My interest in the syndrome started in the middle 1950’s when I was studying a condition that was affecting some of the children who I was seeing in my general practice in England. These children had developed personality changes following acute infections associated with some rather remarkable fits.

Within two years, I had collected about 40 of these cases. They were mostly between 1 and 5 years of age and characteristically became naughty and difficult a few days after developing an acute infections illness, such as measles or gastroenteritis. They were irritable, negativistic and spiteful, their sleep was disturbed, waking up many times in the night crying.

Their appetite was poor, they failed to gain weight and their abdomens were often distended and they had bulky pale offensive stools. This condition usually righted itself after a month or two, even if left untreated, but there were some cases which went on for longer and petitmal-like fits occured.

Summary:

These three common symptoms often occur together and most general practitioners have their own thoughts on what usually cause them. The sharing of these thoughts may enlarge our vision of the possibilities that face us, so may help to reduce personal bias. Special emphasis is placed on the role of infection and food sensitivity in the production of this syndrome. Methods of management are discussed.

The similarity between this pattern of illness and that of mild coeliac disease led me to treating them successfully with a gluten-free diet and to call the condition Pre-Coeliac Syndrome.

One child developed most remarkable fits and it was these that gave the clue that led me to their cause. These particular fits bore a striking resemblance to those occurring in dogs when fed upon wheat flour treated with a gas called agene, as had been described by the late Sir Edward Mellanby in 1946.

He called these fits “Canine Hysteria”; many had searched for the human counterpart of these fits, but had failed to find it and interest had waned.

Comparing the illness of Pre-Coeliac Syndrome with that of Canine Hysteria showed too many points of similarity to be coincidence (see tables I and II). Agene-treated flour was surely the cause of both.

On closer enquiry, I found that Mellanby’s work had been done on puppies and not on fully grown dogs; the latter apparently just became irritable and sullen when fed on agene-treated flour.

Looking at my adult patients then, I came to the conclusion that the depression associated with headache and insomnia that they were developing following infection such as influenza was the likely adult manifestation of agene-treated flour.

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| TABLE 1 |
| Comparison between canine hysteria & pre-coeliac syndrome |
| Canine Hysteria | Pre-Coeliac Syndrome |
| Onset often associated with infection | Onset usually associated with infection |
| Unfriendly and frightened | Unfriendly and frightened |
| Will bite the hand that feeds it | Spiteful and kicks mother and doctor |
| Has very disturbed nights | Has very disturbed nights |
| Abnormal slow unsteady walking | Abnormal slow staggering gait |
| Has dry mouth | Has dry mouth |
| Has characteristic fits | Has similar fits (see Table 1) |
| Has pale, bulky, foul-smelling stools in later stages of the disease | Has pale, bulky, foul-smelling stools, frequently |
| Has severe skin irritation and scratches a lot | Many cases have skin irritation with or without rash |
| Most cases respond promptly to diet which excludes chemically treated flour | Most cases respond promptly to gluten-free diet. |
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The avoidance of all wheat-flour containing foods, their symptoms clearing up within a few days of starting their diet. For convenience, I thought of them as suffering from Headache-Insomnia-Depression syndrome. At the time, the vast majority of white bread being consumed by the people of Britain was made from agene-treated flour. This made the loaf both bigger and whiter. Soon after my studies became known the use of agene as a flour improver was banned by the British Government. The conditions I described then more or less disappeared, but not altogether.

**Present status of the syndrome**
I believe that the Headache-Insomnia-Depression syndrome still occurs, mainly affecting men and women between 20 and 45. Most cases of depression are associated with insomnia and its diagnosis is often doubted when this is absent. However, there is a form of depression which is associated with deep sleep; this form does not respond to the tricyclic antidepressants but appears to respond only to Monoamine-Oxidase inhibitors.

Likewise some cases of manic depressive psychosis sleep well, even when in a deeply depressive phase. It is therefore the addition of headache that helps to distinguish the syndrome from other forms of depression, and usually it is a prominent feature. The headache most often starts in the neck and spreads to the top of the head, though may be experienced anywhere in the head or even may just be a heaviness or a feeling of mental clouding.

**Predisposing causes**
Apart from viral encephalitis itself, the following infections are all capable of being complicated by an encephalitis and thereby can act as precursors to Headache-Insomnia-Depression syndrome:- Infectious: Influenza; Pneumonia; Meningitis; Septicaemia; Mastoiditis; Typhoid; Malaria; Q Fever and Brucellosis. Some more chronic infections such as tuberculosis, syphilis and cystocercosis may also play a part.

Any other conditions which can cause brain damage or atrophy may predispose to the development of the syndrome under discussion. Examples are:- head injuries; vitamin deficiencies such as pellagra; cerebrovascular accidents; anoxia at birth and during anaesthesia; metabolic disorders of renal, hepatic and pulmonary origin; endocrine disorders; alcoholism; childbirth; brain tumours and drug or other poisoning.

All these conditions can be associated with organic psychosis which may be present with...
headache, insomnia and depression and should be born in mind when analysing any particular case.

Heavy metals may be concerned in some instances, bismuth and mercury in old-fashioned medicines, modern lighting creams and aluminium in cooking utensils.

Obtaining a dietetic history

Getting a short description of how the patient feels when eating can be invaluable in these cases.

In Headache-Insomnia-Depression syndrome, the sufferer will often notice discomfort following eating food. His abdomen feels full up and distended, he notices a rapid or irregular heart beat, sometimes with dyspnoea he may also be aware of a feeling of tiredness, sometimes accompanied by excessive sweating.

These symptoms usually pass off after an hour or two, later to be followed by the symptoms of the syndrome itself.

Obtaining a short description of what the patient eats and drinks during a typical day, with the approximated quantities consumed, is well worth the few minutes that it takes to get it. Hippocrates said “The physician who neglects his patients’ diet is a fool.”

Quite often such an enquiry will reveal the intake of surprisingly high quantities of certain foods or drinks which may serve as pointers to the cause. Wheat, oat or maize containing foods, sugar, cool drinks, fruit, milk, eggs and meat may each be taken in absurdly large quantities by some people.

Alternatively there may come to light the regular consumption of foods or drinks known to be common headache producers such as alcohol or those containing methylxanthine (e.g. coffee, tea, chocolate and cola drinks).

Special enquiry should be made regarding white bread intake, because chlorine gas and chlorine dioxide are still allowed to be used as flour improvers in South Africa. They act in a similar way to agene and alcohol or those containing foods or drinks known to be com-

Some people.

Taken in absurdly large quantities by

In warm conditions in country stores.

Therefore the bread made is suspect.

Flour improvers in South Africa. They

Because chlorine gas and chlorine-

Dioxide are still allowed to be used as

Methylxanthine (e.g. coffee, tea, milk, eggs and meat may each be taken in absurdly large quantities by some people.

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Special enquiry should be made regarding white bread intake, because chlorine gas and chlorine dioxide are still allowed to be used as flour improvers in South Africa. They act in a similar way to agene and alcohol or those containing foods or drinks taken during the twelve hours prior to starting an attack can be recorded. After a few such records have been made, a common denominator may be found and a diet diary is acceptable to the patient, an elimination diet is the next step to take.

Should this procedure not be acceptable to the patient, a ‘diet diary’ can be suggested, wherein all foods and drinks taken during the twelve hours prior to starting an attack can be recorded. After a few such records have been made, a common denominator may be found and a suitable challenge with that substance arranged.

Once the causes of the syndrome have been identified, and they are often multiple, the choice lies with the patient whether to avoid them and be symptom free or to go on enjoying consuming the offending foods or drink and suffer the consequences.

Other causes

If one draws a blank on these lines of enquiry, it is worth asking about working conditions or the inhalation of fumes from heaters or about smoking habits; each may give a clue. Detective work, an elimination diet or a diet diary may be needed if these questions fail to produce any pointers.

The most bizarre cause for the Headache-Insomnia-Depression syndrome that I have encountered was sensitivity to hair oil which proved to be the correct etiology in two cases.

Associated hypertension

Headaches are commonly blamed on hypertension, but I often wonder whether the headaches are not caus-

In Headache-Insomnia-Depression syndrome the blood pressure may be considerably raised but this usually falls to normal with the successful treatment of the syndrome.

Psychological aspects

I have purposely refrained from mentioning the purely psychological side of this syndrome, because it is the medical model to which I hope to draw attention. Nevertheless, the psychological aspects cannot be ignored.

Recent distressing event and stress of any sort can precipitate the syn-

Therapeutic considerations

Treating cases of the syndrome with psychotherapy and counselling will usually lead to some improvement as the result of the attention given, but if the condition is caused by metabolic disturbances, it is most unlikely to be fully effective.

Likewise those who fly to antidepressant therapy, with or without psychotherapy, are also likely to be disappointed. The tricyclic antidepressants are not only ineffective but also often seem to produce side-effects.

MAO inhibitors sometimes help in the short term but this benefit soon seems to fade away. Likewise Lithium salts seem to be of no avail.

Where judging from the patient’s history, there seems to be some hormonal imbalance, treatment with progesterone or chorionic gonadotrophin is said by some to be effective but I have not had much experience with these preparations.

Time consuming though dietetic therapy may be, it is well worth the effort. If the offending foods or drinks are not suggested by a careful history, an elimination diet is the next step to take.

Syndrome may occur during pregnancy or following parturition or abortion. The approach can be similar to that which has been described.

In addition, consideration must be given to two possible vitamin deficiencies that can occur at these times, those of Vitamin B6 (pyridoxine) and Vitamin B12 (the cobalamins). Both of these two vitamins are incompletely understood at the present time, so we can only guess at the cause of these deficiencies.

Nevertheless, what is certain is that there is a group which respond dramatically to therapy with either of the two vitamins or to both. Even if we don’t quite know why we are doing it, I believe that it is imperative that we try this form of treatment at the earliest time we can.