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NASAL SINUSITIS IN CHILDHOOD *

BY

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Since nasal accessory sinusitis is almost always the result of colds, other upper respiratory infections such as influenza, or the exanthemata, it is proper to emphasize that the avoidance and correct treatment of these conditions are of the utmost importance.

Children often manage to escape with few infections during their early lives, but it is common to find that their first year or so at school is constantly interrupted by colds. This is scarcely to be wondered at, for it is at school that they first encounter the millions of organisms which exist where people are herded together. In such places as schools, trains, and cinemas it must be almost impossible to breathe air which has not already been in and out of someone else's lungs or which does not contain droplets from the coughs and sneezes of those who have colds. So far the human species has not been able to develop an innate immunity to the organisms that cause upper respiratory infections. It has scarcely had time to do so; for, bearing in mind the history of mankind, it is only recently that people have lived in such close proximity to each other. At a children's hospital such as that of Great Ormond Street it would not be an exaggeration to say that one-third of the patients are suffering from disease which is the result of inhalation of micro-organisms.

Frequency

How frequent is sinusitis in children? That it is common in the early years of life has been demonstrated by many different workers. J. H. Ebbs (1938) recently published the results of the examination of the sinuses of 496 children post mortem. He found disease in 152 instances, or 30.6 per cent. Other investigators have submitted a series of children to antrum puncture: by this means Mollison (1922) observed that 22 per cent. had muco-pus in the antra, and Carmack (1931) 30 per cent. In a series of 100 children at Great Ormond Street I found that twenty-four had muco-pus in the antra (Crooks and Signy, 1936). All these children were from a tonsillectomy list, and obviously had something wrong with their noses or throats, or they would not have been undergoing that operation. Since it had been said that removal of tonsils and adenoids cures sinusitis in children, and also that the condition is only temporary, I punctured the antra of these twenty-four children again six months later to test these statements, and still fifteen of them had muco-pus. Therefore neither of these statements is true. During last year antrum infection was proved by exploratory puncture in over 500 children at my out-patient

department, and approximately the same figure applies to several preceding years.

We have been slow to recognize the importance of sinusitis in childhood. It has long been known that it is common in adult life, and it stands to reason that children are more liable even than adults. They are more susceptible to colds, and their sinuses drain less readily during a cold, since the small nose is so easily blocked by mucosal swelling. We know how frequently otitis media occurs in the young, and the middle ear is, after all, only a specialized sinus off the nasopharynx. And the sinuses are all present in childhood: the antrum exists at birth, and by the third year is a fair-sized cavity; the ethmoid labyrinth contains well-defined cells at birth; and the sphenoid is a definite cavity in the third year. The frontals vary greatly in development, but by the age of 5 or 6 there is usually a good-sized cavity. Therefore there is every reason to expect sinusitis in early life.

The Causation of Sinusitis

By far the commonest cause of sinusitis is a cold, or colds. Influenza, particularly in some epidemics, is often responsible for the onset, and sinusitis may follow any of the infectious diseases which are accompanied by upper respiratory inflammation, particularly whooping-cough. Bathing in infected water is another mode of infection; but so far as children are concerned antrum infection from bad teeth does not arise. Lastly, allergic rhinitis may give origin to secondary sinusitis.

It is true to say that with every nasal cold there is sinusitis. How could it be otherwise when the mucous membrane lining the sinuses is continuous with that of the nose? A radiograph taken during a cold will almost always show some thickening of the mucous membrane in the antra. But usually as the cold gets better the sinuses return to normal. When, however, there is retention of exudate in a sinus during an acute infection, or if inflammation persists in such a cavity after the general nasal infection has settled, sinusitis merits separate consideration. Retention of exudate under tension, due to closure of the ostium by inflammatory swelling, gives rise to headache, localized pain, and tenderness. Persistence of inflammation in a sinus, with an open ostium, induces nasal congestion and discharge. The latter is often of the nature of an overflow, the matter in the sinus accumulating until it has reached the level of the ostium. Normally the cilia wipe the exudate towards the ostium, against gravity if necessary. When they are inflamed they are incapable of doing this.

It is essential to bear in mind that pus in a sinus is, strictly speaking, outside the main body cavity. It is in

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no way comparable to inflammation in a long bone, for instance. Provided the ostium is open drainage is present and there is rarely any increase of temperature or localized pain. These manifestations arise only when the ostium is blocked, and then the condition more closely resembles an abscess elsewhere.

The anatomical peculiarities of an individual nose may make it more liable to sinusitis than is normal. For instance, a deviated septum which presses upon a middle turbinate may completely block the ostia of several sinuses when there is nasal congestion. A small and crowded nose is less likely to maintain adequate drainage for the sinuses during a cold than a good roomy nose, and, of course, a sinus may have an abnormally small ostium. And, last but by no means least, some people are highly susceptible to upper respiratory infections, and appear to have little or no immunity to colds. They are obviously candidates for sinusitis.

Bacteriology

It is interesting to compare the bacteriology of sinusitis with the bacteriology of the nose. When I made my observations upon a series of children nasal swabs were taken from them at the time the antra were aspirated. Whereas the commonest organism found in the nose was the staphylococcus, the pneumococcus was much the most frequent organism in the infected antra. Next commonest in the sinus was the Pfeiffer bacillus, but it was rare in the nose. The *Micrococcus catarrhalis* and the *Bacillus hoffmanni* were common in the nose but rare in the sinuses. The streptococcus was a frequent cause of sinusitis but was not so often found in the nose. The usual causes of sinusitis were therefore the pneumococcus, the Pfeiffer bacillus, and the streptococcus. The common organisms in the nose were the staphylococcus, the *Micrococcus catarrhalis*, and the *Bacillus hoffmanni*. The pneumococcus produces a very thick yellow pus, and one wonders whether this fact gives it pre-eminence as a cause of sinusitis, the pus being too thick to escape from the ostium readily.

There is one special peculiarity about the pathology of sinusitis in children: the bone surrounding the sinuses is more porous than in later life, and osteitis is more likely to arise. I will now proceed to the clinical manifestations.

Acute Sinusitis

Acute sinusitis meriting separate consideration from a generalized inflammation of the nose, sinuses, and throat is comparatively infrequent in childhood, and it only calls attention to itself during the course of such an infection when the discharge cannot escape from the sinus. This happens, of course, when the ostium becomes blocked owing to the swelling of the mucosa encroaching on the narrow opening. It therefore occurs typically at the height of an acute cold or influenza.

SYMPTOMS

These vary with the sinus involved, and usually consist of severe headache, localized pain, tenderness, and an increase in fever. If the antrum is at fault there may be swelling of the cheek and oedema of the orbit. Sometimes osteitis of the maxilla results. An acute block in the ethmoids with osteitis is not very uncommon in the first year or two of life. When severe there is a tender swelling over the upper part of the side of the nose, and the orbit is closed by great oedema. Sometimes the eyeball is immobilized. On several occasions the diagnosis

of cavernous sinus thrombosis was made. It is important to recognize the nature of the illness, because external opening of the ethmoids results in recovery, while neglect of it may end in cavernous sinus thrombosis and death.

TREATMENT

In the first place treatment is conservative. In the great majority of instances the ostium can be made to open and let out the discharge without surgical intervention. The patient will of course be in bed; and it is important to maintain an even temperature in the room. Sudden changes of temperature increase nasal congestion. The main object of treatment is to shrink the inside of the nose till the discharge comes away. There are many preparations of use for this purpose—they usually contain ephedrine and volatile oils. A benzedrine inhaler is effective, and children like it. Inhalations of menthol in hot water are helpful if the child is old enough to use them. In addition the middle meatus of the nose should be shrunk by the application of a cotton-dressed probe dipped in cocaine 10 per cent. and adrenaline 1 in 1,000. Only if these measures fail after trial for a few days should surgery be resorted to, and then it should be as simple as possible: for instance, aspiration of the antrum, but not lavage, which may spread the infection.

It is obvious that acute sinusitis may pass on to a chronic condition in which there is inflammation of the mucous membrane, although drainage has been established.

Chronic Sinusitis

Chronic sinusitis is so often found in the catarrhal child who is liable to colds that it must claim our chief attention. The pathological condition present is catarrhal, or, more rarely, suppurative, inflammation of one or more of the sinuses with continued discharge into the nose. Most often the trouble lies in the antrum. I had come to that conclusion clinically, and was pleased to see that Ebbs in his series of necropsies had found that the antrum was involved more often than the ethmoids and sphenoids added together.

SIGNS AND SYMPTOMS

A series of 100 children with sinusitis at Great Ormond Street was analysed for signs and symptoms of chronic sinusitis, and the following figures are based on this examination. Subsequent observations on many hundreds of children have confirmed them.

Nasal Discharge.—The most frequent symptom was nasal discharge, and of the 100 children eighty-four suffered from it. There is one point to beware of in children. A child hates to have his nose blown, and will try his best to avoid being attacked with a handkerchief. Therefore he tends to sniff nasal discharge backwards into the throat. It is not enough to ask a mother if the nose runs; you must ask if the child sniffs. Very often the mother says there is no discharge, but that the nose is stuffy and full of catarrh. The secretion may be mucoid and clear or yellow and sticky, and is sometimes purulent. Since sinusitis is so often bilateral—the antrum was involved on both sides in sixty-one children and on one side only in thirty-nine cases in this series of 100—the discharge is usually from both sides of the nose. The child is hardly ever free from catarrh, except perhaps for a few summer months. Each cold is accompanied by a streaming nose, which takes several weeks to improve. In short, children with sinus disease are catarrhal, and one could almost go further and say that children with catarrh have sinusitis. In these eighty-four children the average duration of nasal catarrh was two years.

Colds.—Of the 100 children eighty-three suffered from frequent colds. Sometimes the mothers said they were never free from cold—another way of stating that they had chronic catarrh. Colds are the cause of sinusitis, and so we would expect these children with sinusitis to have colds. But sinusitis is also a cause of colds. Sometimes after washing out an antrum a child develops a cold or tonsillitis; active organisms have been released. It is therefore obvious that a discharging sinus may cause a cold, and the vicious circle is complete.

Cough.—Eighty-two of the 100 children suffered from cough. It is a severe hacking cough, often resembling whooping-cough, worse at night and on waking, and is the result of post-nasal discharge through sniffing. If the discharge lies in the nasopharynx the cough is merely a reflex irritation. Unfortunately it may be a much more serious matter. If some lipiodol is placed in an antrum and the child then goes to sleep, some will be found in the lungs next morning. So it is with the purulent discharge from the sinuses. During deep sleep it drops through the open glottis into the lungs, and often serious lung trouble develops. Nearly all bronchiectatics have sinus disease. It has never been proved that the sinusitis is the cause of the bronchiectasis, but it seems a reasonable possibility. I do not believe in the other theory, that coughed-up sputum infects the sinuses. Most likely there is some weakness in the respiratory system, or lack of resistance to disease, which makes both the lungs and the sinuses liable to inflammation.

Snoring and mouth-breathing were present in 62 per cent., and here one must say a word about the "adenoid face." It is a pity that such a term was ever coined, for it has misled all of us. The adenoid face is the face of a child with a blocked nose and nothing more. And adenoids are not the most common cause of a blocked nose even in children. The nasopharynx is a big space, and it needs a good mass of adenoids to block it up. Occasionally such a mass is found, but not more often than, say, once in every five or six operations for the removal of tonsils and adenoids. On the other hand the nose is a narrow space, and is very easily blocked by swelling of the turbinates and accumulation of discharge. In sinusitis the turbinates become swollen, particularly the inferior turbinates over which the discharges flow. In my opinion an "adenoid face" is more often the result of nasosinusitis than it is of adenoids. Of course the two may go together.

Sore throats may occur in sinusitis from mouth-breathing, and tonsillitis may result from infected post-nasal discharge.

Enlarged cervical glands are seldom the result of sinusitis by itself. Lymphatic absorption from an intact sinus is not great.

Headaches are common, and occurred in 44 per cent. They are usually frontal, and are apt to be severe during a cold.

Otitis media occurred in forty-four of the 100 children with sinusitis. Trickling as it does over the orifices of the Eustachian tubes, it is little wonder that post-nasal discharge often leads to otitis media. It is almost an axiom these days that otitis media calls for the removal of adenoids. It also calls for an investigation of the sinuses, and one has often seen persistent otorrhoea clear up after treatment of an infected sinus.

Systemic Effects.—Chronic sinusitis causes general debility, characterized by mental lassitude and a change for the worse in temperament. A child with sinusitis is often morose and ill tempered; he is easily tired, and has

dark rings under his eyes. Sinusitis does not commonly constitute the focus of infection responsible for such diseases as rheumatism or arthritis. Organisms are not readily absorbed from the sinuses, and even the lymphatic drainage is slight.

DIAGNOSIS

This rests upon the symptoms in the first place, but must be supplemented by certain special observations, which are: (1) examination of the nose, (2) transillumination, (3) radiography, and (4) puncture-aspiration.

Examination of the Nose and Throat.—Continued discharge from a sinus causes nasal congestion on the corresponding side, and of course nasal congestion leads to further retention in the sinus; so one expects to see congestion and hypertrophy of the inferior turbinate on the side of the nose corresponding to the sinusitis. The middle turbinate is also often swollen, but is less easy to see. In the middle meatus, or between the inferior turbinate and the septum, there may be an accumulation of mucus or muco-pus. A post-nasal examination would reveal post-nasal discharge. It is difficult to carry out in a child, but often enough a blob of muco-pus will be seen hanging down behind the uvula. The pharynx is usually red and granular.

Transillumination is sometimes useful. If the sinus involved is the antrum, and if the condition is unilateral, a definite finding is obtained with transillumination. Unfortunately circumstances are not often so favourable, for when both antra are infected it is still possible to get a light through them in a child if it is powerful enough. And again if they are poorly developed, or have unerupted teeth in front of them, they appear dull.

X-ray examination is essential. For general purposes one film taken in the naso-mental position is sufficient. It shows the antra, the ethmoids, and the frontals, and the cause of any opacity—whether thick mucous membrane only, or fluid content. Usually the infected antrum shows a uniform opacity made up of thick membrane and retained secretion. In a child a fluid level is rather rare, and indicates a not very thick lining, for such a lining would obscure the level. A good radiograph will always

Puncture-aspiration of the antrum. This position is suitable for either local or general anaesthesia. The cannula reaches the most dependent part of the cavity, and the head is easily held still.

show disease if it is present, and it is unwise to presume a pathological change in a sinus that is clear in such a film.

Puncture-aspiration of the antrum is the final proof of the presence of infected contents in that cavity. It is not such a delicate test of sinus pathology as an x-ray examination, for many a sinus shows changes in the

mucosa in a radiograph but is clear on aspiration or wash. The converse does not hold good. There are two points worth mentioning in regard to puncture-aspiration. It is advisable to culture the fluid aspirated, and it would be useless to aspirate it through the ordinary cannula, since that is contaminated by the withdrawal of the trocar. Therefore a finer cannula is attached to a glass syringe containing sterile saline, and this is passed through the original cannula left *in situ* and the contents are aspirated into the syringe. The position of the head is also important, for the point of the cannula must reach the lowest part of the antrum cavity. This can only be attained by adopting the position I advocate: the child lying on his back with the shoulders on a sand pillow, and the head extended fully (see diagram).

TREATMENT

The treatment of chronic sinusitis is in the first place preventive. Colds must be avoided by improving hygiene and general health and resistance. When they occur the nasal mucosa must be shrunk so that the ostia of the sinuses remain open. If subacute or chronic catarrhal sinusitis persists after a cold general medical treatment is indicated. Only if there is retention of inflammatory products in a sinus is lavage necessary. Operation is reserved for chronic suppurative sinusitis.

As an example, take the child who has all the past winter been subject to repeated colds, and since the last cold a month or so ago has had continuous nasal catarrh. Examination reveals a debilitated sniffing child with a little cough. The inferior turbinates of the nose are swollen. There is a mucoid discharge seen running down the back of the throat. X-ray examination shows swollen mucosa of the antra, and perhaps the opacity is more marked on one side than on the other, suggesting some amount of retention. What is the correct line of treatment? It should be started by keeping the child in a warm, well-ventilated room for a week, the nose meanwhile being shrunk by repeated applications of shrinking drops and by inhalations of menthol. At the same time a vitamin-containing tonic should be given. After that the child should get out whenever the weather is reasonable, and when he has been doing that for a week, the nasal shrinking being continued with, he should go to the seaside. After a month or two on the south coast a radiograph would probably show the sinuses to be clear. Admittedly such expensive and prolonged treatment is out of the question for many children. If so, one may be forced into washing out the antra as the quickest way to get rid of the symptoms. It often works like a charm, but it is no real substitute for the improved general condition and resistance which would have resulted from a holiday at the seaside.

Now consider a more severe example, that of a child who has had constant nasal discharge all the winter. The general condition has suffered a good deal, and a hard barking cough which interrupts sleep at night has developed. Perhaps there has been headache. Radiographs show complete opacity of one or both of the antra. It is unlikely that the line of treatment suggested for the previous case will be rewarded with success. It is necessary to proceed straight away by washing out the sinus in question, and there is no doubt that recovery, even if it does not depend entirely on lavage, will come about much quicker because of it. It is quite possible to wash out the antra of children under local anaesthesia. With a very nervous or difficult child it may be necessary to give a general anaesthetic, but I rarely have to resort to it, especially in hospital practice. According to the find-

ings on lavage the procedure may need to be repeated several times, usually at weekly intervals. The average number of washes necessary in the 100 children I have quoted was three. The treatment as outlined for the milder case should be given at the same time.

Finally, consider the exaggerated example of a child who has had a purulent nasal discharge for several years, and is found on x-ray examination to have an opaque antrum with chronic changes in the mucosa. In my opinion lavage is again indicated, and should be repeated up to a dozen times if there is improvement rather than that an intranasal operation should be resorted to. Of course, if there is as much purulent discharge on the sixth wash as there was on the first, one would probably feel that more radical treatment was necessary.

What is more radical treatment? It is antrostomy—that is, punching as large a hole as possible in the bone of the inferior meatus, between the nose and the antrum. There is then dependent drainage and a large opening through which it is easy to insert a curved tube for washing. I do not consider it such a desirable operation as it sounds theoretically, at any rate in childhood. The floor of the antrum being higher than the floor of the nose during youth, the opening cannot be made very large unless the inferior turbinate is sacrificed, which I am unwilling to do. Also, the hole in the young bone is apt to close in a month or two. Finally, lavage through the opening is little more pleasant than puncture. In spite of its drawbacks, however, it is an operation which has often been followed by good results.

Lastly, there are those cases, even in childhood, in which such advanced disease of the mucosa of the antrum is present that only its removal will alleviate the symptoms. Then a Caldwell-Luc operation has to be done.

We have been discussing the antrum. It is easier to treat than the other sinuses and enables one to present a scheme of treatment more readily. In addition it is far more frequently diseased than the other sinuses in childhood. Disease in the *sphenoid* is more difficult to diagnose and treat. One depends on radiographs even more than in the case of the antrum. Lavage can be carried out through a straight trocar and cannula.

The complicated structure of the *ethmoids* makes them unsuitable for puncture and lavage. In advanced disease it may be necessary to remove the middle turbinate and open the cells, but in less severe inflammation of the ethmoids—and the same applies to the sphenoids—Proetz (1931) has worked out a most valuable form of treatment which he calls displacement. The principle is the introduction of shrinking or therapeutic fluids into the sinuses by means of repeated negative pressure applied to the nose, which is filled with the fluid selected. This form of treatment applies particularly to the ethmoids and the sphenoids, and is of less value in the antrum.

Short-wave diathermy has been used recently, and is of benefit in those conditions of chronic catarrhal sinusitis which are not accompanied by retention of exudate.

Prognosis

What is the outlook in sinusitis in childhood? It is obviously much more favourable than in later life, for two reasons: (1) the young tissues recover more quickly and completely; (2) sinusitis in the adult may have been in existence for years before it is diagnosed.

Sinusitis has a bad reputation, and one is told that it is never cured for life. That is obviously because it

does not fall into the "ectomy" class. Appendicectomy and tonsillectomy leave no room for recurrent inflammation in the organs involved. No doubt removal of the antrum would be followed by a complete cure of antritis. But the cure would be much worse than the disease. It is possible to cure inflammation in a sinus completely by adequate treatment, but of course the sinus remains, and so does the inherent liability to infection of it which caused the original trouble.

Of the 100 children we have been discussing fifty-two were completely cured—that is, they were free of symptoms, and final radiographs showed normal sinuses; thirty-two were improved; and sixteen remained unchanged.

Relation of Tonsils and Adenoids to Sinusitis

Even in a short paper one cannot omit referring to the tonsils and adenoids and their relation to sinusitis. The first question that comes to mind is, "Does infection of the tonsils and adenoids cause sinusitis?" If so it must be either because the adenoids are so large as to block the nasal airway and interfere with ventilation of the sinuses, or because it is a result of surface spread of infection against the normal mucous stream kept up by the cilia. The removal of tonsils and adenoids should cure sinusitis, and it should be uncommon among children who have had their tonsils and adenoids removed. I have already mentioned that of twenty-four cases of sinusitis in children only nine cleared up after removal of the tonsils and adenoids, and they might have done so without the operation. Of the 100 children with sinusitis forty-one had already had their tonsils and adenoids removed completely. The broad conclusion is justifiable that disease of the tonsils and adenoids is not a common cause of sinusitis and that their removal is neither a preventive nor a cure of the condition.

The second question is, "Does inflammation in the sinuses give rise to infection of the tonsils and adenoids?" As the post-nasal stream of mucus is over the adenoids and posterior halves of the tonsils the mechanical possibility of such an infection is evident. It is difficult to draw conclusions from the fact that forty-one of our 100 children had previously had their tonsils and adenoids removed. They may have had the operation done for symptoms which should more properly have drawn attention to the sinuses. Even worse, they may have developed sinusitis as a result of imperfect technique during the operation of removal of their tonsils and adenoids. One has seen that happen. Infected blood runs into the sinuses and sets up inflammation there.

I believe that sinusitis is a common cause of inflammation of the adenoids, and to a lesser degree of the tonsils. The first step in the treatment of sinusitis is the treatment of the sinus itself, and not the removal of the tonsils and adenoids. If the latter are infected and fail to respond to such treatment they should be removed. If there is a large pad of adenoids interfering with respiration, treatment of coexisting sinusitis is not likely to lead to cure until it is removed.

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A CLINICAL EXPERIMENT IN OESTRIN THERAPY

BY

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Oestrin is now well established as a therapeutic agent, but many problems remain to be solved before the most effective mode of administration can be determined. The principle of endocrine therapy is to give the hormone by the most convenient route in such a form and dosage that it will be delivered at the site of effect at a suitable rate, in suitable concentrations, and over as prolonged a period as possible or desirable. The following case illustrates some of the factors to be considered in the use of oestrin.

On February 27, 1936, Mr. Frank Cook did a bilateral ovariectomy, for cysts of both ovaries, on a girl, aged 20, who had suffered for some time from irregular menstrual bleeding. Three days later uterine haemorrhage started and continued for three days. Nine days after the operation hot flushes began to appear. Oestrin was first given forty-four days after operation, by which time the patient was complaining of about twelve hot flushes a day, and during the subsequent two years the case afforded an opportunity for studying the effects of oestrin given by mouth, by injection, and by implantation. In Chart I the number of daily hot flushes is indicated, and is correlated with the dose of oestrin administered.

The Effective Dose of Oestrin for a Recent Castrate

A consideration of the chart shows that the symptoms as measured by the daily frequency of hot flushes began to come under control when oestrone (menformon, Organon) was given in daily doses of 6,000 I.U. (0.6 mg.) by mouth, and after a prolonged period of administration of higher doses remained completely controlled by 5,000 I.U. daily. The case is particularly suitable for this type of investigation, since the daily hot-flushes curve rose rapidly when treatment was discontinued. Later in the patient's history (January, 1937, et seq.) doses increasing from 1,000 I.U. of oestrone by injection had an effect on the symptoms; and later still (October, 1937) 5,000 M.U. of oestriol by mouth* (tridestrin, Paines and Byrne) was found to be a suitable maintenance dose. Finally the implantation of a 14 mg. tablet of crystalline oestrone produced a demonstrable effect lasting over a period of weeks.

Thus it would appear that relatively small doses of oestrin by mouth are effective in controlling the symptoms of acute ovarian deficiency in a castrate. This observation is supported by results obtained in other cases. For instance, the administration of 1,000 I.U. daily for a fortnight, followed by 2,000 I.U. for another fortnight, completely relieved the symptoms of a woman of 54 who was suffering from a moderately severe menopause with six hot flushes a day, and converted a well-marked menopausal vaginal smear into one typical of oestrus.

It is important to determine the minimal effective maintenance dose of oestrin in these cases, for the administration of high doses has certain disadvantages:

1. It may induce uterine haemorrhage, and the patient suffering from the effects of a natural menopause should be

* Oestriol (tri-hydroxy-oestrin) is less potent when given by injection than oestrone (keto-hydroxy-oestrin), but it is more effectively absorbed than oestrone when given by mouth. It therefore appears to be a suitable method of peroral administration of oestrin.