needle of any obstruction. The plunger is withdrawn gently in order to make sure that the tip of the needle is not lying within the lumen of a blood vessel or within the subarachnoid space. Twenty-five cc. of the anesthetic solution is injected slowly into the caudal canal. As soon as the initial dose has been injected the syringe is detached from the needle and a No. 5 French nylon ureteral catheter which has been sterilized in an autoclave is passed through the needle and is advanced until the tip of the catheter is approximately 1½ inches (3.8 cm.) above the sacral hiatus. The catheter is now supported in place while the needle is removed. The catheter is taped to the skin and the region is sealed with adhesive tape to prevent soiling from the perineum. The patient may now be turned on her back and made comfortable. It is important to refrain from advancing the tip of the catheter more than 1½ inches (3.8 cm.) into the caudal canal. If the catheter is placed high in the canal, unilateral anesthesia may result.

Additional injections of 25 cc. of the anesthetic solution are given whenever the patient begins complaining of discomfort.

COMMENT

We believe that the catheter method is much safer than the method of using an indwelling needle. If a needle breaks in the caudal canal, surgical intervention for its removal will be necessary. Indwelling needles also produce an unnecessary amount of trauma inside the caudal canal. The sacrococcygeal ligament acts as a fulcrum, holding the hub of the needle in a fixed position. Every motion of the patient will cause the tip of the needle to sweep the inside of the caudal canal, damaging the vascular plexus and traumatizing the periosteum. This cannot happen if the needle is replaced with a flexible ureteral catheter.

The position of the patient during the initial injection is important. We do not believe we are justified in employing the knee-chest position. If the patient is placed in a modified right Sims position near the edge of the bed it is an easy matter to reach over her and place the needle and catheter in the caudal canal.

We have kept our patients in a slight Fowler position during labor. This prevents the anesthesia from ascending to an unnecessary height and also prevents the fall in blood pressure and nausea which frequently occur if the anesthetic solution ascends to envelop the thoracic nerves.

Our first 25 or 30 patients were anesthetized with 1.5 per cent solution of procaine without epinephrine. In these cases we observed a few who had a sudden lowering of blood pressure followed by a feeble thready pulse, nausea and vomiting. Since that time we have included 2 minims of epinephrine with the initial injection for all patients except those with toxemia. We have not observed evidence of cardiovascular collapse since epinephrine was added to the anesthetic solution, nor have the patients become nauseated.

We have used metycaine for a number of patients and have not been able to demonstrate results superior to those obtained with procaine. Procaine has been used in the majority of our cases because we believe it to be the safest local anesthetic agent available at present.

CONCLUSIONS

1. Continuous caudal anesthesia is satisfactory in most cases.

2. We feel that the use of a ureteral catheter is safer and more comfortable for the patient.

3. Epinephrine should be added to the initial injection of anesthetic solution into the caudal canal in all cases except those of toxic reactions.

4. Continuous caudal anesthesia may be of service in cases of eclampsia, for 3 patients with eclampsia were delivered while under caudal anesthesia without any maternal or fetal death and with apparent control of symptoms of toxemia.

5. Absolute asepsis must be observed at all times.

6. A lower fetal mortality rate than usual was noted.

EXCRETION OF THIAMINE, RIBOFLAVIN, NIACIN AND PANTOTHENIC ACID IN HUMAN SWEAT

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The excretion of vitamins in sweat is of interest from the standpoint of the metabolism of such vitamins in the body and the possible loss of such vitamins by this channel, especially in instances of profuse sweating. Such results also have a bearing on the physiology of perspiration. The amount of sweat vitamins might also conceivably have a bearing on the growth of organisms on the skin, since some of these vitamins have a definite effect on the growth of certain micro-organisms.

One of us has reported on the excretion of ascorbic acid in sweat.[1] An increased excretion of this vitamin was noted in sweat after administration of large doses of the vitamin. Hardt and Still [2] studied the excretion of thiamine as well as of ascorbic acid in sweat after exercise. They concluded that 5 to 15 per cent of ingested thiamine might be the daily loss by way of the sweat and that the giving of 50 mg. of thiamine to their subjects led to an increased excretion of thiamine by this channel. Results on niacin, pantothenic acid and riboflavin do not appear to have been previously reported.

We have studied the excretion of thiamine, niacin, riboflavin and pantothenic acid in heat sweat of human subjects with and without the administration of large doses of these vitamins. The subjects were normal men.

METHODS

Specimens of sweat were collected as follows: The subjects were encased in a rubber bag as far as their necks and were seated in a heat cabinet. Incandescent lamps furnished sufficient heat to obtain 100 to 200 cc. of sweat in twenty to thirty minutes.

Thiamine was determined by the chemical method of Kirch and Bergeim,[3] and niacin,[4] pantothenic acid [5]

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and riboflavin [6] by microbiologic methods. In the thiamine method the sweat was concentrated by evaporation in vacuo in acid solution. In the other methods the sweat was filtered and heated to kill bacteria before analysis.

In certain instances large doses of the vitamins were given by mouth or by intramuscular injection at different periods before sweating was induced. Details of administration and analytic results obtained are given in table 1.

THIAMINE IN SWEAT

Thiamine values varied from <0.06 to 0.60 microgram per cubic centimeter of sweat. The <0.06 microgram value does not indicate a complete absence of thiamine but merely that the amount was too small to be determined by the chemical method used. In general subjects were given a shower bath shortly (usually about forty-five minutes) before sweating was induced. This was done in order that sweat evaporated on the skin might be removed so that the results obtained would approximate as closely as possible the values for the sweat as it poured out by the sweat glands. Nevertheless, some concentration of sweat on the surface of the skin probably occurred in some cases, and some of the values may be somewhat high on this account. This is suggested by the fact that when two successive samples of sweat were obtained the second sample generally showed somewhat lower values for thiamine as well as other vitamins. The lower values in the table are thus probably in general to be given some preference. Further light is thrown on this question by experiments 21 and 22. In experiment 21 two samples of sweat each of 200 cc. were collected, one immediately after the other. The first sweat should have washed the skin well, so that the second sweat should have been a fairly pure secretion. Yet analysis for the vitamins shows little change in values. Nor were the results much different in experiment 22 in which a single specimen was taken from the same subject without previous bathing. Experiment 22 may have been influenced by the fact that on the day of sweating the outdoor temperature was around 95 F. and hence fairly profuse sweating had occurred before the sample was taken. That the influence of evaporation of sweat on the skin in these experiments was not such as strongly to affect the results is further indicated by the reasonable constancy of the findings and by comparisons such as were made in experiments 19 and 20 in which the findings were similar in spite of the fact that in the first test the subject was given two baths at forty-five minutes and five minutes before sweating was induced and in the second case no bath at all was given on the day of sweating.

An average value of 0.2 microgram per cubic centimeter of sweat was obtained. For reasons stated, this figure may be a little high and the value of 0.15 microgram may be more nearly representative. A really definitive average would require a larger number of cases: 0.15 microgram per cubic centimeter would correspond to 150 micrograms per liter of sweat. Hardt and Still [2] found about 90 micrograms per liter in their experiments.

The physiologic significance of these results is not entirely clear. Williams [7] gives figures on the amounts of these vitamins contained in a well rounded diet (2,500 calories). For thiamine he gives a figure of 3 mg. a day. Lane, Johnson and Williams [8] calculate, however, that the thiamine content of the average American diet, such as was consumed by the middle two thirds or three fourth of the population prior to the advent of enriched bread and flour, was about 0.8 mg. per 2,500 calories and that if the use of enriched flour and bread becomes universal the average intake will be increased to about 1.3 mg. per 2,500 calories. Taking the figure of 150 micrograms per liter of sweat, one would have in this amount of sweat about 5 per cent of a good intake or about 11.5 per cent of the 1.3 mg. figure for the average American diet. Under average conditions of temperature and humidity and light work, the amount of sweat may not be much over 500 cc. a day. Any increases in temperature and amount of work readily increase the amount of sweating, so that with warm weather or fairly active work 2 to 3 liters of sweat may be secreted, and with a hot environment and active work considerably larger amounts of sweat may be poured out. With 3 liters of sweat the loss by secretion would correspond to about 15 per cent of intake on a good diet and more than 30 per cent of intake on the average American diet,

TABLE 1.—*Thiamine, Riboflavin, Niacin and Pantothenic Acid in Sweat (Micrograms of Vitamin per Cubic Centimeter of Sweat)*

Experiment	Thiamine	Riboflavin	Niacin	Pantothenic Acid	Type of Diet and Comment
1	<0.06	0.10	0.36	0.43	Regular mixed diet
2	<0.30	<0.05	0.10	0.35	Regular mixed diet
3A	<0.30	0.12	0.25	0.80	Regular diet + thiamine 3 mg., riboflavin 5 mg., niacin 50 mg. and pantothenic acid 10 mg. a day for 4 days; first sweat specimen
3B	<0.30	0.10	<0.10	0.50	Same as 3A; second sweat specimen
4	0.60	0.12	0.30	0.26	Same as 3A for 3 days; no extra vitamin for 2 days before sweating
5	0.15	0.11	0.40	0.25	Regular mixed diet
6	0.30	0.11	<0.10	0.48	Regular mixed diet
7	0.06	0.18	0.15	0.55	Regular mixed diet
8	0.24	0.20	0.10	0.78	Regular mixed diet
9	0.30	0.23	0.12	0.37	Regular mixed diet
10	0.06	0.16	0.12	0.78	Regular mixed diet
11A	0.06	0.20	0.12	0.20	Regular mixed diet
11B	<0.06	0.20	0.13	0.20	Same sweat as 11A but incubated for 24 hours at 37 C. before analysis
12	<0.06	0.03	0.25	0.23	Regular mixed diet
13	0.24	0.25	0.30	0.22	Regular mixed diet
14	<0.06	0.15	0.29	0.23	Regular mixed diet
15	0.06	0.03	0.26	0.20	Day of sweating thiamine 6 mg., riboflavin 10 mg., niacin 100 mg., pantothenic acid 20 mg.; preceding day 1¼ times as much
16A	0.36	0.14	0.46	0.54	Regular diet; sweat before vitamin injection
16B	0.15	0.05	0.35	0.23	Sweat 30 minutes after intramuscular injection of thiamine 10.5 mg., riboflavin 1.05 mg., niacin 35 mg., pantothenic acid 5.86 mg.
17	0.09	0.13	0.30	0.19	Regular mixed diet; 4 days after injection (16B)
18A	0.45	0.13	0.30	0.20	Regular mixed diet; before vitamin injection
18B	0.36	0.14	0.50	0.12	One hour after intramuscular injection of thiamine 15 mg., niacin 50 mg., riboflavin 1.5 mg. and pantothenic acid 8.4 mg.
19	0.30	0.25	0.25	0.28	Regular mixed diet; bath 45 minutes and 5 minutes before sweating
20	0.20	0.26	0.20	0.19	Same as 19 but no bath on day of sweating
21A	0.40	0.20	0.12	0.20	Regular diet; first 200 cc. of sweat
21B	0.30	0.30	0.10	0.30	Same as 21A; second 200 cc. of sweat
22	0.24	0.19	0.15	0.19	Same as 21A but no bath on day of sweating

6. Snell, E. E., and Strong, F. M.: Indust. & Engin. Chem. (Anal. Ed.) **11**: 346, 1939. Silber and Unna.[5]

7. Williams, R. J.: Approximate Vitamin Requirements of Human Beings, J. A. M. A. **119**: 1-3 (May 2) 1942.

8. Lane, R. L.; Johnson, Elizabeth, and Williams, R. R.: Studies of the Average American Diet: I. Thiamine Content, J. Nutrition **23**: 613 (June) 1942.

taking the 1.3 mg. figure. Hardt and Still figured that 5 to 15 per cent of ingested thiamine is lost with moderate temperature and work. It would seem that under average conditions the loss of thiamine in sweat, while appreciable, might not be of great physiologic significance. With profuse perspiration the loss might well be of sufficient concern to warrant special precautions to insure that the thiamine level of the diet did not fall too low. It must, of course, be borne in mind that some persons may excrete more than the average amount on which these calculations are based and some definitely less.

RIBOFLAVIN IN SWEAT

Riboflavin values found for sweat were 0.03 to 0.30 microgram per cubic centimeter, or an average of 0.15 microgram. With some special emphasis on the lower values or reasons previously stated, the average would be nearer 0.12 microgram. This would be 120 micrograms per liter of sweat and a little over 3 per cent of the figures of Williams for a good diet (3.7 mg. a day or about 5.5 per cent of a more nearly average American intake of 2.2 mg.[9] These values are somewhat less than those obtained for thiamine, and the physiologic significance of the losses by sweat may be somewhat less. The loss under average conditions is probably not of great importance but might become so in case of profuse perspiration and diets not optimal for this vitamin.

PANTOTHENIC ACID IN SWEAT

For pantothenic acid values of 0.12 microgram to 0.80 microgram were obtained with an average of 0.34 microgram per cubic centimeter of sweat. As the lower values probably represent more nearly the sweat as secreted, a figure of 0.3 microgram may be more representative. If one considers a good diet to contain about 11 mg. of pantothenic acid, the loss in a liter of sweat would be about 3 per cent of intake, or for 3 liters about 9 per cent. This loss is proportionally similar to the losses of thiamine and riboflavin and may have a similar significance.

NICOTINIC ACID IN SWEAT

Values for nicotinic acid in sweat were obtained varying from 0.1 to 0.46 microgram per cubic centimeter, with an average of 0.23 microgram. This may be slightly high owing to the concentration of sweat on the skin, so that a value of 0.2 microgram may be more nearly correct. This would correspond to 200 micrograms of nicotinic acid per liter of sweat. This would be about 0.5 per cent of the amount in a good diet or about 1 to 2 per cent of that in more usual but adequate diets. The loss of nicotinic acid in sweat could hardly be of physiologic significance.

INFLUENCE OF HIGH VITAMIN INTAKE

Several experiments were carried out in which the person was given large amounts of each of the vitamins studied either by mouth or by intramuscular injection. The results are given in table 1. The results for thiamine are somewhat irregular, so that further study is needed. The results are complicated by the fact that when no special vitamin is given a second specimen of sweat may contain less vitamin than a first specimen, owing probably to the fact that the first sweat washes out any adherent vitamin that may have been concentrated on or in the skin. Also, perhaps, because the effects of administration are somewhat transitory. Hardt and Still found that after one hour of exercise the ratio of thiamine in sweat to that in urine might be 71 : 1 and after an hour and a half only 8.5 : 1. Our results, as far as they go, indicate that injection or ingestion of thiamine in large amounts may have some effect on excretion in the sweat, but such effect is very slight compared with the amounts so administered.

It may be that there is some effect as long as the thiamine in the blood remains very high but that the thiamine is rapidly removed from the blood by the tissues so as not to be readily called on for excretion. This fits in with the fact that the thiamine content of the blood is very low and exists mostly in combined form. We have tested several specimens of sweat for thiamine pyrophosphate by treating the sweat with phosphatase [3] before analysis, and our results have always been negative.

No increase of riboflavin was noted in sweat after ingestion or injection of large doses of this vitamin. Nor were definite significant changes noted in the studies on niacin and pantothenic acid. It seems clear, therefore, that when large doses of the four vitamins studied are given by mouth or are injected intramuscularly a considerable part of this vitamin is not excreted in the sweat. This is probably due largely to the fact that these vitamins do not remain in free form in the blood in high concentration for any long period. This appears to be more probable than that the sweat glands have such an extremely low capacity for excretion of these vitamins, since, as shown by Hardt and Still, under certain conditions the excretion of thiamine in sweat may be greater than that in urine. Under ordinary conditions, however, the twenty-four hour elimination of these vitamins by the urine is much greater than in the sweat. It must also be borne in mind that the combined urine and sweat thiamine do not account for more than a part of the ingested thiamine, apparently because of the destruction of the vitamin in the body.

The losses per liter of sweat of about 3 to 10 per cent of the intake for thiamine, riboflavin and pantothenic acid are not much different from the losses of about 4 per cent for ascorbic acid (about 2 mg. per liter compared with the adult requirement of about 50 mg. a day). Since vitamin C-salt tablets have been reported from the medical division of the du Pont Company as superior to salt alone in cases of profuse sweating, it is possible that the other vitamins might also be helpful under similar conditions.

BACTERIA AND THE VITAMINS OF SWEAT

The bacteriology of the sweat as far as these vitamins are concerned may be considered from two angles. The question arises first as to whether the sweat bacteria destroy or use up the vitamin present or engage in any synthesis. We found on incubating sweat at 37 C. for twenty-four hours that there was some decrease in the thiamine level but no change in the pantothenic acid, niacin or riboflavin levels. Under these conditions considerable bacterial growth occurs and the sweat changes from a p_H of about 5 to one of about 8. It may be that the destruction of thiamine noted was due to the alkalinity developed. However, it does not appear that

9. Stiebeling, Hazel K., and Phipard, Esther F.: Diets of Families of Employed Wage Earners and Clerical Workers in Cities, Washington, D. C., Circular 507, United States Department of Agriculture, 1939.

bacteria are much concerned with either the formation or the destruction of these vitamins on the surface of the skin and that the vitamins found are not of bacterial origin.

Further support for this view was obtained in experiments in which 5 cc. of sweat was added to 5 cc. of plain broth with or without the addition of 20 micrograms of thiamine and incubated at 37 C. for twenty hours. No significant change was noted in the amount of thiamine in either case, indicating that the bacteria of the sweat neither synthesized nor destroyed thiamine under these conditions. The use of dextrose acid mediums in place of plain broth gave similar results, indicating that the p_H of the medium was not a factor. The results are shown in table 2.

SUMMARY AND CONCLUSIONS

Heat sweat was found to contain on the average about 150 micrograms of thiamine, 120 micrograms of riboflavin, 300 micrograms of pantothenic acid and 200 micrograms of nicotinic acid. It is possible that these values may be slightly higher than true values for sweat as secreted by the glands because of the difficulty of entirely avoiding concentration due to evaporation on the skin surface. These values per liter correspond

TABLE 2.—*Sweat Bacteria and Thiamine Destruction and Synthesis*

Five cc. of sweat plus 5 cc. of medium was incubated at 37 C. for twenty hours. Bacterial growth was noted in all cases.

Experiment	Medium Used	Thiamine Present Before Incubation, Micrograms	Thiamine Found After Incubation, Micrograms
1	Plain broth	0	0
2	Plain broth	0	0
3	Plain broth	20	21
4	Plain broth	20	21
5	Acid dextrose broth	0	0
6	Acid dextrose broth	0	0
7	Acid dextrose broth	20	20
8	Acid dextrose broth	20	21

for thiamine to about 5 per cent of intake on a good diet, for riboflavin and pantothenic acid to about 3 per cent and for nicotinic acid to about 0.5 per cent. For average American diets the percentages would be more nearly 10 per cent for thiamine, 5 per cent for riboflavin and 1 per cent for nicotinic acid. The excretion of such amounts of these vitamins cannot be said to be negligible from the physiologic standpoint although perhaps becoming of real importance only in case of rather profuse sweating or on diets low in these vitamins. The elimination of nicotinic acid could hardly be of importance in any case. The losses of the other vitamins are of the same order as losses reported for ascorbic acid in sweat. Since favorable results have been reported in the administration of ascorbic acid in cases of profuse perspiration, it is possible that supplements of other vitamins might be worthy of trial under similar conditions. Ingestion or intramuscular injection of large amounts of these vitamins did not lead to any noticeable or persistent increase of their secretion in the sweat.

These vitamins as found in sweat appear to be a true excretion not appreciably influenced by bacteria on the skin. Sweat contains sufficient of these vitamins to promote bacterial growth provided conditions are otherwise favorable. Thiamine appears to exist in sweat only in the free form.

FAMILIAL TUBEROUS SCLEROSIS (EPILOIA) WITHOUT ADENOMA SEBACEUM

REPORT OF TWO CASES

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Tuberous sclerosis (epiloia, Bourneville's disease) is considered a rare and unusual entity. For this reason its presence as a diagnostic possibility in cases in which epileptiform seizures are present is seldom entertained. Yet the literature on this subject has assumed impressive proportions. In the sixty years from the time Bourneville [1] first described it in 1880 down to 1940 one hundred and twelve reports have been collected dealing with tuberous sclerosis and its related neurocutaneous syndromes (Recklinghausen's neurofibromatosis, angiomatosis cerebri or Sturge-Weber's disease, and von Hippel-Lindau's disease).

In recent years the roentgenologist has become more alert to the significance of metastatic calcifications (calcified plaques) in survey films of the skull as an identifying feature of tuberous sclerosis, and the internist has in turn been stimulated to search for its other characteristic manifestations. With the increasing use of pneumoencephalography, this type of ectodermosis is being more commonly reported, its features are more clearly defined and more light has been thrown on its hamartial nature and its relation to the tumor problem.[2]

In this communication it is our purpose to present 2 cases of familial epilepsy in which the weight of evidence is diagnostic of tuberous sclerosis.

REPORT OF CASES

CASE 1.—W. M. Jr., a white man aged 22, seen April 8, 1941, had a history of epileptic seizures and poor vision. He had been a confirmed epileptic since the age of 2 years. In the week preceding the first visit he averaged eight to ten seizures a day. Well defined mental deterioration and periods of irritability had appeared in recent months. He stuttered and had never been able to pursue any gainful occupation. His father's grandfather was known to have had convulsions. A grandfather and aunt were operated on for "brain tumor." Physical examination revealed no cutaneous lesions and no evidence of facial rash suggestive of adenoma sebaceum. The extremities showed no loss of motor power. Decided mental retardation was present.

The eyeballs were prominent with a widening of the palpebral fissures. There was a horizontal and rotatory nystagmus present with movement to the right. Extensive choroidal changes were present involving both eyes, with a moderately advanced grade of optic atrophy. Large macular atrophic lesions were noted. Myopia of a high grade was found. The lesions were believed by the ophthalmologist to be on the basis of a hereditary macular degenerative process, congenital and colobomatous in origin.

Roentgenograms of the skull showed that the outer table was thick, and a number of calcified deposits were seen

From the Jewish Hospital.
Dr. Samuel Levine rendered aid in the interpretation of the roentgenograms.
Released for publication by the War Department Manuscript Board, which assumes no responsibility, other than censorship, for the contents of this article.

1. Bourneville, D. M.: Contribution a l'étude de l'idiotie; idiotie et épilepsie hémiplégique, Arch. de neurol. **1**: 81-91, 1880.
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