April 28th. The penile sore remained healed, and the surface had assumed an almost normal appearance, except for a small shallow depression remaining to show where original sore had been.

June 17th. Nearly four months after actual healing of sore; no sign of any recurrence.

Undoubtedly the gonorrhoeal complication helped to aggravate the condition and retarded the healing of the ulcer. At the same time it is not unlikely that the antimony tartrate injections and the antimony tartrate taken by mouth helped to light up the old gonorrhoeal trouble. It is, however, unquestionable that the antimony tartrate was the only drug which had any effect upon the sore. Definite signs of healing were observed after the fourth injection, although the patient himself declared that he found improvement after the second injection.

All other local treatment was suspended while the injections were being given, with the exception of an antiseptic wash, night and morning, for the sore, followed by the application of a little dusting powder composed of equal parts of calomel, boracic acid, and iodoform, which had been previously used without the slightest effect.

Altogether, about 3 grains of antimony tartrate were injected intramuscularly over a period of thirty-six days. Only twelve injections were given. Castellani recommends ½ to 1 c.cm. as the dose of his No. 1 formula of antimony tartrate. I began with 9 minims (about ¼ gr. antimony tartrate), and gradually went up to 1.2 c.cm., or ⅓ gr. antimony tartrate, for the last five injections. By mouth, roughly 27 to 30 grains of antimony tartrate were taken over the same period. How much of the cure can be attributed to the oral administration of the drug is difficult to calculate, but it was noted that although the patient was taking 5 to 20 minims of antimony wine three times a day, in gradually increasing doses, from November 4th, 1919, to January 14th, 1920—a period of seventy-one days—without any appreciable effect on the condition of the sore, it is reasonable to conclude that only a very small amount of the drug, subsequently given by mouth, had any definite effect on the process of healing. On the other hand, very definite improvement took place after the fourth intramuscular injection, that is, before the drug given orally could have had time to have much constitutional effect. It is stated that:

"Antimony is slowly absorbed and is taken up from the blood and stored in the liver. It does not appear to have any important influence upon the corpuscles, but diminution in red cells, leucocytosis, and decrease of alkalinity have been recorded." Also, "it is excreted in the intestine, and by the liver, kidneys, and skin" (vide Bruce and Dilling, *Materia Medica*, p. 139).

Some authorities state that it causes peripheral vascular dilatation. Probably the latter action of the drug, a certain amount of leucocytosis, and that part of it excreted through the skin, were the chief sources of improvement in the local condition. The amount of the drug administered orally, acting in the above way, would naturally be infinitesimal, owing to the very slow absorption. Some authorities, among them being Greig and Curjel, consider that the condition is only benefited by large doses of antimony tartrate (1 to 3 grains intravenously). This may be where the disease is extensive and advanced. Other authors have reported cases of failure. The case of the Cantonese woman already referred to was a failure, but it was hardly a fair test case, as the disease was far advanced, involving the clitoris, vagina, the fourchette, both labia minora, and the right labium major. It was impossible to give intravenous injections, owing to the smallness and inaccessibility of the veins, while the intramuscular injections of antimony tartrate, in saline or distilled water (grain ¼), caused several local abscesses, and had to be discontinued. Daniels stated to me that any improvement in such an advanced female case is very improbable.

Fortunately, the case here recorded was definitely localized, and neither advanced nor extensive; also, the progress of spread was extremely slow. It was an ideal case for the administration of the drug by the intramuscular route. The results were so satisfactory, and the cure so quickly attained by this method, that the report of the case may be the means of encouraging some others to use the same treatment. No doubt early cases—before the disease has got a firm hold, and where the ulcer is not extensive—will prove most amenable to the action of the drug intramuscularly.

With advanced and extensive cases it would be useless to treat them otherwise than by larger doses, by the intravenous route, over a more extended period, and in hospital, where the action of the drug and the condition of the patient can be observed carefully from day to day.

SEVEN CASES OF ESSENTIAL PENTOSURIA.

BY

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ALIMENTARY PENTOSURIA is not a very rare condition, particularly in summer when fruits containing arabinose are often eaten in considerable quantities, but essential or spontaneous pentosuria, which is not dependent upon the ingestion of pentose-containing foods, is exceedingly uncommon, some forty cases only being on record. Up to the present no example of the condition has been reported in this country, the published cases having all occurred in America or Germany. Last year we had the remarkable experience of meeting with seven cases, five of which were encountered in one month and the other two a few weeks later. Five of the cases proved to be examples of simple essential pentosuria, inactive arabinose being the only sugar present in the urine, in the other two small quantities of dextrose and pseudo-laevulose were found in addition. One of the patients with pure pentosuria had been treated for diabetes for twenty-six years, two had been dieted along orthodox lines for the same complaint without any improvement for several months, a fourth was referred to one of us as a case of lactosuria, presumably because the sugar in the urine did not ferment with yeast, and in the fifth the presence of sugar had been discovered accidentally, although its nature was not determined, previous to an operation. The remaining cases had been rejected for life insurance owing to the presence of glycosuria.

The majority of the cases of essential pentosuria hitherto described have been Germans, or of German or Russian descent, and a striking proportion have been Jews. Three of our cases were Jews, two were of Greek descent, but the others were purely English in birth and ancestry. A striking feature of the condition is its tendency to occur in several collaterals of a family, and some pentosuriacs have been members of diabetic families. Two of our patients, those of Greek descent, were father and son, but no history of glycosuria in any other member of the family could be obtained. Two of the Jews (Cases 4 and 6) were also related, being uncle and nephew. In this instance there was a family history of glycosuria, the father of the elder patient having been treated by the late Dr. Pavy for many years for diabetes, although he eventually died at the age of 67 from Bright's disease; a niece of the same patient and cousin of the other, consulted one of us and was found to be passing about 50 grams of sugar a day, the whole of which however was dextrose. The family histories of the other cases were free from diabetes or glycosuria, so far as could be ascertained. Six of the patients were males and one was a female. Their ages ranged from 19 to 75 years. These details, with the actual amount of sugar passed and the other more important results of the analyses of the urines, are shown in the following table (Table I). The data for Case 5 are incomplete, as only an odd specimen of the urine could be obtained for examination. The dextrose and pseudo-laevulose were estimated by the methods described by one of us in 1917[1] and the pentose by a modification of Jolles's process carried out as follows:

One hundred c.cm. of the urine are mixed with 150 c.cm. of hydrochloric acid (12 per cent.), and heated in a flask fitted with a reflux condenser for a quarter of an hour in a water-bath. The contents of the flask are subjected to steam distillation and 500 c.cm. of the distillate collected. Of this 100 c.cm. are neutralized with sodium hydrate (20 per cent.), using methyl orange as the indicator, and then made faintly acid by adding one or two drops of half normal acid. A measured quantity of normal sodium hydrogen sulphite is introduced, and the mixture left to stand for two hours. The excess of sulphite is then titrated with tenth normal iodine solution, using starch as the indicator. From the amount of sulphite consumed the percentage of pentose present can be calculated, each cubic centimetre of sulphite corresponding to 0.07595 gram of pentose.

Arabinose does not reduce copper salts as readily as dextrose, and, as the percentage of the sugar excreted is

TABLE I.—*Results of Analyses.*

Case.	Sex.	Nationality.	Age.	Urine.	Sp. gr.	Albumin.	Sugar.							Acetone.	Total Nitrogen.	Urea.	Uric Acid.	Amino-acid Nitrogen.	Indican.	Urobilin.
							Benedict's Test.	Bial's Test.	Rotation.	Fermentation.	Dextrose.	Pseudo-laevulose.	Pentose.							
				c.cm.							gms.	gms.	gms.		gms.	gms.	gms.	gms.	gms.	
1	M.	Greek	47	700	1030	0	+	+	±	0	0	0	2.4	0	8.9	17.2	0.42	0.15	0.007	++
2	M.	,,	22	1,000	1026	0	+	+	±	0	0	0	2.5	0	17.4	32.7	0.66	0 35	0.005	++
3	F.	English	75	800	1030	tr.	+	+	±	0	0	0	3.4	0	8.3	16.5	0.48	0.20	0.024	++
4	M.	Jew	19	1,400	1030	0	+	+	±	0	0	0	3.9	0	19.2	37.5	0.77	0.91	0.005	++
5	M.	,,	40	?	1025	0	+	+	±	0	0	0	?	0	—	—	—	—	—	++
6	M.	,,	48	1,600	1020	0	+	+	−	+	3.2	6 4	3.2	0	18.1	33.9	0.44	0.30	0.006	++
7	M.	English	32	800	1030	0	+	+	+	+	5.0	1.6	1 6	0	9.6	16.8	0.32	0.35	0.008	++

always small, a delayed reaction with a sudden change of colour—especially with Benedict's test—is suggestive. The best confirmatory test for routine diagnostic work is Bial's, but it may also give a reaction with an excess of glycuronic acid, and does not differentiate between the inactive arabinose of essential pentosuria and the l-arabinose of alimentary pentosuria. The results, therefore, need confirmation before a reliable diagnosis can be arrived at. With the help of the polariscope the dextro-rotatory l-arabinose may be distinguished from the inactive form, and a controlled fermentation test with yeast shows that the sugar does not ferment, but the most reliable data are obtained by preparing the p-bromphenylosazone and the diphenylhydrazone, and studying their melting points and rotatory powers. As will be seen from the table (Table I) the urine from all our cases gave a positive reaction with Bial's test. The five cases of pure pentosuria passed urine which did not rotate polarized light and did not ferment with yeast, but in the other two the urine was optically active, and formed gas when submitted to the action of yeast owing to the presence of other sugars. The results obtained with p-bromphenylhydrazine and diphenylhydrazine are shown in the following table (Table II). For comparison the standard results given by racemic or inactive arabinose and l-arabinose are also shown.

Owing to the limited amount of material available in some instances, and an inability to secure a further supply of diphenylhydrazine when our pre-war stock had been exhausted, we were unable to carry out all the tests in every case, or to obtain invariably a pure product for the determination of the melting-point, but the results as they stand are sufficiently exact to suggest that inactive arabinose was the pentose present in all, and that this was undoubtedly so in three of the cases is proved by our having been able to isolate the pure sugar and study its properties. The isolation was carried out by the following procedure.

Method.

The diphenylhydrazone was first prepared. The urine was thoroughly mixed with one-tenth its volume of a saturated solution of lead acetate, boiled and filtered. The filtrate was treated with sodium sulphate until the lead had been completely precipitated, and this precipitate was filtered off. The clear solution was now evaporated to one-third of its volume and twice this volume of alcohol added. After standing for two hours it was again filtered and the sugar present in the filtrate estimated. For each gram of sugar found to be present 1.4 gram of diphenylhydrazine hydrochloride and 1 gram of sodium acetate were added, and the mixture boiled in a water-bath, under a reflux condenser, for two hours. The crystals which appeared on cooling were filtered off and recrystallized two or three times from aqueous pyridine until a constant melting-point was obtained.

From this purified product the sugar was separated by the action of formalin. For each 3 grams of the diphenylhydrazone contained in a flask, there were added 12 c.cm. of formalin (40 per cent.) and 20 c.cm. of water. The contents of the flask were well shaken for an hour, and the flask was then heated on a water-bath for another hour. After cooling the solution was extracted with ether three times and evaporated down to a small bulk. On standing the sugar crystals separated out, and were purified by recrystallization from absolute alcohol.

The urine of three of our cases treated in this way yielded small white crystals which melted at 163-4° C., and in solution were optically inactive, thus corresponding to inactive arabinose. In order to prove that the sugar was actually arabinose, however, it was oxidized with bromine and the barium salt of the acid formed was prepared.

One gram of the sugar was dissolved in 10 c.cm. of water and 1 gram of bromine and 1 gram of barium carbonate added. The mixture was allowed to stand at the room temperature for three days, then boiled and filtered from the excess of carbonate. The barium salt was precipitated from the filtrate with absolute alcohol, filtered off, purified by recrystallization, and its barium content determined. This was found to work out at 36.9 per cent., a close approximation to the theoretical yield of 36.92 per cent. by barium arabonate, and thus proving that the sugar separated from the urine was arabinose. Further evidence in support of this conclusion was obtained by preparing the r-arabonalactone, which has a melting point of 98° C. One gram of the barium salt, prepared as above, was dissolved in 10 c.cm. of water and decomposed with a stream of carbon dioxide gas. The precipitated carbonate was filtered off and the filtrate evaporated on

TABLE II.—*Polarization and Melting Points.*

	p-bromphenylosazone.		p-bromphenylhydrazone.		Diphenylhydrazone.		Isolated Sugar.	
	M. P.	Rotation.	M. P.	Rotation.	M. P.	Rotation.	M. P.	Rotation.
L-Arabinose	196-200°	+	160-2°	+	216-8°	+	130-160°	+ 104-5
R-Arabinose	200-202°	±	160°	±	204-5°	±	163-164°	±
Case 1	202°	±	−	−	204°	±	−	−
Case 2	200°	±	−	−	203°	±	−	−
Case 3	202°	±	160°	±	205°	±	164°	±
Case 4	200°	±	−	−	200°	±	−	−
Case 5	200°	±	−	−	−	−	−	−
Case 6	200°	±	−	−	205°	±	163°	±
Case 7	200°	±	−	−	205°	±	164°	±

a water-bath to a small volume. On standing, hard white crystals separated out and were found to melt at 98° C.

Inactive arabinose is made up of equal parts of the dextro-rotatory and laevo-rotatory varieties, and although the difference in its optical activity and the rotatory powers, melting points, and solubilities of its derivatives are sufficient to distinguish it from these two sugars, the actual separation of its constituents furnishes the most conclusive proof of its composition. We therefore attempted to effect this, and were successful in isolating the laevo-rotatory sugar from one specimen and the dextro-rotatory sugar from another. The recovery of both from one sample was impossible owing to the small amount of material available.

Separation of Laevo-rotatory and Dextro-rotatory Sugar.

In order to obtain the laevo-rotatory sugar 1 gram of the r-arabonalactone, prepared as described above, was dissolved in water and mixed with a saturated solution of brucine, cooled, and the brucine salt filtered off. This was suspended in water, shaken with barium hydrate, filtered, and the filtrate extracted five times with ether to remove the excess of brucine. The watery solution was then decomposed with carbon dioxide and the resulting barium carbonate filtered off. The solution, which was now found to be dextro-rotatory, was evaporated on a water-bath, and the lactone which separated out was re-crystallized from alcohol. It was found to have a melting point of 95° C. On being dissolved in water and treated with sodium amalgam the lactone gave a sugar which yielded a phenylosazone with a melting point of 160° C., and 0.2 gram dissolved in pyridine-alcohol showed a specific rotation of + 1.10°, proving that the sugar was l-arabinose.

The dextro-rotatory moiety of the sugar was separated from another sample as follows: One gram of the purified sugar, prepared as before, was mixed with 1 gram of sodium acetate and 1 gram of l-menthyl-hydrazine and heated in a water-bath for two hours. On cooling, the product which separated out was recrystallized from alcohol, and found to have a melting point of 131° C., corresponding to d-arabinose-l-menthylhydrazone. From this the free sugar was separated by the action of formaldehyde. On preparing the phenylosazone it was found to have a melting point of 160° C., and 0.2 gram dissolved in pyridine-alcohol had a specific rotation of − 1.1°, corresponding to d-arabinose.

The source of origin of the inactive arabinose found in the urine in essential pentosuria has been the subject of much debate and many experiments. That it is not derived from the carbohydrates of the food is shown by the fact that their complete withdrawal has no influence on the excretion of the sugar in the urine. There is some evidence that it may be related to the proteins in the diet, however, for Klercher [2] found that the output varied considerably during the day and that there was a certain parallelism between the amount excreted and the total nitrogen content of the urine. Klercher and Janeway [3] also observed a diminished excretion on a purin-free and milk diet. Neuberg [4] has advanced the hypothesis that the parent substance may be galactose, and in support of this are the observations of Tintemann [5] and Klercher that a slight increase in the amount of pentose in the urine followed the administration of galactose or lactose, especially in the first few hours after the sugar was taken. Bial and Blumenthal, on the other hand, failed to find any such increase. We had the opportunity of carrying out a number of experiments bearing on this question on one of our patients who went into a nursing home for observation. In this case the administration of lactose on two occasions, once alone and later along with oatmeal porridge, milk, bread, and coffee, had no effect on the amount of arabinose appearing in the urine, even in the hours immediately succeeding the meal. When all carbohydrate food was withdrawn the excretion of the pentose was practically unchanged, but as the protein was diminished the output of pentose fell from 3.2 grams to 0.5 gram daily, and then gradually rose again to its former level as the protein intake was increased.

It is noteworthy that the urine of all our cases of pentosuria contained an excess of urobilin and showed a high excretion of amino-acid nitrogen, a combination which we have come to regard as indicative of defective functioning of the liver; moreover, in the case where continuous observation was possible, we found that the output of arabinose varied with the amount of urobilin and the quantity of amino-acid nitrogen excreted. We have also noticed that alimentary pentosuria has been associated with an excess of urobilin and a high amino-acid nitrogen in the urine. We are therefore inclined to conclude that pentosuria is dependent upon defects in the functional activity of the liver. In some cases it is probably due to a congenital, or possibly an acquired, abnormality, which results in the imperfect metabolism of a pentose of protein origin, thus giving rise to essential pentosuria, while in others it is merely an inability to destroy the pentose derived from foods containing it, with the result that alimentary pentosuria follows their use.

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A NOTE ON THE TREATMENT OF CUTANEOUS ERYSIPELAS WITH BRILLIANT GREEN.

BY

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ERYSIPELAS is a disease to which little attention is paid in these days, though formerly it used to be regarded with respect and even dread. Probably there are few diseases which have been treated in so many different ways or with so many different topical applications. During the war, when streptococcal infections of wounds were prevalent, it was not a very infrequent complication, but the prognosis rarely gave rise to anxiety, and isolation of erysipelas cases is not now regarded as essential for the well-being of other patients in the wards. The reason is not far to seek. To be logical all streptococcal infections should be segregated, and the fact that the infection has reached the superficial layers of the skin, and is therefore more apparent to the eye, is not a sufficient argument in favour of isolation. Furthermore, it is well known that, except at the extreme age periods of life, erysipelas is not a dangerous disease, and in previously healthy patients the mortality is very low. These patients may be very ill for a time, and the rash may spread almost all over the body, but with intelligent treatment and good nursing the outlook is almost always favourable, even when the lesion originates in connexion with a serious wound. With the abolition of sepsis in clean surgical wounds erysipelas has retired to a place of little importance. Cases, however, are still admitted to hospital in fair numbers, and at St. Thomas's they are taken into the isolation block reserved for obviously septic cases. During the last eighteen months I have been in charge of these beds in the hospital, and therefore I have had the opportunity of observing many examples of this disease and of comparing the relative merits of a large number of topical applications. It has enabled me to come to conclusions as to whether topical applications are of real value, and also which of the many in use may be relied upon to limit the disease and to ease the patient's distress.

In 1909 I published, in conjunction with Dr. P. N. Panton, some observations on erysipelas and allied infections,[1] in which we emphasized the facts that erysipelas is usually a streptococcal inflammation of the epidermis, but that the streptococci are of many different strains. From this, and by subsequent clinical observations, it is realized why the treatment of this condition by stock serums and vaccines is not conspicuously successful. Otherwise it would appear that such treatment ought to be efficacious. I have since been keenly on the look-out for any evidence that topical applications really influence the disease. It was at one time held that the extension of the rash in the skin could be limited by incisions outside the affected zone, by scarification, or painting a ring of silver nitrate around it, but these methods have all been abandoned owing to their lack of success. In some cases, at any rate, there is a coincident streptococcal lymphangitis, and this may account for failure. Perhaps such examples should be termed phlegmonous, or cellulo-cutaneous erysipelas, but anyhow these cases are difficult to separate from the purely cutaneous ones.

A whole legion of topical applications has been employed in the treatment of this disease; they have been used for two purposes—namely, to give comfort to the patient, and to limit the spread of the infection. The first is undoubtedly of importance since in some cases there is intolerable itching which disturbs the patient's rest, but the second is the supreme test of all local treatment.