We may classify the symptomatic treatment of pain into four groups: (1) analgesic drugs, with either a central or a peripheral action; (2) interruption of the pain pathways, suppressing the transmission of impulses to a conscious level; (3) psychosurgery, altering the affective interpretation of stimuli which have reached conscious level; and (4) psychotherapy, including suggestion, altering in a wider sense the interpretation of pain stimuli.

The abolition of pain in some cases after bilateral adrenalectomy (West *et al.*, 1952) is an interesting phenomenon and is not solely related to the disappearance of metastases in bone and other tissues. The mechanism of pain suppression in these cases is not yet understood. Riddoch (1938) noted that pain is "the only aspect of sensation accompanied by endocrine, autonomic, and motor reactions of a protective kind." Cannon *et al.* (1929), as the result of experiments on cats, pointed out that the reaction to pain probably depends on the state of the sympatho-adrenal system. After bilateral adrenalectomy the entire endocrine response to stress, and therefore to painful stimuli, is altered. The outpouring of adrenaline is abolished, but this may not be the only or the most important factor.

Summary

Observations were made during the treatment of 77 unselected consecutive cases of pain arising from a number of causes.

Types of pain include post-herpetic neuralgia, painful amputation stump and phantom limb, headache not associated with hypertension or gross neurological disease, brachial neuritis, causalgia, central pain, and several others.

Numerous forms of treatment are discussed, including peripheral nerve blocks, injection of local anaesthetic into interspinous ligaments, intrathecal alcohol, vasodilator drugs, and psychotherapy.

It is stressed that no complaint of pain except that of the malingerer should go untreated. The pain of the neurotic may cause as much disability, and therefore require treatment just as much, as the pain due to malignant disease.

Since pain is often of mixed origin, a combined therapy which employs both physical and psychological methods is often the most rewarding.

I wish to thank Dr. W. Ritchie Russell and Dr. C. W. M. Whitty for permission to publish these cases and for invaluable direction throughout the study. Professor P. C. Cloake kindly gave permission to publish Case 18.

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PROPHYLACTIC SULPHADIMIDINE IN CHILDREN SUBJECT TO RECURRENT INFECTIONS OF UPPER RESPIRATORY TRACT

BY

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Mass chemoprophylaxis to reduce the incidence of infections of the respiratory tract was successfully employed in the American Services during the last war, and its efficacy was conclusively demonstrated in controlled trials. With the appearance of sulphonamide-resistant streptococci, both in the armed Forces and in the civil population, chemoprophylaxis declined in popularity. The reduction of infections with group A streptococci has proved effective in preventing recurrences of rheumatic fever in susceptible subjects, and prophylactic sulphonamides and penicillin have both been used for this purpose for many years.

The problem of the child who is subject to frequent infection of the respiratory tract is constantly before the family doctor and the paediatrician. Attempts have been made to reduce the number of these infections by giving a small dose of a sulphonamide or penicillin daily to such children. Lapin (1948) reported a successful trial with oral penicillin in hospital out-patients. Siegel and Julianelle (1945) gave prophylactic sulphadiazine for 15 weeks to 30 mentally defective children in an institution, but during the trial period the number of acute infections in both treated children and controls was very low and no benefit was demonstrable from the use of the drug. Finke (1953) records the results of submitting 100 Rochester schoolchildren to different prophylactic regimes over a period of 10 months. The number of infections of the respiratory tract was 2.5 per child in treated cases and 4.3 in controls, and in a study of older children the number of days lost from school in those treated was half that in the controls.

The purpose of this paper is to describe the results of a trial of prophylactic sulphonamide therapy in a group of children awaiting tonsillectomy on account of recurrent infections of the upper respiratory tract.

Plan of Investigation

The children attended the hospital at intervals of eight weeks for a period of eight months between August, 1954, and May, 1955, and were submitted to a clinical trial on the double blind principle. Two kinds of tablet were made. Tablet A contained calcium carbonate 60% and calcium lactate 40%, and tablet B sulphadimidine 0.5 g. Both were flavoured with aniseed and were identical in appearance and very similar in taste. Each child acted as his own control. Half the group received calcium tablets for the first four months followed by sulphadimidine for four months, and the course was reversed for the other half. The identity of the tablets was not revealed to the clinical assessor until the end of the trial, so that the observations by all concerned were unprejudiced. The family doctors were fully informed of the nature and purpose of the trial and were requested to record details of the patients' illnesses treated by them on a form which was returned to the hospital by the mother at the child's next visit. The tablets were normally continued during an acute illness, but any

other treatment required was left to the discretion of the family doctor. The mother kept her own record of the child's illnesses and absence from school.

At each visit the child was weighed and a full history of any infections suffered during the previous eight weeks noted, as were infections occurring in other members of the household. The nose and throat were examined and further clinical examination was made if indicated. Only febrile illnesses of more than two days' duration were included in the final figures, and the specific fevers were excluded. Infections of the respiratory tract were classified as tonsillitis, otitis media, bronchitis, and pneumonia. Coryza was noted, but was included only when associated with one of the above. After consideration of the history and the details supplied by the family doctors it was possible to fit most of these infections into the groups mentioned. Illnesses for which the family doctor had not been called were included, as it was thought that in this way a more accurate picture of the child's health was obtained, for parents vary so much in their liability to consult their doctor. This is especially so if the illness follows a familiar course. When the symptoms appear the mother often carries out the treatment given by her doctor in a previous attack and does not call him unless the child's condition gives cause for concern. As the mother did not know whether the child was having calcium tablets or sulphadimidine her observations were unbiased.

Selection of Cases.—The purpose of the trial was explained to the parents of children whose names had recently been placed on the waiting-list for removal of tonsils and adenoids for repeated attacks of tonsillitis. Only those living within a few miles of the hospital were circularized, and the first 60 who wished to be included in the trial and agreed to attend regularly were accepted.

Dosage.—Children weighing 60 lb. (27 kg.) or less received one tablet daily, and others two tablets (each sulphadimidine tablet contained 0.5 g. of the drug).

Results

Only 48 children completed the trial satisfactorily. Twelve were excluded—three on account of refusal to take the tablets, one who developed a rash which may have been due to sulphonamide sensitivity, and five who were unable to attend regularly owing to unforeseen circumstances. One child in each group had his tonsils removed at another hospital shortly after the trial began, and the parents of another ceased to attend after four months as the child had three attacks of tonsillitis while taking calcium tablets.

Various indices of the state of the children's health throughout the trial were used. The results of the different observations are detailed below and analysed statistically in Table I.

Incidence of Acute Infections of the Respiratory Tract.—It will be seen that the children had 25 acute infections while taking sulphadimidine, compared with 60 on the calcium tablets, and this difference is highly significant ($P<0.001$).

TABLE I.—*Effect of Prophylactic Chemotherapy on the Incidence of Acute Respiratory Infections, Absence from School, and Number of Visits by G.P.*

	Sept-Dec., 1954		Jan.-April, 1955		Total		χ^2 Calculated on Total
	Ca	S	Ca	S	Ca	S	
Acute tonsillitis ..	26	10	20	11	46	21	
Bronchitis and pneumonia	3	1	5	0	8	1	
Otitis media	2	0	4	3	6	3	
Total ..	31	11	29	14	60	25	13·6 ($P<0·001$)
Absence from school in weeks ..	37	13½	43	16½	80	30	21·83 ($P<0·001$)
No. of visits by G.P. ..	20	12	21	13	41	25	3·41 ($P<0·1$)

Ca=Calcium. S=Sulphadimidine.

Absence from School.—Thirty-seven children were of school age, and while they were taking sulphadimidine the total absence from school, excluding that due to the specific fevers, was 30 weeks, compared with 80 weeks when on calcium tablets, a highly significant difference ($P<0.001$).

Number of Illnesses Treated by the Family Doctor.—The doctor was called to treat a total of 25 illnesses in children taking sulphadimidine and 41 in those taking calcium tablets. This figure includes visits for illnesses classified as "colds," but visits to children with infectious fevers have been excluded from the total. The effect of sulphadimidine is not statistically significant ($P<0.1$).

Tonsillar Hypertrophy.—The size of the tonsils was assessed at every interview, each tonsil being considered separately and placed in one of three categories—namely, not visible beyond the pillars of the fauces, classified N; meeting or almost meeting in the midline, classified ++; and intermediate in size between the two, classified +. By this means it was possible to compare the size of the tonsils at the beginning and end of the periods on suphadimidine and calcium tablets. The results are shown in Table II, from which it will be seen that there was a significant diminution in the size of the tonsils while on sulphadimidine. Generally speaking, the increase in size was related to recent infection. The initial appearance of the tonsils and the degree of hypertrophy bore no relation to the number of attacks of tonsillitis or the response to chemotherapy.

TABLE II.—*Effect of Prophylactic Chemotherapy on Size of Tonsils*

Size of Tonsil	Sept.-Dec., 1954		Jan.-April, 1955		Total	
	Ca Tablets	Sulphadimidine	Ca Tablets	Sulphadimidine	Ca Tablets	Sulphadimidine
Diminished ..	3	6	1	4	4	10
Unchanged ..	11	21	16	13	27	34
Increased ..	5	2	12	2	17	4

χ^2 (on totals)= 11·4. $P<0·01$.

TABLE III.—*Effect of Prophylactic Chemotherapy on Size of Tonsillar Glands*

Size of Tonsillar Glands	Sept.-Dec., 1954		Jan.-April, 1955		Total	
	Ca Tablets	Sulphadimidine	Ca Tablets	Sulphadimidine	Ca Tablets	Sulphadimidine
Diminished ..	5	6	1	2	6	8
Unchanged ..	9	20	19	13	28	33
Increased ..	5	3	9	4	14	7

χ^2 (on totals)=3·03. $P<0·2$.

Size of Tonsillar Glands.—This is shown in Table III and is not statistically significant, but tonsillar glands were classified only as palpable or not palpable, and therefore diminution in size would be recorded only if the glands were no longer felt. The finding of persistently enlarged tonsillar glands is taken by many to indicate chronic tonsillar infection, and it might be anticipated that such children would not respond so well to prophylactic chemotherapy. Sixteen children had large, firm tonsillar glands at the onset of the trial, and the glands remained unchanged throughout the period of observation. In this group there were 16 attacks of acute infection of the upper respiratory tract in children on calcium tablets (average 1 per child) and 10 on sulphadimidine (average 0.6 per child), while the corresponding figures for the 32 children without chronic tonsillar gland enlargement were 44 (average 1.4 per child) and 15 (average 0.5 per child). The average time off school for those with and without chronic glandular enlargement was 1.8 and 3.4 weeks per child respectively, so there is nothing in these figures to suggest that the finding of persistently enlarged tonsillar glands implies a less favourable

response to prophylactic chemotherapy or a higher incidence of acute infections.

Nasal Obstruction.—This was extremely variable. It was absent throughout the period of observation in 14 cases and persistent in 7. It developed in 8 children receiving calcium tablets and in 5 receiving sulphadimidine. In the remaining cases it varied from visit to visit. Chronic nasal obstruction did not appear to increase the predisposition to acute respiratory tract infections and was uninfluenced by prophylactic chemotherapy. It was often associated with poor appetite, disturbed nights, and persistent cough. Otitis media occurred in 8 children, and in 7 of these nasal obstruction was present for most of the observation period.

When the individual cases were reviewed it was found that most of the children had fewer and milder acute illnesses and much less absence from school during their four months on sulphadimidine. All things considered, 28 fared better on sulphadimidine than on calcium tablets, 3 were worse, and in 17 there was no appreciable difference. Thirty children were given calcium tablets for the first four months, and the 20 who completed the trial had a total of 46 acute illnesses in eight months (average 2.3 per child), while of 30 children who started the trial on sulphadimidine 28 who completed it had a total of 39 acute illnesses (average 1.4 per child) in the same period. This difference is significant ($\chi^2=4.91$, $P<0.05$), and suggests that the benefit conferred by prophylactic chemotherapy is maintained after treatment is discontinued, at least for a few months.

Toxic Effects of Sulphadimidine.—Four days after starting sulphadimidine one child developed an irritating macular rash confined to the trunk, and the tablets were discontinued. The rash persisted for three weeks and finally cleared with desquamation of the skin. His blood count remained normal and there was no constitutional disturbance. He was excluded from the trial. Routine examinations of the blood were not carried out on these children.

Acute Coryza.—It is not surprising that the incidence of acute coryza was unaffected by prophylactic chemotherapy. Thirty-five "colds" were recorded while calcium tablets were being taken, and 40 with sulphadimidine. Coryza often occurred in several members of the household at the same time, but acute tonsillitis was recorded in only two instances in the family when the patient was affected.

Weight.—The average gain in weight while taking calcium tablets was 1 lb. 11 oz. (0.77 kg.) in four months, and while on sulphadimidine it was 1 lb. 9 oz. (0.71 kg.). Loss of weight was recorded on eight occasions only in the 96 periods of four months, and only twice did it exceed 8 oz. (0.23 kg.). Lost weight had normally been regained by the next visit and only one child weighed less at the end than at the beginning of the trial, in spite of the fact that eight children had an unsatisfactory winter with repeated illnesses.

Discussion

The results of the trial show that sulphadimidine was an effective prophylactic agent. It was used in preference to penicillin for several reasons. Penicillin is the drug of choice for use against group A streptococci, as it is more effective than the sulphonamides in eradicating streptococci from the throat, but a careful study of exudative pharyngitis and tonsillitis has shown that only about 25% of cases are due to beta haemolytic streptococci (Commission on Acute Respiratory Diseases, 1944). The prophylactic dose of penicillin is not known with certainty even for the prevention of group A streptococcal infections. The dosage of sulphadimidine used in this trial was that recommended for sulphadiazine in the Medical Research Council's (1955) therapeutic trial in rheumatic fever. Dosage of a similar order has been used prophylactically for this purpose for over ten years, and, in spite of the greater popularity of penicillin recently, sulphonamides have well withstood the test of time. The appearance of antibiotic-resistant staphylococci in hospitals and among hospital out-patients is a cause for concern at the present time, and this was regarded as an important contraindication to penicillin prophylaxis. The disadvantage of sulphonamides is, of course, their toxicity, but in doses of up to 1 g. daily serious toxic effects are estimated to occur in 1:10,000 cases and mild toxic reactions such as transient dermatitis in 1:200 cases (Coburn and Young, 1949). It is felt that these figures justify the use of chemoprophylaxis by the family doctor if the mother is warned to discontinue the tablets should a rash appear and return to her doctor as soon as possible.

Stollerman (1954) advised against giving sulphonamides in therapeutic doses to these patients for treatment of acute infections, as this seems to precipitate toxic effects. The development of resistant strains of streptococci was formerly a serious drawback to the use of chemoprophylaxis. The problem arose mainly in small closed communities, and now that other drugs are available it is not regarded as of great practical importance. The value of sulphonamides in the treatment of acute infections of the upper respiratory tract is somewhat doubtful (Macdonald and Watson, 1951; Landsman *et al.*, 1951). At all events, chemoprophylaxis leaves the family doctor free to use penicillin as his first line of attack in dealing with acute infections of the respiratory tract and staphylococcal skin infections, without the fear that he might be dealing with organisms made resistant to penicillin. Sulphadimidine is a relatively soluble sulphonamide of low toxicity and cost. It was taken without difficulty by the children when flavoured with aniseed. Three children refused to take the calcium tablets similarly flavoured.

In 1954 approximately one in seven of all the new out-patients attending the Hospital for Sick Children, Great Ormond Street, was suffering from recurrent infections of the upper respiratory tract. Over 20 years have passed since Kaiser (1932) published the results of a carefully planned trial designed to determine the results of tonsillectomy in 2,200 children followed for ten years after operation and compared with a similar group not subjected to surgery. The effectiveness of the operation in reducing the incidence of acute pharyngitis and cervical adenitis was still evident after ten years, and some initial improvement resulted in children with recurrent otitis media. When the operation was carried out in children subject to repeated "colds," sinusitis, pneumonia, or bronchitis, no definite benefit was demonstrated. These observations were made, of course, before the advent of chemotherapy or antibiotics. Spence and Taylor (1954) estimated that, in Newcastle-upon-Tyne, children admitted to hospital for tonsillectomy form one-quarter of the total admissions of children under 14 years. At the Hospital for Sick Children, Great Ormond Street, the proportion is one-sixth of all the admissions. One in ten of the paediatric beds in Newcastle is occupied by a child undergoing tonsillectomy.

Most of the 48 children in the trial were referred to hospital when symptoms had been present for one or two years, and during the winter under observation were much improved compared with the previous winter, the incidence of acute tonsillitis being approximately halved. The numbers were 154 attacks for the winter 1953–4 and 67 for the winter 1954–5. The first figure must be accepted with reserve, as it was obtained by questioning the mother on her first visit and includes attacks of acute tonsillitis treated by the family doctor only. These observations do suggest, however, that some children, at least, are recommended for tonsillectomy when their susceptibility to infection of the upper respiratory tract is beginning to decline, and it is a common observation that such infections are very frequent during the first two terms at school. The majority of children start school during the winter months, when opportunities for outdoor activities are at a minimum and the seasonal incidence of streptococcal infections is at its height.

Chemoprophylaxis is well worth a trial by the family doctor when he is called to treat a child who has suffered two or three infections of the upper respiratory tract in a comparatively short period. If it is instituted promptly and continued for a few months for one or two winters,

hypertrophy of the tonsils and adenoids might be avoided. It can be used for children awaiting tonsillectomy as in this trial, for at the present time most hospital waiting-lists are long and there is often a delay of over a year before the operation is carried out. Some doctors and many parents believe that once the tonsils have been pronounced "infected" they will remain so. Indeed, children are often referred to the ear, nose, and throat surgeon after their first attack of tonsillitis in the belief that further attacks can be confidently expected in the future and will be avoided if the tonsils are removed. The length of hospital waiting-lists for tonsillectomy encourages this practice. It is felt that the judicious employment of chemoprophylaxis and the prompt treatment of severe acute infections with penicillin will bring about a considerable reduction in the number of children requiring removal of their tonsils and adenoids and avoid much illness and loss of time from school.

Summary

Forty-eight children awaiting tonsillectomy were observed for eight winter months. Each child received either prophylactic sulphadimidine or calcium tablets. Half began with 0.5 g. of sulphadimidine daily, while the other half received a calcium lactate tablet identical in taste and appearance. The groups were changed after four months. The trial was conducted on the double blind principle.

Twenty-eight children fared better on sulphadimidine, 3 were worse, and in 17 there was no appreciable difference. During the period on sulphadimidine 25 acute infections were recorded, absence from school totalled 30 weeks, and the family doctor was called to treat 25 illnesses. The corresponding figures for the period on calcium tablets were 60 acute infections, 80 weeks lost from school, and 41 illnesses requiring treatment by the doctor.

Tonsillar hypertrophy and cervical adenitis were favourably influenced by chemoprophylaxis.

Chemoprophylaxis did not seem to affect nasal obstruction or reduce the incidence of the common cold.

Reasons for using chemoprophylaxis in preference to penicillin prophylaxis are discussed.

It is considered that chemoprophylaxis is worth a trial as an alternative to tonsillectomy in children subject to recurrent infections of the upper respiratory tract and, if instituted promptly, would result in a reduction of the number requiring this operation.

I am indebted to Professor R. S. Illingworth, who suggested the need for an investigation along these lines, and to Professor G. M. Wilson, who gave valuable advice on the planning of the trial and presentation of the results. I thank Mr. H. S. Sharp for kindly allowing these observations to be made on his patients; Dr. R. E. Bonham-Carter and Professor A. Moncrieff for encouragement and advice; Dr. C. Carter for advice on the statistics; the family doctors who gave information about their patients; and Imperial Chemical (Pharmaceuticals) Ltd. for supplying the tablets and for their successful efforts to make them palatable and acceptable to the children.

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SENSORY RADICULAR NEUROPATHY IN A DEAF CHILD

BY

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A number of cases have been described by various authors under different titles which may well be variants on one syndrome—characterized by painless ulcers of the feet, arthropathy, and deafness. The early literature includes four cases in one family described by Brüns (1903) as "syringomyélie lombosacrée familiale probable." Göbell and Runge (1914) reported a series of nine cases of "lumbar syringomyelia" without deafness in a single family covering two generations. Guillain and Thévenard (1929) published a report of a similar family. Hicks (1922) reported that 34 members in one family had perforating ulcers of the feet; and deafness was present in 10. In 1949 Murray Jackson reported 26 cases of "familial lumbo-sacral syringomyelia" in one family covering four generations. He noted that in this family there was an associated spina bifida occulta.

In 1940 a symposium of cases was described under the title of "L'acropathie ulcère-mutilante familiale" by Thévenard, Van Bogaert, André, and Goethals-Borin, with further post-mortem findings. The authors concluded that the cases described were examples of sensory radicular neuropathy.

The following case falls into this clinical group; it is of interest because the disease appeared at an unusually early age.

Case History

The patient was born on February 20, 1947. He was the second of three children of healthy parents; both siblings were healthy. There was no history of perforating ulcers of the feet or of deafness in the family (which has been traced back as far as the great-grandparents). The patient and his father and elder sister are left-handed.

The mother was in poor general health during pregnancy. Labour was rapid and the child was rather shocked at birth, but soon recovered and thereafter made satisfactory progress. At the age of 15 months, while he was crawling round the garden, he cut his knee badly and yet did not cry. His parents had been aware, since then, that he did not feel pain as acutely as their other children.

At 2½ years he could walk and feed himself, but made no attempt to talk and took no notice when spoken to. He was certified as an imbecile and committed to an institution.

In November, 1950 (aged 3½ years), he burnt his right forearm by putting it into boiling water. A year later he received a third-degree burn on the left thigh from sitting on a too-hot bedpan. These injuries seemed to be painless. In December, 1950, he developed a painless indolent ulcer on the plantar aspect of the left great toe, which took four months to heal. A few months later it broke down again despite rest in bed. The toe was therefore amputated. In September, 1953 the neighbouring toe developed an ulcer. This healed when he was confined to bed, but broke down as soon as he was allowed to walk about.

Findings

On examination he was a friendly little boy, of normal physical development. The occipitofrontal circumference of the skull was 20 in. (50.8 cm.). He was of normal intelligence and left-handed. The cranial nerves were normal in all respects except for the eighth nerve.