

times a day before meals and for children 10 mg. a day for each year of apparent (not chronological) age, the total daily amount of the drug for children being divided also into three doses. The efficiency of the treatment was checked by the use of seven consecutive daily NIH post-treatment swabs. The patients were treated in four series, as follows:

One series of 107 patients received enteric coated gentian violet tablets N. N. R. daily for a period of ten consecutive days. Post-treatment swabs taken in these cases from ten to twenty-one days after the completion of the treatment indicated that ninety-seven, or 91 per cent, were negative for pinworms.

Thirty patients were treated with enteric coated tablets over a period of eight days, were allowed to rest for seven days and were then treated for an additional period of eight days. Of these thirty patients twenty-seven, or 90 per cent, were negative on post-treatment swab examinations taken between the fourteenth and twenty-first days following the end of the treatment.

The third series involved the treatment of nineteen individuals with enteric coated tablets over a period of sixteen days with a week's rest between the eight-day treatment periods. Of these patients eleven, or 58 per cent, were negative on post-treatment swab examinations made from the forty-second to the forty-eighth day following the end of the treatment.

In the fourth series sixty-eight patients were treated with gentian violet tablets provided with a water soluble coating designed for disintegration in the small intestine at approximately four and one-half hours after administration. These patients were given the sixteen-day treatment with the usual seven days rest period between two eight-day courses. The tablets were given one hour before meals. Fifty-four, or 79 per cent, of the sixty-eight patients were negative for pinworm ova on seven consecutive daily post-treatment swabs taken from the forty-second to the forty-eighth day following the end of the treatment.

A certain percentage of the treated patients suffered reactions in the form of nausea, vomiting, diarrhea and abdominal pain but the reactions were of a temporary nature and quickly subsided when the dosage of the drug was reduced or the treatment was discontinued for a period of a day or two.

Contraindications for the use of gentian violet include concomitant infestations with *Ascaris lumbricoides*, moderate to severe cardiac, hepatic or renal disease, alcohol and diseases of the gastrointestinal tract.

The minimum lethal dose of gentian violet for rabbits was 22 mg. per kilogram of body weight daily for a period of six days. One dog tolerated a dose of 35.4 mg. per kilogram daily for eighteen days. No pathologic tissue changes have been found to account for the death of experimental animals succumbing to the administration of gentian violet.

Gentian violet was found to be eminently superior to some and superior to all the other methods of therapy tested under similar conditions and checked by the same technic. Because of its relative cheapness, its ease of administration and its relatively high degree of efficacy, the drug is apparently of greater value than are other known drugs for the treatment of pinworm infestation in families in which many individuals may be infested and in which simultaneous treatment of all infested individuals appears to be necessary for the control of the condition.

Clinical Notes, Suggestions and New Instruments

A GREAT CRAVING FOR SALT BY A CHILD WITH CORTICO-ADRENAL INSUFFICIENCY

LAWSON WILKINS, M.D., AND CURT P. RICHTER, PH.D.
BALTIMORE

Special food cravings or aversions have received only passing interest in modern medicine and have been almost entirely neglected in modern nutrition. This is due to the prevalent view that appetite cannot be trusted as a guide to the proper selection of foods. Results of experiments on rats using the self-selection technic indicate, on the contrary, that a very close relationship exists between appetite and nutritional needs of minerals and vitamins, as well as of fats, carbohydrates and proteins. In human beings there are only a few instances which throw light on the relationship between appetite and dietary needs. Davis¹ reported that when very young normal children were given free access to a large number of natural foods they made selections which resulted in normal growth and development. She also reported that a child with vitamin A deficiency took large amounts of cod liver oil and thereby caused the deficiency symptoms to disappear.

During the past year we had occasion to make in this hospital a clinical observation which demonstrates in a very striking way the close relationship between appetite and nutritional needs. The endocrinologic aspects and the full medical history of this case have been reported in detail by Wilkins, Fleischmann and Howard.² The following data were taken from their history:

REPORT OF CASE

D. W., a boy aged 3½ years, admitted to the Harriett Lane Home for Children, showed a marked development of his secondary sex organs. His penis and testes were as large as those of a 12 year old boy. The prostate was fairly well developed; spermatogenesis was absent. Over the pubis there was a rather abundant growth of long dark hair. The voice was deep and the laryngeal cartilage was as prominent as that of a full grown man.

The skin on his scalp and body had a slightly brownish hue; the alveoli of the nipples were pigmented and the gums over the upper incisors showed a patch of brownish pigmentation.

His blood had a low sodium and a high nonprotein nitrogen content. Other physical observations were negative.

In the hospital the boy did not seem to be especially ill. He behaved like a very defective child, growling and snarling in an incoherent manner when attempts were made to examine him. He was offered the regular ward diet. His appetite was poor and he ate but little of the food. When feedings were forced, he vomited on several occasions. Seven days after admission he suddenly died.

Postmortem examination revealed that both adrenals were large. There was hyperplasia of the androgenic or prenatal zone cells, with marked diminution of the normal cortical cells. The testes were composed of similar cells crowding out the seminiferous tubules. Otherwise no pathologic changes were found. The precocious development of the secondary male sex characteristics was thought to be due to the embryonic hyperplasia of the androgenic zone of the adrenal. It appeared that death from adrenal insufficiency resulted from destruction of the electrolyte-controlling elements of the adrenal cortex.

One of the interesting features of this case was the presence of a great craving for salt. After his death it was learned that from the age of 12 months the child had eaten salt in large quantities. In addition, he had been given saline enemas

These observations form part of a study of the "Influence of Hormones on Appetite," supported by the Committee on Research in Endocrinology of the National Research Council.

From the Harriett Lane Home for Children and the Psychobiological Laboratory, Henry Phipps Psychiatric Clinic, Johns Hopkins Hospital.

1. Davis, Clara M.: Self Selection of Diet by Newly Weaned Infants, *Am. J. Dis. Child.* **36**: 651 (Oct.) 1928.

2. Wilkins, Lawson; Fleischmann, W., and Howard, J. E.: Endocrinology, to be published.

every second or third day because of constipation. Subsequently a full account was obtained from the parents concerning the onset and development of this craving. The following letter, which is one of the most extraordinary documents on behavior on record, was written by the parents in response to a few questions regarding their child's special appetites:

"Dear Dr. ———:

"Since receiving your letter it has been on my mind constantly to remember as nearly as possible the correct answers to all of your questions. We want to thank you for your very nice letter and are glad to help in any way we can.

"Some of the things I am writing you I know are not direct answers to your questions, but indirectly I feel that they may be of some help to you and perhaps explain how we had studied D—— and his peculiarities. Of course, in the beginning we knew that he was very sick, but did not know his true condition or what to expect.

"We had such a hard time trying to find milk to agree with him that I remembered exactly when each kind was changed; but when he first started eating salt I didn't think it was so important until later when he started craving it.

"With his feeding problems we only gave one new food at a time and took particular notice of the reaction it had on him. At six months we still didn't have any one milk to agree with him for any length of time except mother's milk. At this time Dr. ——— told us to start giving him strained vegetable soup and beef broth. He liked it, but as soon as it touched his tongue he would gag and bring up everything he had in his stomach unless I made it very thin with the beef broth. About a month later we started giving him strained vegetables; but, no matter what it was, he would bring it all up immediately unless it was very thin, practically liquid. At this time the doctor told us to give him crackers and zwieback; but as soon as he got any crumbs or little pieces of food on his tongue he would gag and bring up everything else. I would keep trying him from time to time thinking that perhaps the next time he would do better.

"When he was around a year old he started licking all the salt off the crackers and always asked for more. He didn't say any words at this time, but he had a certain sound for everything and a way of letting us know what he wanted. This was the first we had noticed his wanting the crackers or salt. Finally he started chewing the crackers; but he only chewed them until he got the salt off, then he would spit them out. He did the same with bacon, but he didn't swallow the pieces. When he was about sixteen months old, crackers were the first food he chewed and swallowed; but it was quite a while after that before he would chew up and eat a whole cracker. He would usually just make a mess of them eating the salt off.

"In an effort to try to find a food that he would like well enough to chew up and swallow, we gave him a taste of practically everything. So, one evening during supper, when he was about eighteen months old, we used some salt out of the shaker on some food. He wanted some, too. We gave him just a few grains to taste, thinking he wouldn't like it; but he ate it and asked for more. This was the beginning of his showing that he really craved salt, because this one time was all it took for him to learn what was in the shaker. For a few days after that, when I would feed him his dinner alone at noon, he would keep crying for something that wasn't on the table and always pointed to the cupboard. I didn't think of the salt, so I held him up in front of the cupboard to see what he wanted. He picked out the salt at once; and in order to see what he would do with it, I let him have it. He poured some out and ate it by dipping his finger in it. After this he wouldn't eat any food without having the salt, too. I would purposely let it off the table and even hide it from him until I could ask the doctor about it. For it seemed to us like he ate a terrible lot of plain salt. But when I asked Dr. ——— about it, he said, 'Let him have it. It won't hurt him.' So we gave it to him and never tried to stop it altogether. After we gave it to him all the time he usually didn't ask for it with his dinner; but he wouldn't eat his breakfast or supper without it. He really cried for it and acted like he had to have it. Foods that he ordinarily wouldn't touch he would eat all right if I added more salt to them. He would take the shaker and pour some out on his plate and eat it with his finger, but we always tried to keep him from getting what we thought would be too much for him. He never did care much for zwieback, toast or bread or for cooked potatoes, but he did like raw potatoes, raw carrots, celery, tomatoes, lettuce and different other foods if he could dip them in salt. If I didn't give it to him, he always asked for it. At eighteen

months he was just starting to say a few words, and salt was among the first ones. We had found that practically everything he liked real well was salty, such as crackers, pretzels, potato chips, olives, pickles, fresh fish, salt mackerel, crisp bacon and most foods and vegetables if I added more salt. We never tried to force him to eat a food; I always tried to prepare the same food in a way that he would like it. Spinach and green beans were his favorite vegetables. By letting him taste different foods he learned to like quite a variety, although he was three years old before he really ate a good meal by chewing it and swallowing it. In the meantime, I kept feeding him strained foods with the beef broth. . . . As he grew older and ate better, he very seldom brought up his meals any more. But he always wanted a lot of vegetable juice on his foods before he would eat them. If I didn't give it to him, he would ask for it and would eat everything good; but he wanted the salt too. By the time he was three years, I could reason with him and make him understand when he had enough of anything. At the time we had no idea as to the amount of salt he ate, or what the result would be if he didn't have it; but we have measured it now and would say that he ate between three quarters to one teaspoon of plain table salt a day in addition to all his foods being saltier than ours. If he ate a food without it, I let him go; but if he wanted more salt in it, I added a little more. Many times I tried to make him think I added it, but he always knew the difference with the first taste. Some days he may have had a little more or less than the amount stated, which is, as we would judge, the average.

"He would not eat anything sweet, though. Mostly everything with much sugar in it he would either bring back up or *just wouldn't eat it*. He would not eat cereal with sugar and milk on it. I would always strain his cereal into his glass of milk and let him drink it. Wheaties, or any small amount of dry cereal I tried to give him, he would not eat with sugar and milk but wanted it dry with salt sprinkled on. He *did not* like candy, cake, custards, puddings, etc. He did eat a little ice cream or jello.

"He was a very observing baby and, even in his sickly condition, started noticing pictures in books when he was six months old. He always liked books, and we would read to him quite a lot. When he was about two years old he began reading the pictures himself. He would get out one book after another and never seemed to grow tired of reading them. Many times he surprised us by knowing and recognizing things in the pictures we hadn't even noticed. And by the time he was three and a half he knew a few words by sight. When he was two and a half he loved to hunt for the attractive pictures of the good foods in the magazines. He learned to know what all the foods were and made believe he ate them. It was surprising to us to see how this improved his appetite at meal time, for it was at this time that he started chewing his foods better and acted like he really enjoyed them. Another thing that helped him learn to eat was because he became interested in cooking. Many times he would play for an hour or more making believe he was cooking his Daddy's supper and imagining all kinds of foods he was cooking.

"There was no other one food that he seemed to crave like salt, except water. Many people seemed to think this was because he ate so much salt, but he liked lots of water to drink from the time he was four months old. At six months, if he showed him a bottle of water and one of milk, he would take the water in preference to the milk *every time*. And in studying him, we found that by giving him lots of water he would be able to belch easier and so keep his milk down better. He learned to know himself that it helped him. As soon as he knew what the word 'water' meant, he would cry for it every time he heard the word mentioned. And when he saw the river or the ocean, he always thought he had to have some to drink until we were finally able to explain to him that it wasn't drinking water. But up until the time we took him up there he still wanted water every time he saw anybody else drink it. He always asked for it many times between meals; and if there was water on the table at meal time he would rather drink it than eat his meal. And if we let him drink and eat too much without making him stop to belch in between, his food would come back up almost every time. Also, if we let him cry much, he could not keep anything in his stomach.

"At home he acted and played the same as any perfectly normal child. But the doctor had told us not to take him anywhere among people because of contracting contagious diseases, which he didn't think D—— could pull through. The result was that he was afraid of strangers; and when we brought him up there it was the first time that he was among

complete strangers and strange surroundings. We had never been away from him ourselves before. Either my husband or I were always with him to take care of him.

"I hope that I have answered all of your questions satisfactorily and also that at least part of what I have written will be of some help to you. In order to remember the answers as nearly correct as possible, it was necessary for me to recall D—'s whole life. If there is anything at all that I have omitted don't hesitate to let us know. We will be glad to answer it if we can. As for the different kinds of milks we gave him and the age when each one was changed, also his growth and development, I had those recorded on the backs of the pictures I sent you sometime after we returned from up there.

"Hoping we have been able to help you in your studies and perhaps some children in the future, we are,

"Yours very truly,

"MR. AND MRS. —."

COMMENT

The full significance of the craving for salt by this child can be obtained from a review of our knowledge of salt craving by adrenalectomized animals.

It is well known that in rats kept on the ordinary stock diets symptoms of insufficiency develop and the rats die within ten to fifteen days after adrenalectomy. Death occurs largely because of the excessive loss of sodium chloride in the urine and the resulting changes in the internal osmotic conditions.³ It is known that the survival time can be increased and the mortality rate decreased by increasing the salt content of the food until it approximates the amount of salt lost in the urine. Further, it was shown that when adrenalectomized rats have access to salt in a container separate from the food they will ingest large amounts of salt and, as a consequence, keep themselves alive and free from symptoms of insufficiency.⁴ Some of the rats ingested from fifteen to twenty times as much of a 3 per cent salt solution thirty days after adrenalectomy as they had in the last ten day preoperative period. That the increased salt appetite depended on the loss of the adrenals was demonstrated by the observation that adrenals successfully implanted to the anterior chamber of the eyes caused the craving to disappear entirely.

This increased craving for salt manifested by adrenalectomized rats is not an isolated instance of a mineral or food craving which is closely related to dietary needs. We⁵ have reported that parathyroidectomized rats have an increased appetite for calcium, magnesium and strontium salts, which are known to decrease parathyroid tetany, and that they have a decreased appetite for phosphorus. We found also that pregnant and lactating rats given free access to a large selection of minerals, vitamins, purified (or nearly purified) fats, proteins and carbohydrates, all in separate containers, make selections in accordance with their needs. They increased their intake of calcium, phosphorus, protein and fat.

There can be little doubt, then, that with his increased salt craving the 3½ year old boy with deficient adrenal cortical tissue made an effort to maintain a normal internal salt balance. Apparently he started as early as eleven months after birth. During the two and one half years previous to his entrance to the hospital he must have kept himself alive by eating large amounts of salt. In the hospital he was not given free access to salt but was given the regular ward diet, which contains the normal amount of salt and, as a result, died suddenly.

The basis for special cravings has not yet been established. We do not know whether the adrenalectomized rats eat large amounts of salt because the ingestion of salt makes them feel better or because their taste for salt has changed—in other words, that in their salt deficient state they become chemotrophically attracted to salt. In favor of the latter view is the observation that adrenalectomized rats have a greatly decreased

threshold for salt. They distinguish distilled water from salt solution in a 1:33,000 concentration, while normal rats do not make this distinction until the salt solution reaches a concentration of 1:2,000.⁶ Such minimal amounts of salt as are received in drinking a few cubic centimeters of a 1:33,000 solution could not possibly have any physiologic effect. This boy also showed a positive reaction to salt when he first tasted it in pure form in very small quantities on the top of soda crackers. It is not readily conceivable that such a small amount of salt could have had any detectable effect on his deficiency condition.

SUMMARY

A boy aged 3½ years with deficient adrenal cortical tissue, manifesting various symptoms of adrenal insufficiency, had a marked craving for salt. On the basis of observations made on adrenalectomized rats, it would seem that this boy, by increasing his salt intake, kept himself alive for at least two and one half years.

A NEW TUBE FOR USE IN THE TREATMENT OF EMPYEMA BY OPEN DRAINAGE

LEON J. LEAHY, M.D., BUFFALO

It appears to be generally accepted that cases of empyema must be individualized and the proper treatment instituted to meet the conditions present. The chief factors influencing this are the age of the patient, the character of the exudate and the presence of complications. In most large series it is noted that the vast majority of cases require open drainage, such other methods as aspiration and closed drainage being reserved for the instances in which it is felt that the open method is either unsafe or not warranted. At times one of these procedures is used as a preliminary measure before establishing open drainage.

In instituting and maintaining open drainage I have encountered several difficulties which, although of a minor nature, could easily contribute to chronicity or recurrence if they were not recognized early or handled properly. The first of these has to do with the prevention of the tube from either slipping into the pleural cavity or coming out with the dressing. Sutures through the tube are satisfactory only until such time as they slough through the skin. A safety pin inserted through the tube and held to the chest wall with adhesive tape is an acceptable makeshift. However, the strips become readily loosened by the moisture from drainage and irrigations, thus allowing the tube to slip out of the pleural cavity unless care is exercised. As the inner end of the sinus closes very readily after the end of the tube has come out of the pleural cavity, reintroduction of the tube is often unsatisfactory. The next problem has to do with the inner end of the tube; it can easily

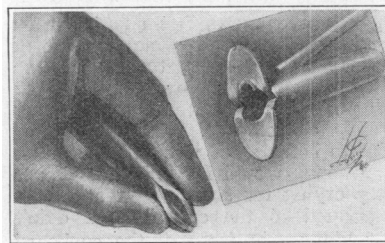


Fig. 1.—Tube and flanges bent forward for introduction into the pleural cavity.

be allowed to project into the pleural cavity for a distance of 1 or 2 inches, and with the use of modern gum rubber tubing it is difficult to recognize this fact even on the x-ray film without the injection of an opaque substance. I feel that if the end of the tube is not at the level of the parietal pleura the portion of the pleural cavity about the drainage tube is not kept emptied. This is in spite of secondary openings made in the sides of the tube, as these seem to become plugged with fibrin or granulations. There is the added factor of increased morbidity because the lung in reexpanding comes in contact with the end of the tube, and I feel that the speed of reexpansion

3. Loeb, R. F.: *Proc. Soc. Exper. Biol. & Med.* **30**: 808 (March) 1933. Harrop, G. A.; Soffer, L. J.; Ellsworth, Read, and Trescher, J. H.: *J. Exper. Med.* **58**: 17 (July) 1933. Rubin, M. I., and Krick, E. T.: *Proc. Soc. Exper. Biol. & Med.* **31**: 228 (Nov.) 1933.
4. Richter, C. P.: *Am. J. Physiol.* **115**: 155 (March) 1936.
5. Richter, C. P., and Eckert, J. F.: *Endocrinology* **21**: 50 (Jan.) 1937. Richter, C. P., and Eckert, J. F.: *Am. J. M. Sc.* **198**: 9 (July) 1939.

6. Richter, C. P.: *Endocrinology* **24**: 367 (March) 1939. From the Department of Surgery, University of Buffalo School of Medicine. The instrument is made by the George P. Pilling & Son Company, Philadelphia.