cyanosis." The salient features here are psychological instability, weakness, chronic headache, and cyanosis without associated dyspnoea, occurring almost exclusively in women. While it is just possible that some of these cases may be idiopathic, it is now recognized that the majority are due to the ingestion of aniline antipyretics. The self-administration of drugs is often denied by these patients, and careful search may be necessary to find the actual cause of the sulphaemoglobinaemia. Case I suffered a relapse some months after dismissal. This patient was admitted to another hospital and a normal ventricular system was demonstrated by cisternal encephalography. She was then examined by a psychologist, who reported that the symptoms were psychological in origin. Case II presents many different features. Here the drugs were taken to obtain relief from pain caused by an organic condition. The pain of rheumatoid arthritis, as in the case reported by Coxon and Crawford (1940), or of rheumatic myalgia as in the case here described, may be the prime factor. Both sexes may be affected, psychological instability is not present, and the tendency to habit formation is not marked.

The mode of formation of sulphaemoglobin is the same whether it is produced by aniline itself or one of its derivatives. According to Snapper (1925), the circulating haemoglobin is sensitized by aniline derivatives and can thus unite with traces of sulphide absorbed from the intestine. Snapper induced sulphaemoglobinaemia in men by administering aniline compounds and sulphur. Outside the body, however, aniline and its related compounds have no effect on haemoglobin. It appears that aniline compounds are oxidized to the corresponding phenyl-hydroxyl amines and *p*-aminophenols in the blood stream and that these substances affect haemoglobin. Gley (1937) and Morgan and Anderson (1940) have demonstrated that both these substances, when added to blood, lead to the rapid formation of sulphaemoglobin if a trace of sulphide be present, and to methaemoglobin if sulphide be absent. Methaemoglobin can be produced only with difficulty by giving aniline antipyretics alone (Harrop and Waterfield, 1930). Further, methaemoglobin is highly unstable in the blood stream, being rapidly converted to haemoglobin (Stadie, 1921), and large quantities are required to produce cyanosis. Such cyanosis lifts within 24 to 48 hours after withdrawal of the drug, and is more likely to appear in acute than in chronic poisoning.

Finally, there is some evidence in favour of the view that coloured oxidation products of *p*-aminophenol are present in the blood after the ingestion of aniline compounds and that these are partly responsible for the cyanosis. Leslie (1939) described a case of acute acetanilide poisoning in which marked cyanosis was not associated with any change in the blood pigment and was considered to be due to the presence of some coloured derivative of acetanilide in the blood. Lundsteen, Meulengracht, and Rischel (1938) described 11 cases of chronic acetanilide poisoning with cyanosis, and were able to demonstrate a chocolate-coloured derivative of *p*-aminophenol in the blood of one of their cases which was specially investigated. It is difficult, at present, to assess the importance of this coloured *p*-aminophenol derivative in the production of cyanosis. In the majority of cases of chronic poisoning with aniline antipyretics, including the two described here, the cyanosis has been adequately, if not completely, accounted for by the presence of sulphaemoglobin in the blood.

Summary

The clinical and laboratory findings in two cases of sulphaemoglobinaemia due to aniline antipyretics are described. The method of formation of the abnormal pigment and other factors which may contribute to the cyanosis are discussed.

I wish to express my indebtedness to Dr. John Gracie for permission to investigate cases under his care, and to Drs. S. V. Telfer and G. H. Bell for their advice and help.

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THE CHILD WITH FREQUENT COLDS

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In this article are given the results of a comprehensive investigation of 100 school-children suffering from frequent colds. At the invitation of the County Medical Officer, the children were referred by the school medical inspectors in the area of South-West Essex to a special clinic established at the hospital for the purpose of investigating this prevalent condition. The children were mostly drawn from middle-class and artisan families. The main part of the investigation consisted of clinical, x-ray, and laboratory examinations, and note was also taken of the environment and development of the children. While our chief purpose was to establish the clinical characteristics of the child with frequent colds, we also considered the problem of which department in a hospital should be responsible for their examination and should advise on their treatment.

It was inevitable that a number of children suffering from asthma and hay-fever should be referred to such a clinic. If these are excluded the history of the disorder is a typical one. The children usually began to suffer from frequent colds when they started attendance at school. They complained at first of blockage of the nasal passages followed by a mucous discharge which after a few days became muco-purulent. Often there was also a mild upper respiratory infection, with slight cough but little sputum. The general constitutional disturbances always found in an adult suffering from coryza were absent. The cold will last about two weeks, and then the child may be free for a few weeks until the next attack. This cycle will continue right through the winter and may often be present during the summer months, though the colds are usually less severe in the warm weather. In a small number of cases there was continuous muco-purulent nasal discharge between the attacks. Many of these children had had these frequent colds for as long as three years. While the children remain fairly well in spite of these frequent attacks, both the parents and the education authorities show concern at the amount of schooling lost. Some parents are also anxious lest the frequency of the attacks denotes some constitutional deficiency or even serious organic disease—e.g., tuberculosis.

We have examined 130 children, the findings in the first 100 of which are given below. There were 59 boys and 41 girls in this series. Four children were between the ages of 1 and 5, 69 between 6 and 10, and 27 between 11 and 15 years.

History

Their birth weights were all within normal limits, and they all developed normally from birth, reaching the usual milestones at the expected ages; 88 had been breast-fed and 12 bottle-fed; and 95 were given cod-liver oil and orange juice or other additional vitamins to supplement a normal diet. Only 2 children were in the habit of going to bed late. We analysed this series with regard to previous infectious diseases and found that 84 had had measles, 59 whooping-cough, 3 diphtheria, 59 bronchitis, 23 tonsillitis, and 14 otitis media. The majority of them had been vaccinated and immunized against diphtheria. No definite relation was found between any of these infectious diseases and the onset of colds. In 33 cases the mothers complained that their children snored at night and were mouth-breathers. Twenty-one children had had their tonsils and adenoids removed before being seen by us, mainly for the relief of frequent colds, and of these 18 were not improved. A near relative of 26 children had suffered from tuberculosis and of 22 from an allergic condition.

Clinical Examination

These children all showed normal weights and heights for their age and sex, and appeared to be well developed and of normal intelligence, with the exception of 3 who were slightly

backward. None showed evidence of rickets. Their temperatures, pulse, and respiration rates were normal. Eight had carious teeth. Tonsillar enlargement of varying degrees was present in 39 and the adenoids were prominent in 27. In no case was there complete nasal obstruction, and the adenoid facies was rare. We specially observed the shape of the thorax of these children, and found that in 17 it was definitely barrel-shaped, in 5 alar, and normal in 78. In no case was serious lung disease found, but 8 showed a few scattered rhonchi and occasional rales. The heart, abdomen, and central nervous system were normal in all cases. No serious organic disease was therefore found on clinical examination.

Investigations

A number of laboratory tests were done on every child. The haemoglobin in 2 cases was between 60 and 70%, in 6 between 71 and 80%, in 45 between 81 and 90%, in 16 between 91 and 95%, and in 31 over 95%. The white count was between 6,000 and 10,000, and in no case was there a leucocytosis. The differential count showed some interesting features. Only 3 had increased eosinophils, but there were more than 40% of lymphocytes in 53 of the patients, showing a relative lymphocytosis. The urine was normal in every child. B.S.R. (Westergren) was done in one-third of the children, and was within normal limits. Twelve children had a positive Mantoux (1:1000), and 5 of these had positive family histories. None of them showed any other evidence of tuberculous infection, and there was no relation between the positive Mantoux reaction and anaemia or frequent colds. X-ray examination of their chests showed mild catarrhal changes in 49, particularly in the right lower zone, and also slight increase in the hilar markings. Skiagrams of their sinuses showed definite opacities in one or both maxillary antra in 51, and this was the most common abnormality found in the investigations done on these children. The radiographic appearances were thought to be due to mucosal swelling and thickening in the majority of cases, and only 3 showed opacities thought to be caused by actual pus in the sinuses.

Each child was also tested for allergic skin sensitivity to the common air-borne inhalants by the intradermal method, and to the pollens and the main food groups by the scratch test. In all, 14 groups covering 60 substances were used. No food sensitivity was discovered in any child. Eleven children showed positive reactions; 4 of these were cases of hay-fever and had marked sensitivity to pollens, and 5 were cases of bronchial asthma showing marked sensitivity to air-borne inhalants, those most frequently incriminated being house dust, feathers, horse dander, cat, dog, cow, wool, and furs, in that order. The remaining 2 cases gave positive skin reactions to air-borne inhalants, but the symptoms for which they had been referred were not regarded as allergic. The skin-testing was done independently of the history-taking and clinical examination, and therefore any bias in its interpretation can be excluded. It is interesting that in every case where an allergic factor was diagnosed it was confirmed by skin tests. At the clinic at this hospital for children suffering from respiratory allergy, in which skin sensitivity tests are done, 80% show positive reactions. This is in marked contrast to the present series, only 11% of which had positive skin reactions to the common air-borne inhalants. Two other features distinguishing the two groups are the absence of radiological abnormality of the nasal air sinuses in the allergic group and the low incidence of eosinophilia in the present series as opposed to the allergic.

The cervical, axillary, and inguinal groups of glands were carefully examined, and enlargement of the cervical chain of glands was noted in 30 cases. This was usually found in patients with enlarged septic tonsils. In addition, however, many children showed enlargement, sometimes to a considerable extent, of the other groups of lymph glands. This generalized glandular enlargement seems to be common in children who have an active septic or tuberculous focus, though often no obvious cause can be found. Twenty children with adenopathy had several additional investigations done to see whether further light could be thrown on this clinical problem—namely, the Paul-Bunnell test, Wassermann reaction, and biopsy of a small gland in 6 cases. All these tests proved negative, and the results of the routine investigations in no way differed from those

obtained in children with no generalized glandular enlargement. The glands studied histologically showed activity only in the germinal centres, and the general structure of the gland was quite normal.

No bacteriological examination of the muco-purulent nasal discharge was made. Many workers have investigated its flora and the results are well known.

Conclusions

From these investigations we learn that the child with frequent colds is of normal development, build, and intelligence, and does not suffer from any other organic disease. Though minor degrees of anaemia occur, the children cannot be regarded as physically defective. The onset of the attacks at the beginning of school suggests that the continuous contact with infection is an important aetiological factor. No definite relation was found between the colds and developmental abnormalities, upbringing, previous illnesses, or contact with tuberculous infection. No conclusion can be drawn from the lack of improvement after tonsillectomy, as naturally the children who improved after this operation would not be sent to the clinic; but we believe that in the absence of other indications, such as infection of the tonsils or nasal obstruction due to adenoids, surgical removal of the tonsils and adenoids will be relatively ineffective as a measure designed to prevent frequent colds. No allergic aetiological factor could be established. Investigation of the blood, the Mantoux test, and special investigations with regard to glandular enlargement, though of general interest, did not throw any light on this condition. These frequent colds are due to inflammatory reactions of the mucous membrane lining the nasal passages and air sinuses, and give rise to few general constitutional disturbances in children. A filterable air-borne virus seems to be responsible, aided by other organisms such as the pneumococcus, *Sr. viridans* and *haemolyticus*, staphylococcus, *Micrococcus catarrhalis*, or *Haemophilus influenzae*, which set up secondary infection. Repeated colds may cause nasal obstruction, and there may be arrest of nasal development and failure of muscular control over nasal respiration. These factors predispose the child to further infection.

We think that the treatment of this condition is entirely a problem for the ear-nose-and-throat surgeon, who should keep these children under supervision in a special clinic where they can receive conservative and operative treatment. A general medical or surgical, paediatric, or allergic clinic should not have to deal with these children, as, apart from the local conditions affecting the nasal passages, sinuses, and throat, no other abnormality could be discovered.

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Dr. Douglas Lothian, resident medical superintendent of the Down Mental Hospital, Downpatrick, in his report for 1944 records that 39 patients were treated by the electro-convulsive method during the year, and 9 of them were discharged recovered, 3 being cases of dementia praecox and 6 suffering from depression. Two other cases of depression made such considerable improvement as to warrant the expectation that they would soon be discharged, as did 1 case of dementia praecox. Three cases of dementia praecox made an apparent recovery, but relapsed later; 2 cases made some improvement, but relapsed completely later. Forty-seven patients recovered without electro-convulsive therapy, but with psychotherapy and occupational therapy; these included 18 cases of dementia praecox, 16 depressions, 7 anxiety neuroses, 5 manias, and 1 paraphrenia. The other recoveries included a case of general paralysis of the insane treated by trypanamide and bismuth, 2 cases of arteriosclerotic confusion cleared up by careful attention to living habits, 1 case of uraemic confusion, and 2 cases of mental disorder resulting from alcoholism.