficulties.

The circulation in the lobes of the gland can be visualized most easily in preparations which have been prepared by the injection of the vascular system with India ink. It is found that the main arteries to the gland branch into interlobular arteries, which send smaller branches into the single lobes. These arteries continue toward the central canal, where they split up into capillaries which run parallel to the tubular glands toward the periphery of the lobe. A section cut perpendicular to the tubular glands (fig. 4) shows that the capillaries are interspersed between the glands, much as in the papilla of the kid-
The salt gland of the gull consists of longitudinal lobes about 1 mm. in diameter; each lobe has a central canal with the branching secretory tubules arranged radially around it. (Drawing by M. Cerame-Vivas.)

ney where the vasa recta are interspersed between the limbs of Henle’s loop. A diagram of the circulation (fig. 5) shows how the blood flows parallel to, but in the opposite direction from, the flow in the tubular gland.

Is There a Countercurrent System in the Salt Gland?

The arrangement just described can, of course, be recognized as a countercurrent flow, and no renal physiologist is unaware of the importance of the countercurrent multiplier system in the elaboration of a concentrated urine in the kidney. However, in the case of the salt gland, the countercurrent flow cannot be used to explain the elaboration of a concentrated fluid. A countercurrent multiplier system consists of a tube which has been turned back on itself to form a loop; but in the salt gland we have 2 unconnected tubes running in opposite directions. This is typical for a type of countercurrent exchange system which is particularly well suited for obtaining the same concentration in the outgoing fluid from one tube as in the incoming fluid in the other (fig. 6). In other words, the system in the salt gland seems ideal for the elaboration of a secretion which is isotonic with plasma, and the high concentrations which are actually produced cannot result from a countercurrent multiplier system.

It is true that the direction of the blood flow may be opposite to what we have assumed for there is always some doubt about

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Figure 2

The salt gland of the gull consists of longitudinal lobes about 1 mm. in diameter; each lobe has a central canal with the branching secretory tubules arranged radially around it. (Drawing by M. Cerame-Vivas.)

Figure 3A

In cross section the lobe of the salt-secreting gland shows the central canal and the radial arrangement of the secretory tubules. In the lower right hand corner an interlobulay vein and an artery are visible.

Figure 3B

In higher magnification the peripheral ends of the secretory tubules appear as closed tubes without any similarity to the glomerular apparatus of the kidney. However, the peripheral part of the tubule has smaller cells and an appearance which differs from the more central parts.
the interpretation of histologic sections. But even if the blood flow were the reverse of what we have suggested, with the flow in the same direction as the fluid in the gland, the arrangement would still not be a multiplier system. We must therefore conclude that, although there is a countercurrent flow, the countercurrent multiplier principle cannot be used to explain the function of this particular gland and its ability to elaborate highly concentrated solutions.

**Nervous Control**

The nerve supply to the salt gland is rather complex and not easily worked out because the nerves in the head of the bird have a complex course with frequent anastomoses. The gland is innervated from a ganglion in the orbit, the ganglion ethmoidale. This ganglion is supplied by a relatively large branch of the ophthalmic nerve, and a smaller one from the facial nerve, as well as by sympathetic fibers. Apparently nonmyelinated fibers from the ganglion penetrate the bone to reach the gland. Electric stimulation of the ophthalmic nerve causes no secretion, but if the small branch from the facial nerve is stimulated, a fluid of the usual composition, rich in sodium chloride is secreted. As far as we can establish, the branch of the facial nerve continues back toward the inner ear; it is reminiscent of, and could be homologous to, the chorda tympani which stimulates salivary secretion in mammals.

The secretory nerve apparently is parasympathetic in nature.\textsuperscript{10} Stimulation of the cervical sympathetic chain causes no secretion and injection of epinephrine blocks secretion from the gland. Acetylcholine, if injected in a proximal artery, causes the gland to secrete; if injected in the general circulation it will, of
The arrangement of the blood vessels and capillaries in the lobes of the salt gland indicates that the capillary blood flow is countercurrent to the flow of secreted fluid in the secretory tubule. (Drawing by M. Cerame-Vivas.)

course, be hydrolyzed before it reaches the gland. The parasympathomimetic substance methacholine (Mecholyl) also causes the gland to secrete.

**Effect of Anesthesia**

One difficulty in the study of the function of the salt gland is that the secretion is blocked by anesthesia. Secretion can always be induced in the nonanesthetized bird by an osmotic load, for example by the injection of hypertonic sodium chloride. Within a few minutes, sometimes within 1 minute of an injected load, secretion will begin. However, since anesthesia immediately blocks secretion, many further experiments, in particular those involving surgical procedures, cannot be carried out.

**Osmoreceptor Reflex**

The effects of anesthesia, of nerve stimulation, and of osmotic load, indicate a sequence of control as suggested in figure 7. The term osmoreceptor is used, rather than salt receptor, because the gland responds not only to salt loads, but to osmotic loads in general. If a hypertonic solution of a nonelectrolyte such as sucrose is infused, the gland begins to secrete a fluid of the usual composition, with a high concentration of sodium chloride. This indicates that the secretion occurs in response to an osmotic load, rather than to the concentration of sodium or chloride in the plasma.

**Carbonic Anhydrase in the Salt Gland**

It has frequently been proposed that carbonic anhydrase plays an important role in ionic transport mechanisms. Since the salt gland is an organ which apparently has no other function than the transportation of sodium chloride, it seems well suited to a study of the possible role of this enzyme in the mechanism of transport. Many schemes which have been suggested to account for ionic transport involve bicarbonate and car-
bionic anhydrase in an ion exchange system. With Dr. T. H. Maren, in 1958, we found that the salt gland is rich in carbonic anhydrase.

Of considerable interest is the observation that the carbonic anhydrase inhibitor, acetazolamide (Diamox), when injected into a bird whose gland is actively secreting, blocks the secretion almost instantaneously. This result indicates that carbonic anhydrase is essential to secretion, but it does not prove that the block is in the ionic pump of the secreting cells. A possible explanation is that the block could be somewhere else in the pathway indicated in figure 7. To examine this possibility experiments were done to determine if the gland retains its ability to secrete in the presence of the enzyme inhibitor. This has actually been found to be the case: direct stimulation of the gland with methacholine gives a secretion of the usual composition, showing that the ionic pump can work in the presence of a carbonic anhydrase inhibitor. Another possible interpretation, however, is that the inhibition of the secreting cells is a matter of relative concentrations, and that, if the stimulus is strong enough, the gland starts secreting in spite of the presence of the inhibitor. Further work on this point has been done by Dr. James Larimer, a former student of mine, in Dr. Maren’s laboratory.

The Role of Acetylcholine in Secretion

It is possible that the parasympathetic nature of the gland affords a clue to the mechanism of ion transport. The secretion occurs in response to the release of acetylcholine from the stimulating nerve. This pattern is reminiscent of other systems in which acetylcholine has an important influence on the movement of sodium, such as in the depolarization of the muscle fiber and of the nerve fiber. Recently, the Hokins of the University of Wisconsin have demonstrated that slices of the salt gland in vitro, when incubated with acetylcholine, show a greatly increased turnover of phosphatidic acid, as evidenced by radiophos-
phorus tracer experiments. The Hokins suggest that phosphatidic acid is an integral part of the sodium pump in the gland, and that it may be the actual ionic transport agent itself.

In a recent series of papers Scethorne has described histologic and histochemical studies of the nasal gland of ducks and pigeons. The gland of the domestic duck, like that of the mallard, its wild ancestor, does secrete salt, but the gland of the pigeon does not. In the gland of the duck there is a moderate amount of alkaline phosphatase, and a high content of succinic dehydrogenase. Not all glands have a high content of succinic dehydrogenase; it seems probable that the presence of this enzyme in the salt gland may be closely related to the energy which is required to perform an exceptionally high level of osmotic work.

Obviously, much work remains to be done on this unique gland, which apparently has no other function than that of transporting sodium chloride and therefore seems to be eminently suited for studies of processes involved in ionic transport. I believe that it is too early to say whether the transport is due to a sodium pump or to a chloride pump. My personal guess is that it may be a chloride pump, but I have no real support for this notion except that the proportion of sodium to potassium in the secreted fluid may indicate that the cation follows passively. In either case, I expect that future work will answer the question. At this time I can only say that if there is any organ in which an ionic pump and its metabolic ramifications can be studied in its pure form, the salt gland of marine birds almost seems to be designed for this purpose.

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Water as a Substrate for Life

Water, of its very nature, as it occurs automatically in the process of cosmic evolution, is fit, with a fitness no less marvelous and varied than that fitness of the organism which has been won by the process of adaptation in the course of organic evolution.

If doubts remain, let a search be made for any other substance which, however slightly, can claim to rival water as the milieu of simple organisms, as the milieu intérieur of all living things, or in any other of the countless physiological functions which it performs either automatically or as a result of adaptation.—L. J. Henderson. The Fitness of the Environment. Boston, Beacon Press, 1958, pp. 131-132.
The Salt-Secreting Gland of Marine Birds

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