

### Discussion

Obviously no statistically significant results can be expected from such small numbers. They can merely indicate the investigations which may usefully be done in the future, so that a truer estimate of their value may be obtained in this particular quandary of the undiagnosed pyrexia. It is of little use to compare, between groups, these measurements as made in patients who do not present with pyrexia of obscure origin: if this was done, the whole circumstances would be altered. For instance, to some extent it is probably for the very reason that the cases of subacute bacterial endocarditis were not anaemic that they were not diagnosed and thus excluded from the series.

The results can be compared with those of other series. In the United States of America in 1907, Cabot's three long-continued fevers were due to typhoid, sepsis, and tuberculosis. Alt and Barker (1930) found, between 1913 and 1930, that in patients discharged with pyrexia of unknown origin the predominating groups were tuberculosis, a tumour, or rheumatic fever. Hamman and Wainwright (1936) divided 90 similar patients followed up into 36 with low-grade long-continued fever and 54 with high fever. In the first group only 10 were diagnosed with certainty, 2 of whom had pulmonary tuberculosis, 2 renal carcinoma, 1 Hodgkin's disease, and 3 brucellosis. Of the second group, 34 were diagnosed with certainty. In them tuberculosis, sepsis, syphilis, or malignant tumour predominated. Keefer (1939) collected 80 cases of prolonged fever of obscure origin and found tuberculosis in 8, tumour or reticulosis in 16, coccal infections in 20, and brucellosis in 6. Keefer and Leard (1955) have published their experiences.

In Sweden, Böttiger (1953) followed up 158 patients discharged between 1940 and 1949 with no diagnosis of the fever made. After a minimal follow-up of two years, diagnosis was made in 35. Of these, 11 had malignant tumours, 10 had non-specific infections, and 6 had tuberculosis. Two of the "non-specific" infections were cases of subacute bacterial endocarditis.

### Summary and Conclusion

A survey of 113 patients presenting with pyrexia of obscure origin has been made. Three groups predominated among the eventual diagnoses. These were tumour or reticulosis, tuberculosis, and subacute bacterial endocarditis. This predominance was even greater in the prolonged fevers and in cases remaining undiagnosed longest despite investigation.

In distinguishing between the groups, help may be obtained from the age and from the common and simple investigations—haemoglobin, erythrocyte sedimentation rate, white-cell count, and plasma albumin.

The present study points to the importance, in cases with pyrexia of obscure origin, of the three groups in regard to duration, difficulty of diagnosis, and need for early treatment. The value of the common investigations will be defined only when a much larger series of these patients is considered.

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## REGULAR USE OF LAXATIVES BY SCHOOLCHILDREN

BY

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Several papers in recent years have dealt with the routine administration of medicaments to children without medical advice. The *Practitioner* (1955) commented on the lack of precise information on the extent of this time-honoured custom and went on to quote figures from the report of the Medical Officer of Health for Bolton for 1954. These revealed that, of 503 infants investigated, 5.8% received teething powders and 12.2% received aperients regularly in the first year of life. Since so-called teething powders are, in fact, usually laxatives, it follows that 18% of infants were being given these regularly in one form or another.

Gordon (1951) investigated 1,499 infants and observed that 41% of healthy breast-fed babies did not have daily motions in their early months. He then went on to speculate whether the purging of infants had any connexion with chronic constipation in subsequent adult life.

The *British Medical Journal* (1955) mentioned that many children were still given a regular weekly laxative, and condemned as potentially dangerous the use of calomel and of castor oil. Shortly afterwards Creery (1955) referred to the common administration of magnesia to infants for the relief of alleged constipation. This occurred at some time to 79% of the children investigated, and in a quarter of these cases the initial recommendation was said to have been made by one of the professional personnel of a welfare clinic.

I have referred (Reid and Reid, 1954) to the fact that approximately 5% of consultations at a group of child welfare clinics were concerned with "constipation"—by which was usually meant a normal two- to three-day bowel rhythm in healthy infants or children.

### Present Investigation

In order to obtain some idea of the extent of the use of laxatives in children an inquiry was conducted during 1953 in the course of routine medical examination of school entrants and leavers in that area of Buckinghamshire which lies from Bletchley northwards.

In the case of entrants (who were almost all 5 years old) the mother was asked by the medical officer or health visitor whether the child was ever given "medicine," and, if so, how often. A note was made of this information in the case of medicines whose action was apparently directed towards the bowels. Such medicines accounted for the vast majority given. In the case of school leavers (usually about 15 years old, or slightly older in the cases of grammar and technical school pupils) the child was asked the same question directly, as comparatively few mothers attended the medical inspections of this age group.

It was soon found that almost all children received laxatives from time to time, and it was therefore decided to record only those who received such medicine regularly at least once weekly. The results are summarized in Table I.

From this it will be seen that an appreciable percentage of children received regular laxatives, the proportion of girls being higher than that of boys in each age group, but a decline in frequency was apparent in each sex from the age

of 5 to the age of 15. This decline was proportionately greater in boys than in girls.

The overall frequency of administration of laxatives to the 191 children who received them regularly is given in Table II. Whilst over four-fifths of these children were purged once weekly, 9.4% received such treatment twice or thrice a week, and 7.9% more frequently. Of the 15 children in the last category, one child received laxatives three or four times weekly, 11 received them daily, and 3 received them twice daily. The types of laxatives used by these children are shown in Table III.

TABLE I.—Number Taking Laxatives at Least Weekly

	5 Years Old			15 Years Old			All Children		
	Boys	Girls	Total	Boys	Girls	Total	Boys	Girls	Total
Total No. investigated	289	258	547	329	236	565	618	494	1,112
No. taking laxatives regularly	51	67	118	30	43	73	81	110	191
% ditto	17.6	26.0	21.6	9.1	18.2	12.9	13.1	22.3	17.2

TABLE II.—Frequency of Regular Use of Laxatives in 191 Children

	No.	%
Once weekly	158	82.7
Twice or thrice weekly	18	9.4
More than " " "	15	7.9

TABLE III.—Type of Laxative Used Regularly in 191 Children

	No.	%
Anthracene	97	50.8
Saline	61	32.0
Phenolphthalein	15	7.9
Mercurial	6	3.1
Lubricant	6	3.1
Hydragogue	4	2.1
Other	2	1.0

**Anthracene.**—Of the 97 children using such laxatives regularly, 90 took them in the form of so-called syrup of figs, the purgative principle of which is, in fact, usually senna.

**Saline.**—Approximately one-third of the children in this group received a preparation of magnesium hydroxide; most of the remainder had preparations containing magnesium sulphate.

**Phenolphthalein.**—Of 15 children who received this, 11 had it incorporated in chocolate and 4 in chewing-gum.

**Mercurial.**—All 6 children in this group received a proprietary preparation whose active principle, at the time of the inquiry, was calomel.

**Lubricant.**—Liquid paraffin was the basic ingredient in all cases.

**Hydragogue.**—Four children took proprietary pills containing one or more laxatives of the hydragogue group.

### Discussion

In considering the types of laxatives used, it is possible to condemn calomel as undesirable. In infants and toddlers there exists an absolute contraindication to its use, and it seems likewise undesirable that older children should regularly ingest a mercurial preparation of which some proportion is absorbed. Calomel is no longer used in the proprietary preparation taken by the children in this survey. It has been replaced by phenolphthalein.

It might perhaps also be legitimate to criticize the regular use of liquid paraffin in children, in view of the finding of Boyd and Doll (1954) that an appreciable excess of patients suffering from gastro-intestinal cancer took liquid paraffin compared with a control group suffering from other diseases.

Any consideration of the effect of the other laxatives, from a purely pharmacological point of view, must be related to the dosages employed. It was not possible to tabulate

these, as the various forms, even of the same type of laxative, differed widely in their pharmacological content. Further, in the case of chocolate or chewing-gum laxatives, and where household preparations such as infusion of senna were used, assessment of the dose was impossible. Typical doses of syrup of figs and of saline powders were one or two teaspoonfuls weekly, but some children had more heroic doses, such as 3½ teaspoonfuls of syrup of figs plus one cascara tablet weekly or one tablespoonful of syrup of figs weekly. One child received a dessertspoonful of syrup of figs and one an indefinite amount of phenolphthalein chocolate laxative thrice weekly. One 15-year-old girl received a teaspoonful of syrup of figs twice daily and complained of frequent colicky pains in the abdomen. These soon ceased once her mother was persuaded to stop administering the medicine.

From a psychological point of view the regular taking of laxatives by children is undesirable. It was clear that most children in this survey had taken them since infancy, and it was also clear that parents in general, and mothers in particular, regarded purgation as part of their duty towards the healthy upbringing of their offspring. It was no doubt this maternal conviction which accounted for the fact that, at the ages of both 5 and 15, proportionately more girls than boys were in receipt of regular laxatives. The week-end appeared to be the traditional time for assaulting the bowels, and it was apparent that the ritual of the family purge still held sway in many homes.

This ritual of weekly purgation was remarked upon by Stein and Sklaroff (1952) in their survey of the health of an urban community in Edinburgh, when they also noted that four out of five households bought some form of laxative. Perhaps no surprise should be expressed at the widespread use of laxatives, because, after all, purgation has been an honoured form of therapy since the earliest times. The supposed importance of frequent family purgation was stressed by Cheyne (1724) in his *Essay of Health and Long Life*, in which he proclaimed: "So true is old Verulam's Aphorism: Nihil magis conducit ad Sanitatem & Longaevitatem quam crebrae & domesticae purgationes." Similarly, the practice of purgation is in modern times probably world-wide. For example, Saunders (1954) remarks that, in Mexico, the idea that the maintenance of health requires a periodic purging of the stomach and intestinal tract is commonly held, and goes on to point out that the idea of a "clean" interior is also an important component in American folk medicine.

The regular use of laxatives or, for that matter, their use when not specifically indicated, is undesirable, because the habit is apt to remain throughout life, with the prospect of ever larger doses being required with advancing age. There lies the road to chronic constipation and to that familiar sight of hospital wards—the patient whose life is centred around the problem of when his bowels can next be blasted into reluctant activity.

Even more undesirable is the danger that the regular taking of laxatives may have a much wider effect by helping to engender the belief that good health is synonymous with the ingestion of pharmacological preparations. Only very rarely during the survey was it indicated by a parent that a child did not require medicine because a proper diet was relied upon to regulate the bowels.

At the same time, parents must not be blamed for administering substances which they undoubtedly believe to be beneficial to the health of their children. They must rather be taught that proper diet, an adequate fluid intake, and a prompt response to the call to stool are the only measures necessary to keep their children's bowels in order, and that, in the case of some children, it is not normal to have a daily motion. Of all the children in the present survey who were not taking regular laxatives, approximately 5% had a bowel movement only every second or third day.

A large amount of money is spent annually on advertisements whose apparent aim is to persuade the British public that they require laxatives. The cost of that campaign is

no doubt borne by the profits reaped in consequence of its success. The *British Medical Journal* (1954) has referred to the role of family doctors in dissuading mothers from the routine administration of unnecessary medicaments to their offspring. Both they and all health workers, especially those whose efforts are chiefly directed towards infants and children, must play their part in discouraging the regular use of laxatives and the attitude of mind which accompanies it.

### Summary

The regular taking of laxatives by a group of school entrants and leavers is investigated. Over 17% of these children took them at least weekly, proportionately more girls than boys doing so at each age. The practice was commoner among entrants than among leavers.

The frequency of administration and type of laxative used are analysed.

The undesirable nature of such medication is discussed.

I am indebted to the health visitors of the North Bucks Division and to my wife for help in conducting this survey, to Professor A. Mair for advice, and to Dr. G. W. H. Townsend, county medical officer, for permission to publish this article.

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## UNUSUAL NEUROLOGICAL COMPLICATIONS AFTER SUDDEN WITHDRAWAL OF CORTISONE

BY

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It is well known that reactions may occur during treatment with cortisone and corticotrophin and when these drugs are withdrawn. In the case here described a severe and unusual illness occurred when the patient inadvertently stopped taking cortisone, with which she had been treated for a long period.

### Case Report

A married woman of 38 was admitted to Addenbrooke's Hospital on March 26, 1953, in a comatose state. She had suffered from severe rheumatoid arthritis for 14 years, and for the previous 18 months had been having cortisone, with considerable benefit. During this period she had had some evidence of hypercortisonism: moonface, gain in weight, acneiform lesions, and difficulty in healing trivial wounds.

After 100 mg. intramuscularly daily for the first six days the usual maintenance dose was 50 mg. daily, at first intramuscularly and later orally. For the two months before admission the dose had been higher—75 mg. orally—on account of an increase in severity of the disease.

Ten days before admission she accidentally doubled the dosage of cortisone to 150 mg. daily, having misread instructions supplied. Seven days later she realized her error and discontinued the drug. The next day she com-

plained of headache and difficulty in sleeping, which she attributed to worry about her children, who had tonsillitis. Her joints were a little more painful. On the third morning after stopping cortisone she was found in bed in a comatose state.

On admission a comatose, well-nourished woman with joints showing rheumatoid changes was seen; she was rousable by painful stimulation. Her temperature was 105° F. (40.6° C.), pulse 140. Her face was moon-shaped, with acneiform lesions. She was not dehydrated or oedematous, and not cyanosed. Medium crepitations were heard at both lung bases. Her B.P. was 90/60.

Examination of the abdomen revealed no abnormality. Central nervous system: fundi normal, pupils reactive; tone generally flaccid; tendon and abdominal reflexes absent; plantar responses flexor.

*Investigations.*—Blood urea, 24 mg./100 ml.; serum potassium, 18.3 mg./100 ml.; serum sodium, 311 mg./100 ml.; serum calcium, 8.8 mg./100 ml.; Hb, 14 g./100 ml.; W.B.C., 15,000; neutrophil leucocytosis. Urinary 17-ketosteroid excretion, 6 mg./day. C.S.U.: protein+, otherwise normal. E.C.G. normal. Lumbar puncture: normal pressure and fluid.

*Treatment and Progress.*—She was treated with tepid sponging, fluid by intragastric Ryle tube, and penicillin. The intravenous injection of 50 ml. of 50% glucose had no effect. After 24 hours the right pupil was larger than the left. The next day the coma was lighter but she was unable to speak; she was at times conscious; there was pronounced weakness of the arms and legs, with some return of tone and tendon reflexes. Her arthritic joints were obviously very painful on slight passive movement and were much more swollen than when she was on cortisone.

On the fifth day she attempted to speak, but had severe dysarthria and was seen to be very labile emotionally, alternately weeping and laughing. A Parkinsonian tremor appeared in the hands; 24 hours later the feet were involved; by then the pupils were again equal. She was started on 25 mg. of cortisone daily, later increased to 50 mg. Six days after admission the temperature became normal; there was some dysphagia and almost complete bilateral palatal palsy which disappeared in a few days. Fourteen days after the onset of the illness her tremor was most pronounced, involving both upper and lower limbs. Benzhexol hydrochloride was given with good effect.

Her speech improved slowly, but after 30 months it remains slow, halting, and slurred, being confined to short sentences. She is still emotionally labile, but to a much less degree. She can sit up, but is unable to feed herself or to stand unsupported, having generalized loss of power in the limbs. There is now wasting compatible with disuse atrophy; the tendon reflexes are diminished, the plantar responses are flexor, and there is no sensory loss. Slight intermittent tremor of the hands remains.

### Discussion

In this case, in which cortisone was withdrawn suddenly after a long period of therapy, the two features we would stress are the acute illness, presumably due in part to acute adrenal insufficiency and in part to cerebral lesions, and the permanent neurological sequelae.

Acute adrenal insufficiency, which may occur and prove fatal, can appear as sudden circulatory collapse, decrease in blood pressure, increase in pulse rate, or perhaps an elevation of temperature, and may cause the patient to lose consciousness quickly (Salassa *et al.*, 1953a, 1953b). In these circumstances the serum electrolytes may be normal (Thorn, 1949), whilst most of the features of chronic adrenal insufficiency will be absent.

Fatal adrenal insufficiency has been reported on several occasions. Fraser *et al.* (1952) described the case of a 34-year-old man with rheumatoid arthritis who died in severe shock two days after operation. He had been on cortisone for only two months, with an average daily dose of 50 mg.,