Summary.

Ionization of the nasal mucous membrane with a 1 per cent. solution of certain drugs, especially alepol, produces in many cases an apparently complete cure of leprotic lesions in this site.

It is particularly effective in otherwise negative cases where infection of the nasal mucosa persists, but even cases which have not yet undergone other treatment react.

The ulcers heal and nasal breathing becomes freer after treatment.

Some of the cases have been consistently negative for two months, which is the longest period that had elapsed between the conclusion of treatment and the writing of this paper.

If these results are confirmed it is clear that in a large number of cases the duration of segregation may be considerably curtailed.

REFERENCE.

¹ Wade and Solis: *Journal of the Philippine Islands Medical Association*. Vol. 7, April, 1927, No. 4, p. 111 et seq.

THE COMBINATION OF ANILINE DYES AND RADIATION IN THE TREATMENT OF TUMOURS.

BY

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ANILINE dyes have been widely used in attempts to cure cancer in the human subject, and various claims have been made. Recently Mr. Frank Coke has been using preparations of the fluorescein series. The best results were obtained with sodium fluorescein, and he is of opinion that better results are obtained by a combination of this drug and hard x rays, than with x rays alone. The fluorescein was administered by local external application and by the mouth. Mr. Coke suggested to me that possibly some specific fluorescent action might be taking place. The following experiments have, therefore, been carried out to test this idea.

A slow-growing rat sarcoma was used. Small pieces, approximately 1 c.mm., were exposed to gamma radiation from two radium applicators of 110 mg. $\text{RaBr}_2 \cdot 4\text{H}_2\text{O}$, having an area of 2 by 2 cm. It was found that whereas three hours' exposure *in vitro* killed the tumour cells, exposure for two and a half hours resulted in no more than delayed growth, when inoculated into rats, as shown in Table I.

TABLE I.—Growth of Slow Sarcoma after Two and a Half Hours' Exposure to Gamma Radiation *in vitro*.

	Days after inoculation—							
	5	7	10	12	14	17	19	21
Rat 1	5×4	6×5	8×6	10×6	13×8	16×11	18×12	22×16
Rat 2	3×3	5×4	7×5	11×6	14×7	16×9	19×10	21×13
Rat 3	o	3×3	5×5	6×6	9×8	12×10	15×10	15×15
Rat 4	o	o	o	6×4	7×5	8×6	11×7	15×11
Rat 5	4×4	5×5	6×5	7×6	8×7	10×9	13×12	14×14
Rat 6	3×3	4×4	4×4	5×5	6×6	7×6	9×7	17×3
Rat 7	o	o	o	o	5×5	8×6	10×7	10×7
Rat 8	o	5×5	6×5	11×6	9×8	10×9	12×11	12×12
Rat 9	4×4	5×4	5×4	5×5	6×5	7×5	8×5	8×7
Rat 10	o	o	o	o	o	o	6×6	6×6

In each of the tables the figures represent the size of the tumours in millimetres. o=Small nodule not measurable.

Small pieces were likewise exposed to various concentrations of fluorescein in Locke's solution, and it was found that 1/80 per cent. solution applied for six hours had no decided effect on the rate of growth of the tumours resulting from the inoculations (Table II).

TABLE II.—Growth of Slow Sarcoma.

	Days after inoculation—											
	5		7		10		12		14		17	
	C	E	C	E	C	E	C	E	C	E	C	E
Rat 1	o	o	6×5	9×5	10×6	14×6	14×8	20×8	16×10	24×14	19×14	33×18
Rat 2	8×5	o	9×5	6×5	12×7	10×6	14×8	12×7				
Rat 3	o	o	o	o	4×4	8×4	7×5	10×6	10×10	14×11	18×11	20×12

C=Control. E=After six hours' treatment with 1/80 per cent. fluorescein.

To test whether the combination of the two agents exhibited any specific effect, exposures of two and a half hours to gamma radiation, and of five hours to 1/200 per cent. fluorescein, were used. The exposures were made in the following manner:

- Eighteen pieces for two and a half hours in 1/200 per cent. fluorescein, Locke's solution. Then for two and a half hours in 1/200 per cent. fluorescein, Locke's solution, and exposed to gamma radiation at the same time. Then for two and a half hours in Locke's solution, after washing in Locke's solution to remove the dye.
- Eighteen pieces for two and a half hours in Locke's solution and exposed to gamma radiation at the same time. Then for five hours in 1/200 per cent. fluorescein, Locke's solution.
- Eighteen pieces, control, for seven and a half hours in Locke's solution.

A and B, therefore, had precisely the same exposures to gamma radiation and to fluorescein; the only difference was that in A the radiation was applied *after* fluorescein treatment, and in B *before* fluorescein treatment.

The fifty-four pieces of tumour were inoculated into nine rats, six pieces into each rat, and the resulting tumours are shown in Table III. There it is seen that the two

TABLE III.—Growth of Slow Sarcoma under Conditions given in the Text.

	Days after inoculation—															
	5			8			11			15			17			
	A.	B.	C.	A.	B.	C.	A.	B.	C.	A.	B.	C.	A.	B.	C.	
Rat 1 {	—	—	o	—	—	8×7	—	—	12×10	—	—	18×14				
Rat 2 {	—	—	o	—	—	8×8	o	—	12×10	4×4	—	16×14	6×5	—	L. Ts.	
	—	—	o	—	—	6×5	o	—	9×9	o	—	14×11	4×4	—		
Rat 3 {	—	—	o	—	—	7×5	—	—	10×7	—	—	12×9				
	—	—	o	—	—	8×7	—	—	13×9	—	—	15×11				
Rat 4 {	—	o	o	—	o	7×7	—	o	11×9	—	9×7	L. Ts.	—	13×10		L. Ts.
	—	—	o	—	—	8×7	—	o	12×9	—	3×3		—	5×5		
Rat 5 {	o	—	o	o	—	7×6	o	—	9×8	6×5	o	13×11	9×9	3×3	16×14	
	—	o	—	o	—	—	o	—	—	7×6	o	—	9×9	o	—	
Rat 6 {	—	—	o	—	—	5×5	—	—	8×8	—	—	12×9				
	—	—	o	—	—	5×5	—	—	7×7	—	—	10×9				
Rat 7 {	—	—	o	—	—	6×5	—	—	8×8	—	—	12×11				
	—	—	o	—	—	4×4	—	—	7×5	—	—	10×9				
Rat 8 {	—	—	o	—	—	6×5	—	—	9×7	—	—	12×10				
	—	—	o	—	—	4×4	—	—	6×4	—	—	9×8				
Rat 9 {	—	—	—	—	—	—	—	—	—	—	—	—	—	—		
	o	—	o	o	—	o	o	—	4×3	5×5	—	8×6	8×8	—	12×10	

would not produce this result. Here also there was summation, but no evidence of any specific action.

These results, in which more than one agent is brought to bear on a pathological condition, at any rate suggest that the summated action of several agents may be a better form of treatment than the pushing of a single agent to near the limit of the patient's tolerance.

REFERENCE.

¹ Mottram, J. C.: *British Medical Journal*, January 28th, 1928, p. 132.

"DEBILITY" IN CHILDREN AND CYCLICAL VOMITING.*

BY

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ALL physicians are familiar with the large group of children who are brought for advice regarding the most varied symptoms, for which no adequate cause can be found, and yet which do not seem to be directly due to some antecedent illness such as scarlet fever, measles, or tonsillitis. Such children are for the most part labelled "debility," and are either given tonics or sent away to the country or seaside, the unlucky ones having their tonsils removed first. It is this group which forms the bulk of all the cases attending any out-patient department for diseases of children.

The object of the present communication is to show that, although the symptoms for which these children attend are varied, yet the common underlying set of causes are of the same nature as those found in the cyclical vomiting of children; in other words, that the "debility" and cyclical vomiting to be described hereafter may be regarded as the minor and major manifestations of one disorder, bearing to each other much the same relation as petit mal and grand mal in epilepsy. Further, it is desired to emphasize the frequency with which cyclical vomiting occurs in children of all classes, and not only among the well-to-do, as is commonly taught. Finally, it is hoped to show that both the minor and the major forms of this disorder are easily preventable by the same treatment.

In September, 1923, a group of 30 children suffering from attacks of cyclical vomiting was collected, observed, treated, and followed up for the following three years. It was then believed that this disorder was rare in children of the hospital class, but it soon became evident that this was not the case. On two separate occasions a census of such cases was taken in the out-patient departments of two London hospitals, and it was found that approximately 30 per cent. of all children over 2 years of age gave a history of typical attacks. Since then it has become apparent that cyclical vomiting in children of the social class that makes use of hospital out-patient departments is so frequent that it is regarded by the parents as a normal accompaniment of childhood. They regard it as a "bilious attack" attributable to indiscretions of diet, and do not as a rule consider it sufficiently important to require medical attention. Probably for these reasons, and because attacks rarely occur in children already in institutions, it has been regarded by the profession as an infrequent condition in hospital class children.

Early in the investigation an attempt was made to study the conditions in the blood and urine before, during, and after the attacks. At first several cases were admitted to hospital, but in none of them did attacks supervene. It therefore became obvious that in-patient observations of this disorder were impracticable, and the cases under observation attended as out-patients at fortnightly intervals. After some months it was noticed that, though new cases of cyclical vomiting were seen, none of those already under observation had further attacks, though no special treatment had been undertaken. In order to secure regular attendance malt extract had been given to all the cases as a placebo; but on further investigation it was found that it was the malt which was preventing the occurrence of

attacks, and that sugar in other forms had a similar result. Thereafter all children with this complaint were given extra sugar as a routine, with the result that in the great majority of over 200 cases treated the attacks have been entirely prevented.

It is now well known that the whole subject of cyclical vomiting is intimately related to that of ketosis. Frew¹ in 1911 showed that acetonuria was present in 61.2 per cent. of 662 children admitted to hospital for various reasons. It was first shown by Marfan² that attacks of cyclical vomiting were regularly accompanied by excess of ketone bodies in the urine. Gamble, Ross, and Tisdall³ state that the amount of acidosis present (reduction of serum bicarbonate of blood) is fully accounted for by the excess of ketone bodies in the blood. Ross and Josephs in 1924⁴ produced attacks of cyclical vomiting in children by starvation, and from a study of the blood sugar under these conditions suggested that hypoglycaemia was probably an essential feature of the attacks. Brown and Graham⁵ in 1926 also studied the blood sugar, plasma bicarbonate, and ketone bodies in the blood and urine of children given a ketogenic (high fat and low carbohydrate) and an anti-ketogenic (high carbohydrate and low fat) diet, and also the effects of treating the resulting ketosis with sugar, alkalis, and alkalis plus sugar. They concluded that sugar was the most useful method of treatment. Investigations on the children forming the subject of this paper show that, at least in many cases, there is not a progressive fall of blood sugar culminating in an attack. On the contrary, the blood sugar often remains normal right up to and during the early stages of the attack, though later it may fall quite suddenly to a very low figure, though not necessarily with any increase in the symptoms present. These facts, together with the knowledge that the prophylactic administration of sugar usually prevents attacks, suggests that the underlying defect is a too rapid depletion of the glycogen reserves of the liver in the circumstances existing at the time. To understand how this glycogen depletion is brought about it will first be necessary to consider the symptomatology of the condition, and then the predisposing and exciting causes.

The cardinal signs and symptoms of cyclical vomiting are extraordinarily constant. They are lassitude, drowsiness, headache, pyrexia, vomiting, and marked muscular prostration. Abdominal pain is frequently complained of, even before vomiting sets in, and constipation is generally present, though diarrhoea accompanies the vomiting in some cases. Pyrexia is invariably present at the outset, and often reaches 103° F. on the first day. In the complete absence of pyrexia cyclical vomiting is unlikely to be the correct diagnosis. The muscular prostration may be extreme, with transient squints, loss of knee-jerks, and carination of the abdomen. In such a case drowsiness may give place to actual coma, and not infrequently there is a mild jaundice with pale-coloured stools. The urine is as a rule acid, scanty, high-coloured, and contains an excess of acetone bodies. Often the attacks are preceded by a prodromal stage lasting from a few hours to a day, with lassitude, anorexia, and headache. Sometimes a sense of chilliness or actual shivering precedes the attack. The vomiting is persistent, and is brought on by the mere sight of food. The vomited material is usually acid, and is often highly coloured with bile. The attacks generally last two or three days and then gradually and spontaneously remit, leaving the child after a few days in normal health. Attacks usually begin at about 3 or 4 years of age, and continue at regular or irregular intervals until 12 or 13 years of age, when they tend to become less frequent and less severe, and by the time of puberty they have generally ceased altogether. Sometimes at puberty the attacks are replaced by symptoms of migraine. In some instances cyclical vomiting commences in infancy, though usually in an atypical form.

It is well recognized that cyclical vomiting only occurs in children with an inherited or acquired nervous instability. On examining the causes which excite the actual attacks it is found that they fall into three main groups, of which the first is by far the most important. They are: (1) mental excitement, such as occurs when attending parties, during examinations, and so forth; (2) infection accompanied by

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