THE INFLUENCE OF THYROID ON WATER METABOLISM IN MIGRAINE

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It is common for patients suffering from migraine to say that they pass urine in larger quantities than is normal at the height of an attack or immediately afterwards. Liveing (1873) gives instances of this in migraine and also in some cases of asthma: " the quantity of limpid water passed in the early part of the paroxysm, white as pump water passed in the students' funking room, or like the urine of hysteria or that of nervous headache". Fisher (1918), a medical man, observed that he passed large quantities of pale coloured urine during attacks of migraine.

Wolff *et al.* (1956) discussed the two varieties of fluid accumulation in patients with vascular headache of the migraine type. In the first type there is local oedema at the site of the headache which occurs at the stage of vascular dilation. According to these authors, this oedema is associated with a lowering of the deep pain threshold, and is therefore an important part of the mechanism of the headache. In the second type there is a generalized oedema often coincident with the headache. They stated that it commonly occurred during periods of increased alertness and driving activity, and that, while it could be induced in patients subject to migraine attacks without starting a headache, it could also be abolished without preventing a headache. They therefore thought that this type of oedema was not related to the mechanism of the headache, but they did not explain the significance of the phenomenon.

Campbell *et al.* (1951) found evidence that migraine patients differed from normal in their salt and water excretion following drinking large quantities of water. In brief, migraine subjects excreted an increased amount of sodium in the 4 hours after the test, compared with normal subjects whose sodium excretion was reduced (see figure 1). There are changes in the blood sodium concentration before, during, and after attacks, with a marked rise

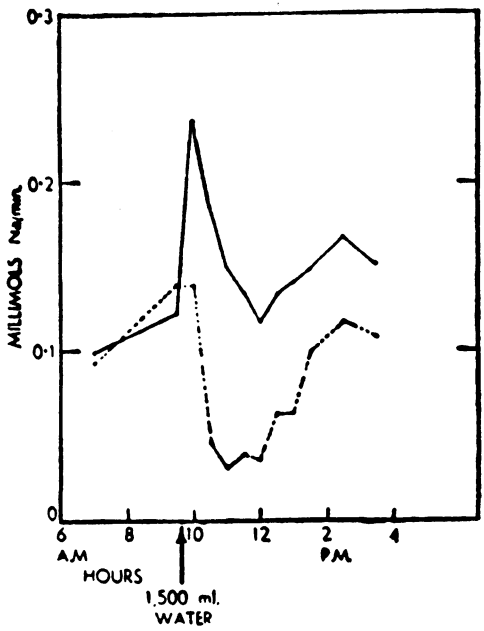

Figure 1

Rate of sodium excretion after 1,500 ml. of water by mouth given at 9.30 a.m. —— = Average excretion for 16 cases of migraine. - - - = Average excretion for seven normal control subjects.

Figures 1 and 2 are shown with the kind permission of the editor of the *British Medical Journal*, and appeared in the *British Medical Journal* with the reference Dorothy Campbell *et al. Brit. med. J.* (1951), **2**, 1424.

in the prodromal phases and a rapid fall at the height of an attack and in the recovery period (see figure 2). These changes may be associated with a lowering of the blood albumen concentration indicating a haemodilution. Worked in terms of Govaert's formula —Colloid Osmotic Pressure = (5.5 x Alb.) + (1.4 x Glob.)—one of our patients whose level between attacks was 27.5 c.m., showed a marked fall in the colloid osmotic pressures in the prodromal stages, i.e., to 18.2 c.m. Hg. Therefore it was assumed that with a rise in blood Na concentration, there is an increase of circulating body fluid. The significance of these phenomena is at present merely a matter of speculation.

The fundamental studies of Verney (1956) on the neural control of the anti-diuretic secretion of the posterior pituitary demonstrated how emotional tension could cause retention of water in the body. Acting through a centre in the hypothalamus, these changes are physiological and reversible, and presumably meet some biological need brought about by the state of emotional tension. When,

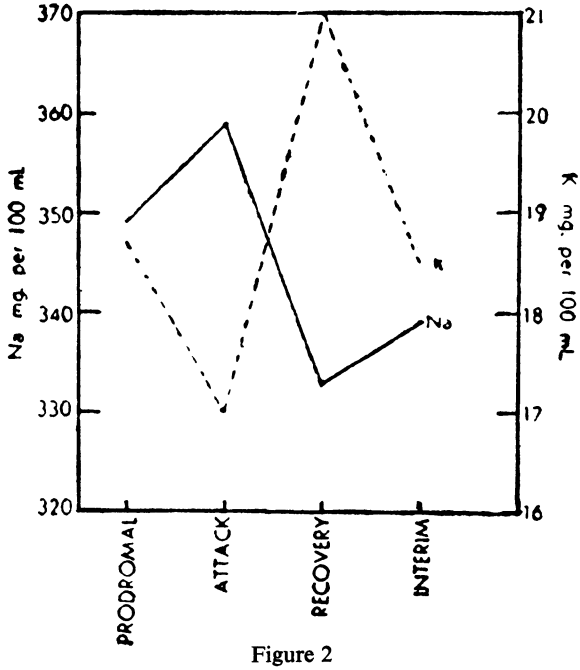

Figure 2
Inverse variation in sodium and potassium levels in the serum during the migraine cycle (average of 31 cases).

through conditioning, the original stimulus fails to arouse emotional tension, the changes do not take place. It is possible that the anti-diuretic hormone plays a part in the prodromal rise in weight from fluid retention experienced by migraine patients, but it would not account for the evidence of sodium retention.

Harris (1948) says " It would seem that there is normally a balance between the specific anti-diuretic action of the neuro-hypophysis and a diuretic influence of the adeno-hypophysis. It is possible that the pars distalis [of the hypothalamus] stimulates water excretion by an action on general metabolism, or indirectly through the thyroid or the adrenal cortex, or by some unknown means ".

Recently several writers have shown that adreno-cortical hormones are increased in the blood and in the urine under conditions of emotional stress. For example Hill *et al.* (1956) studied university boat race crews. They found that the rise in the circulation of adrenal steroids started on the eve of the big race and affected the manager as well as the crew. Bayliss (1955) showed that anxiety, frustration, and fear lead to increased plasma steroids.

Wolff (1953) writes of a private communication in which it is reported that:

". . . adaptive patterns including repressive processes were associated with retention of fluid electrolytes. Inversely, diuresis and loss of electrolytes was noted in subjects exhibiting expressive features of tranquillity after stress . . .

Periods of striving accompanied by tension may be associated with retention of water and electrolytes, followed by a diuresis when tension subsides."

Since that time much has been written on the hormone aldosterone which is secreted by the adrenal cortex. This hormone promotes sodium retention and excretion of potassium. Recent research has suggested that it is controlled by changes in the volume of extra cellular fluid. There is a " neuro-humor " formed in the diencephalon which causes the adrenal cortex to secrete aldosterone. As far as is known, no work has been done up to the present to determine whether aldosterone plays a part in the weight changes in migraine patients, though the secretion of this hormone may influence the changes in weight shown in the diagrams.

Experiments on laboratory animals have shown how the hypothalamus is closely linked with the functioning of the anterior pituitary gland through secretions passing into the blood channels which are common to both.

A chance observation by Brown (1943) that urea which acts as a diuretic is useful in treating some patients with migraine, lends support to the idea that this disorder is affected or conditioned by the balance of salt and water in the body. However, diuretics by themselves are disappointing therapeutically, and this confirms the belief that water and salt retention plays little part in the direct causation of the main symptoms of migraine. Nevertheless, day to day observation of fluctuations in weight gives the clinician a useful indication of the instability of the metabolic background of the migraine subject; and from the point of view of therapy designed to prevent attacks, these observations are of value and can be of help in prophylactic treatment of the condition.

Material

Most of the patients were seen at the Migraine Clinic of the Birmingham and Midland Eye Hospital, and a few in the course of general practice. Only patients with frequent disabling attacks of migraine appeared to yield any clues in this attempt at understanding the metabolic background of the disorder. In the course of this enquiry a surprisingly large variety of headaches were described by the sufferers and their friends as migraine with little evidence to support their contention. The position is further complicated through migraine sufferers being also subject to tension headaches, where the source of the pain is in the scalp and neck muscles. Differentiation is not always easy on the history alone, and it is therefore essential to find some objective evidence of functional changes in the body which are associated with the psychosomatic disorder we call migraine. We are fortunate in having the changes in the body fluids to help us in this, whether

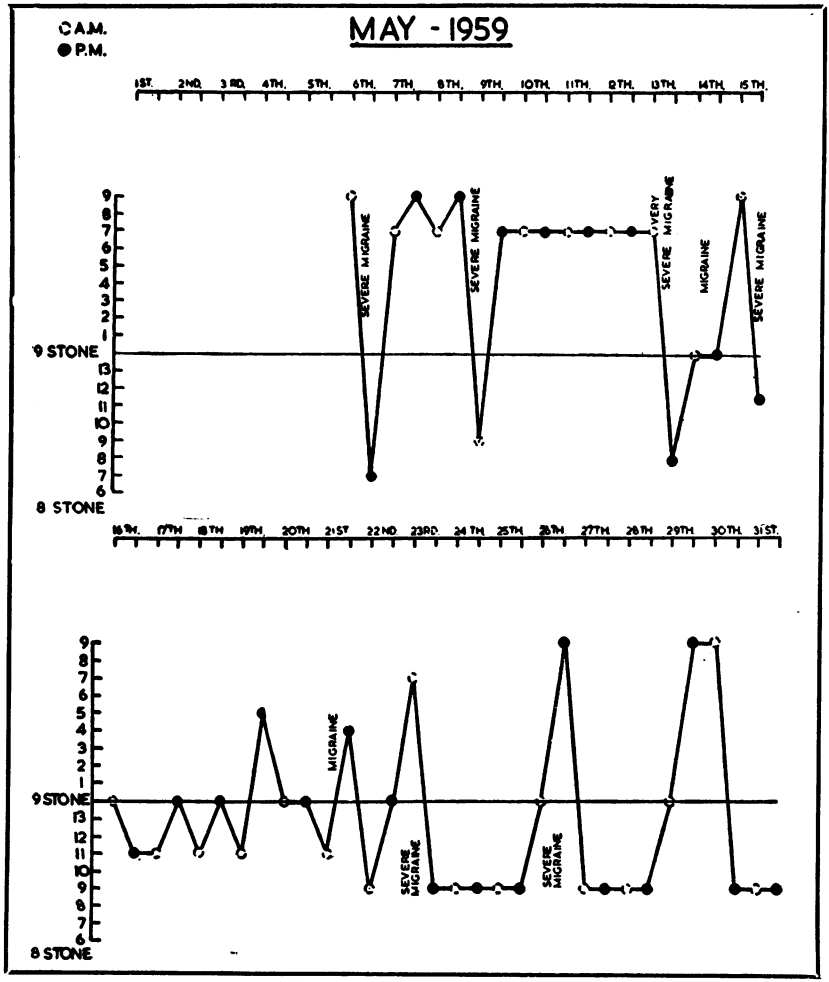

Figure 3
Showing rapid changes in weight (*continued on page 91*).

connected with the migraine symptoms, or merely associated and concomitant phenomena as Wolff *et al.* (1956) thought them to be.

Observations on Diurnal Weight Changes

Patients were asked to weigh themselves stripped after emptying the bladder, first thing in the morning and again on retiring to bed at night (see figure 3). The changes noted are also reflected in some cases by alteration in girth measurements (see figure 4). This patient shows the increase of weight during the day with a fall during the

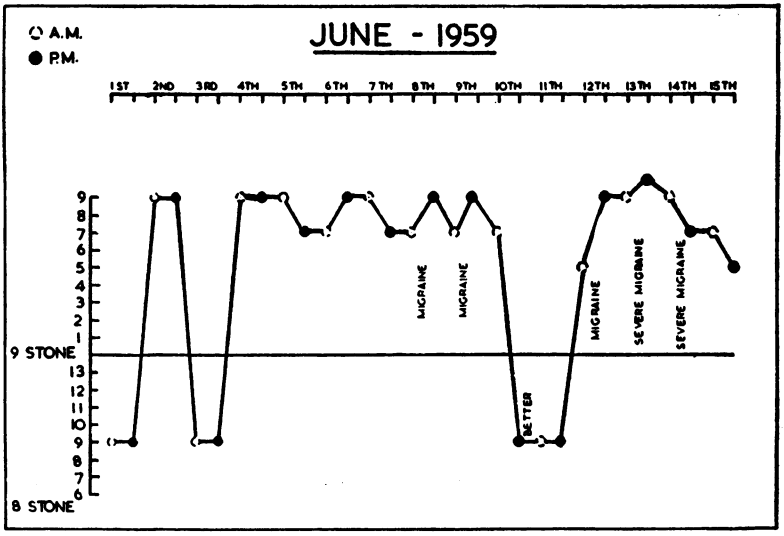

Figure 3 *(continued)*

night, which is typical of most migraine subjects who have kept records. This may be due to the activity of the supra-renal cortex being greater during the day than during the night, as judged by urinary 17 keto-steroid excretion where this has been measured in migraine patients (see also control in figure 11). We also see the well-known weight increase in the pre-menstrual week (see figure 5), which may have something to do with the special tendency of migraine to occur just before or on the first or second day of the menses. Both sexes show similar weight changes though they seem to be more pronounced in women than in men. The reason why women are more constitutionally prone to migraine than men is very likely connected with the hormonal tides of the menstrual cycle.

Treatment with Thyroid

Dr A. C. Crooke (private communication, 1957) of the Birmingham United Hospitals suggested that small doses of thyroid should be given to see what effect this treatment had on the periodic weight changes, as thyroid hormone is essential for normal biological rhythms and for homeostasis (Richter, 1957).

Richter described the influence of the thyroid hormone on biological rhythms in animals and man. He started by discussing the periodic changes in mood of psychiatric patients, the cycles varying from patient to patient from 2 days to as much as 18 months. He quoted the case of a manic-depressive who showed changes in the body weight according to his cyclical changes of mood. There

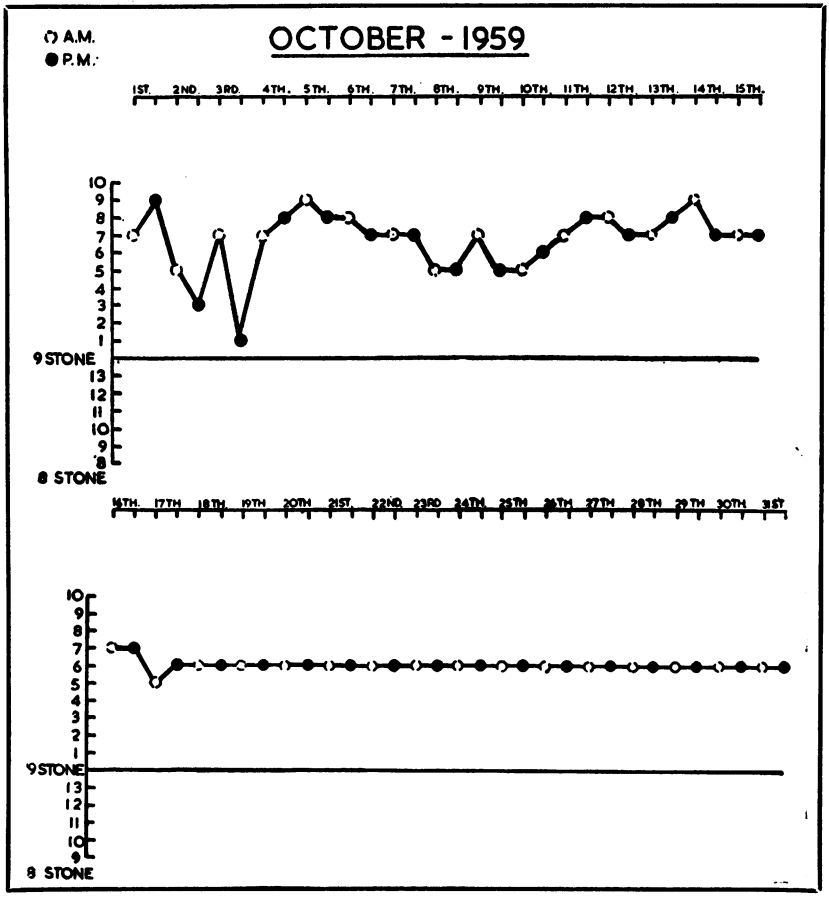

Figure 3a

In same patient as Figure 3, showing reduction in weight changes after thyroid treatment.

are other periodic diseases such as periodic fever, recurrent arthralgia, and periodic leucopenia, and sometimes these patients improve with thyroid treatment. He went on to show that the normal activity phases associated with oestrus cycles in rats were affected by interference with the thyroid in a third of the experimental animals, in such a way that the activity phase was shorter in each cycle. He showed that the thyroid gland is essential for some naturally recurring physiological functions in the rat, besides the role it plays in the neuro-endocrine harmony and balances of the body.

Migraine often occurs in regular cycles or shows some recognizable periodicity. Many patients describe transient changes in mood in

the prodromal stages, varying from depression to euphoria but quite characteristic for each patient: there are also the weight swings. Accordingly, patients were treated with small doses of thyroid not exceeding gr. $\frac{3}{4}$ daily in addition to any sedatives they might have been having previously. This had a striking effect on the weight swings in many but not all our cases (see figures 6, 3, and 3a). Many of these patients started to put on weight while on thyroid to an extent which caused them anxiety. Mrs. W. (figure 5),

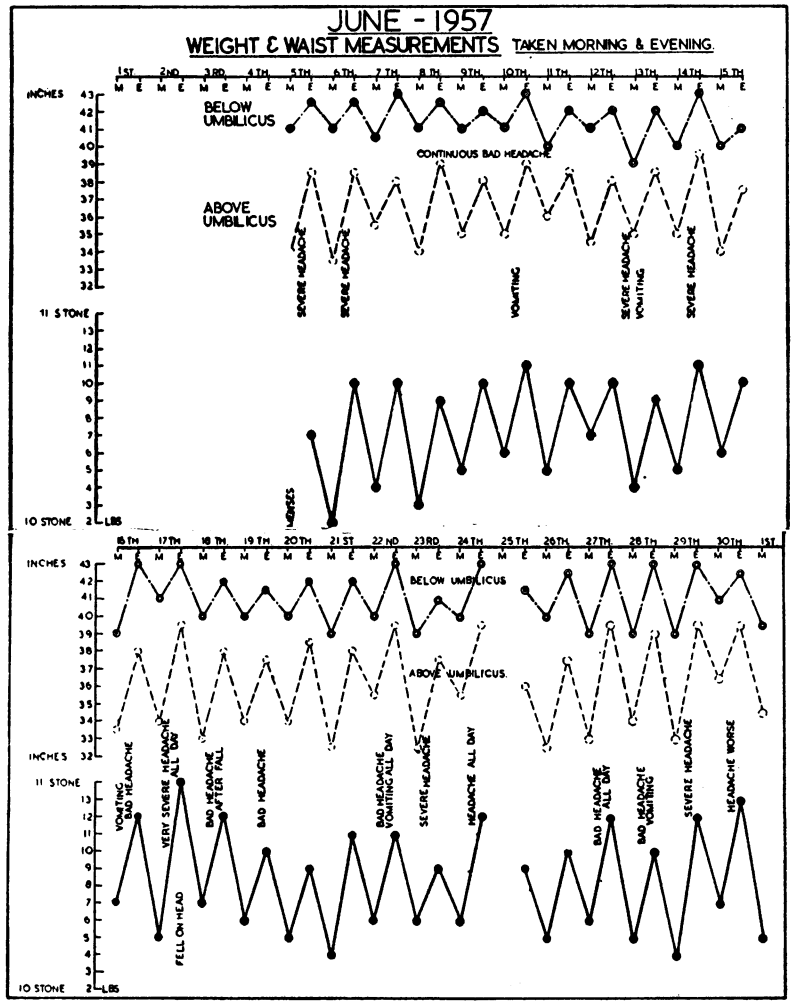

Figure 4

Showing diurnal changes in waist measurements as well as changes in weight in same patient.

increased from a basic weight of 8 st. 9 lbs when the treatment started, and rose to 10 st. 11 lbs.

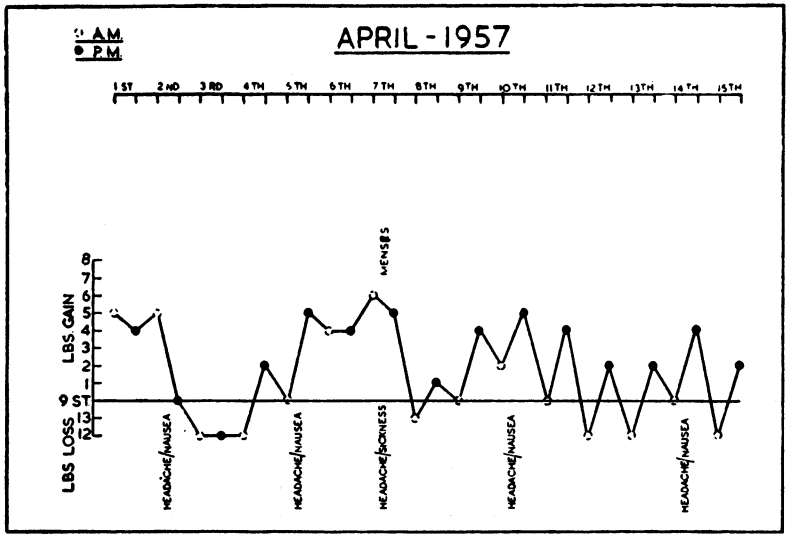

Figure 5
Showing typical menstrual rise in weight.

A number of patients chosen on the basis that they were subject to disabling attacks of migraine with vomiting at least once a fortnight were asked to keep diurnal weight records. For 3 or 4 weeks they continued on whatever treatment they had been taking: then small doses of thyroid were started. As it takes many days for thyroid hormone to exert its full effects, the first 3 weeks on this treatment were ignored, and the weight records covering the period from the third to the sixth or seventh week of thyroid treatment were used for comparison with the period prior to treatment.

The results in terms of average diurnal swing before and after treatment are given in table 1. It will be noted that the only exception in this group is a man, but at the time of writing he has been free from migraine for 6 weeks in spite of having little change in his average diurnal weight swing. This group has been selected on the basis of (*a*) severity of their migraine which has not responded to routine treatment, and (*b*) ability to keep reliable records for 10 to 12 weeks.

All these patients have had relief of symptoms following taking small daily doses of thyroid. Cases 1 and 9 had dummy tablets given on a double blind basis prior to having the true thyroid. A full double blind trial has not been done yet owing to the length of time which it takes, and the severity and disabling nature of

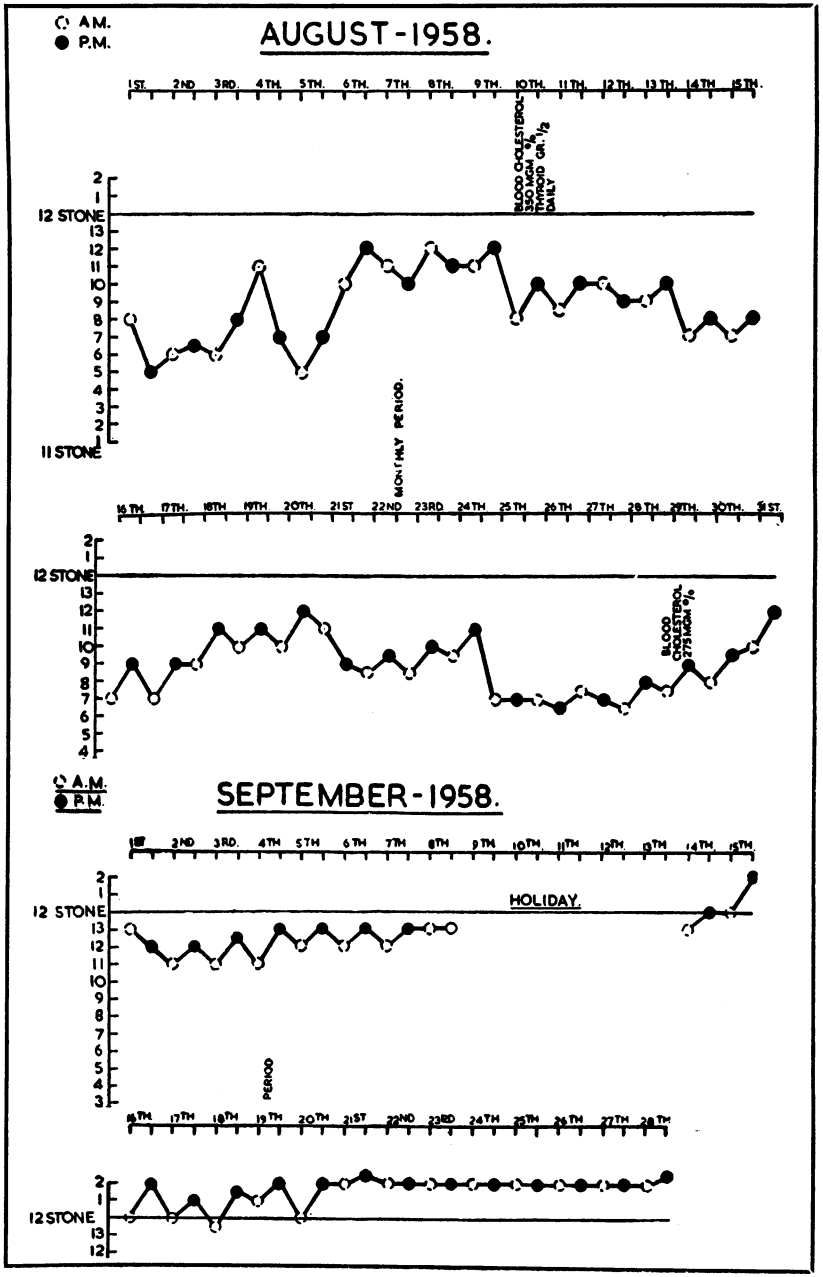

Figure 6

Weight graph showing effect of thyroid treatment, i.e., reduction in weight changes plus general increase in basic weight.

TABLE I

PATIENTS SHOWING DIFFERENCE IN AVERAGE DIURNAL WEIGHT CHANGE, BEFORE AND AFTER THRYOID TREATMENT

	Patient	Average diurnal variation Before thyroid (interval of 3 weeks)	After thyroid
1.	Mrs. C.	10.0 lbs	3.9 lbs
2.	Miss B.	3.8 lbs	1.1 lbs
3.	Mrs. A.	8.1 lbs	4.2 lbs
4.	Miss H.	3.2 lbs	2.7 lbs
5.	Mrs. W.	2.0 lbs	1.8 lbs
6.	Mrs. G. W.	5.1 lbs	1.4 lbs
7.	Mr. W.	4.9 lbs	5.0 lbs
8.	Mrs. P.	6.4 lbs	2.3 lbs
9.	Mrs. F. C.	9.1 lbs	3.9 lbs
10.	Miss E.	6.1 lbs	4.5 lbs
11.	Mrs. S.	3.1 lbs	2.3 lbs

the migraine of the patients selected; however, dummy thyroid tablets have been given in the 3 to 4 weeks prior to giving genuine thyroid.

There are serious difficulties in assessing the degree of relief of migraine symptoms, not only because many of the patients confuse tension headaches with migraine, but as Kennedy (1959) says in a paper on clinical trials:

" Comparisons between treated and untreated, the possibility of spontaneous remissions, the estimation of degrees of improvement or of biological changes and the need to vary the dose, not only make it necessary to take into account the operation of chance, but bring the number of variables under consideration beyond the simultaneous compass of human scrutiny."

Results of thyroid treatment. On an arbitrary scale of disability arising from migraine (see table II), all these patients have benefited

TABLE II

SEVERITY AND FREQUENCY RATING

Severity

Carries on with work or household duties	= 1
Off work for two to six hours	= 4
Off work for six to twenty-four hours	= 6
Off work for twenty-four to forty-eight hours	= 8
Unable to do regular work	= 10

Frequency of symptoms

Once a week	= 3	for each of the following symptoms
Once every fortnight	= 2	
Once a month	= 1	

1. Scotomata.
2. Headache characteristic of migraine.
3. Vomiting.
4. Other neurological symptoms, e.g.vertigo paraesthesiae, aphonia.

Other symptoms if present in a month score (1) each.

1. Fat intolerance.
2. Other food intolerance.
3. Regular prodromal symptoms, e.g., tension headache, hunger, changes of mood, etc.

TOTAL = 25.

greatly from having thyroid as compared to the pre-thyroid phase, vomiting being the first symptom to disappear. In addition over 60 other migraine patients have had small doses of thyroid for longer or shorter periods. None have been made worse by this treatment; two women have had no symptomatic relief and no change in the diurnal variation in their weight. In both these cases there are states of severe chronic anxiety tension with emotional immaturity.

It is obvious that migraine patients do not suffer from thyroid deficiency in the usual sense of the term, and indeed some may give the impression of hyperthyroidism. Theoretically, this paradox might be resolved if it could be shown that any deficiency was temporary and functional rather than due to a morbid pathological condition. There is circumstantial evidence that this may be so.

Thyrotrophic hormone. One of our patients, a spinster, aged 35, suffered very severe attacks of migraine at such frequent intervals that her condition might have been termed " status migrainous ". Tests done at various times had shown evidence of diurnal weight swings, high blood sodium levels, and a high blood cholesterol. She was referred to Dr Crooke at the Endocrine Unit at Little Bromwich Hospital. He has kindly given his permission for his report to be quoted.

It says: Investigations were entirely negative, except for the radio-iodine uptake figures which are abnormal in a most unusual way, and indeed in a way which has not been observed here before. The initial uptake was very low, frankly in the myxoedema range, but the response to T.S.H. was even exaggerated above normal. This would suggest that the original low figure was due to a deficiency of T.S.H. secretion, but there was no other evidence of hypopituitarism. The iodine uptake was repeated and it was again low. This is of particular interest in view of the recent suggestion that some of the patients with migraine and cyclical phenomena and weight changes may respond to thyroid.

Blood cholesterol levels. It was thought that if there was any functional thyroid deficiency in migraine, those patients getting frequent severe attacks might show other evidence of this. Therefore 51 consecutive cases of migraine, subject to attacks at least twice a month, had their serum cholesterol estimated prior to treatment. The results are given in figure 7 and the age distribution in figure 8. The average for the whole group is 284.4 mg. per cent, which is a high figure if one accepts the standard of normality given by many British authorities, which is 150 mg.—250 mg. per cent. (Sampson Wright (1952) and Sheila Sherlock (1955)).

Russell Fraser (1955) writing of hypothyroidism states: " It (the blood cholesterol) is usually but not always raised over 250 mg. per cent in plasma ". But serum cholesterol levels may change rapidly in any individual, and are to some extent dependent on diet (Rivin 1958). In this series all the patients were on a low

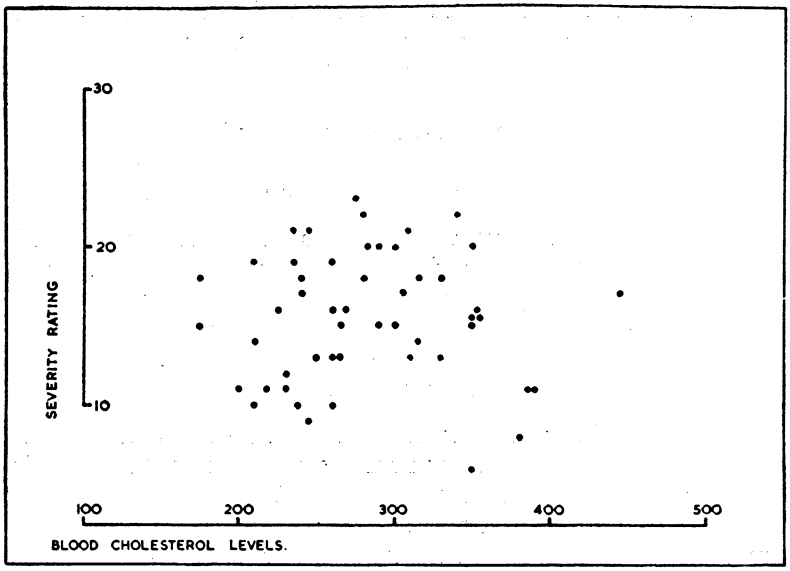

Figure 7
Showing blood cholesterol levels compared with severity and frequency of migraine.

fat diet, as they were intolerant of fatty and greasy food, which gave them indigestion, and which in many cases would precipitate attacks of migraine. All the blood specimens were collected in the afternoon. The known tendency for serum cholesterol levels to rise with increasing age appears in this group, most of those with levels above 300 mg. per cent being 40 years old or more. Two cases are included in figure 7 with high serum cholesterol levels, whose migraine, though frequent had a low severity rating. Both were 29 years of age; one a curate, the other a housewife. Both suffered from periodic depression as well as having a long history of migraine; the curate had had episodes of depression with suicidal thoughts from the age of 16. In our experience,

10—14	15—19	20—24	25—29	30—34	35—39
2	3	3	8	4	9
40—44	**45—49**	**50—54**	**55—59**	**60—64**	**65—70**
6	8	5	1	0	2

Figure 8
Age distribution (51 patients).

endogenous depression as opposed to reactive anxiety is unusual in migraine, but attention is drawn to these two cases, as there may be a link between them and the patients with periodic depression mentioned by Richter.

Clinical Observations—Some factors tending to precipitate migraine

There are many factors which can precipitate migraine attacks (Hay, 1954), and in each case these must be sought for, and dealt with as far as possible.

Fatigue. Migraine has been known to occur with fatigue, such as may follow events causing unusual excitement or emotional tension to the patient. This was fully described by Liveing in 1873. An attack of any severity is always followed by feelings of exhaustion and sometimes coldness which may be bad enough to bring about a temporary state of collapse or even unconsciousness. The attacks terminate, or can be made to terminate with a long relaxed sleep, after which the patient is restored to normal health, and he may find it difficult to realize how ill he felt only a short time before. Some patients attempt to " fight off the attacks " or to " snap out of it " with or without the help of ergot drugs, only to relapse shortly into further attacks of migraine; they then suffer a succession of attacks until they are forced to give up and go to bed, the victims of their driving and over-conscientious personalities, or of the ill-judged advice of their friends. The clinical state in these circumstances may be termed " status migrainous ".

When patients keep accurate records of their attacks, it may be seen that migraine tends to occur in cycles. This periodicity may coincide with the menses or be related to premenstrual tension. It may also be related to certain acquired habits or rhythms of life. Weekend migraine is quite striking; out of 140 new cases 15.6 per cent had attacks at the weekend. Many interesting clinical histories will bear this out, and in those who work on Sundays such as clergymen, there is a tendency for the migraine to begin on Mondays or on their day off. There appears to be a rhythm of over-activity followed by exhaustion based on the week's work. The migraine starts at the point of exhaustion and relaxation, following the over-activity.

One of the earliest of the acquired rhythms is that of sleep depending on the alternation of day and night. This develops in infancy and becomes of fundamental importance with its own diurnal changes in the physiological state of the body. Migraine is related to sleep rhythms in the majority of cases. There is a tendency for the attacks to start in the early hours of the morning or on rising from bed. Many patients sleep badly, having either frank insomnia,

or they are restless with grinding of teeth, talking in their sleep, or even sleep-walking. Nightmares and vivid dreams referring to people known to them, or to recent events in their lives are common. Sleep brings with it no refreshment, and the day begins with feelings of exhaustion, irritation, and sometimes headache either of the tension variety or true migraine. It would seem that though consciousness may be lost, the body and brain remain active, so that sleep is associated with somatic tension rather than with relaxation. There is also the suggestion that unless fatigue accumulated over a period of time is fully discharged by restful sleep, the effort required on awaking to cope with the usual daytime activities is sufficient to precipitate an attack. The diurnal weight swings shown in some of the diagrams would indicate that these patients do not have the normal physiological changes associated with the sleep rhythm.

Endocrine factors. Mention has already been made of the incidence of migraine in patients showing weight gain in the premenstrual tension syndrome. There is also a tendency for some women to have migraine about the time of ovulation. Oestrogen preponderence over progesterone has been given as the cause of premenstrual tension, as has already been mentioned. Most of the menstrual migraine occurs on the day preceding or on the first day of the menses, though it is not uncommon for attacks to start on the third day or later. A sudden drop in oestrogen activity might be more important than the oestrogen activity itself. It is well-known that the onset of migraine is in many cases at puberty, when it may replace childhood symptoms of periodic vomiting or acidosis. Later in the childbearing age, pregnancy is associated with relief from migraine in most, but not all patients; this is the basis of the well-known treatment of migraine with injections of urinary gonadotrophins from pregnant women, a measure often of therapeutic value.

Special senses. Excess of light or noise can both precipitate migraine, especially if the patient has been put into a sensitive state by other factors such as fatigue or premenstrual tension. Some patients are sensitive to glare and flicker, and are liable to have migraine after watching films at the cinema, or the flicker of the television screen, though one patient in this series rather surprisingly goes into a deep sleep on watching television, whereas normally he suffers from insomnia.

Psychological factors. It is well known that states of emotional excitement giving rise to states of tension can be followed by an attack of migraine. There is a large literature on the psychological background of migraine, but two features are noticeable in nearly every case. Firstly, these people are highly active and imaginative.

Should the outlets for their energy prove to be unsatisfactory, a state of somatic tension arises which may become chronic. Secondly, and closely related to the first feature, is a type of obsessive thinking which prevents them from laying a problem on one side to turn their attention to other matters, or to get any sort of relaxation. Thus easily galvanized to activity by a variety of stimuli, they become tense, and remain in this condition until the stimulus has ceased to act upon them, either through appropriate action bringing with it a sense of satisfaction, or through removal of the stimulus. Many migraine sufferers are more conscientious than the average (Hay, 1952).

Miscellaneous factors. There are many factors which patients consider to be important in causing their migraine. Common among these is travel. Functional hypoglycaemia is of great importance in some types of migraine. A sensitivity to fatty and greasy foods is well-known, but it is probably of a different category to the specific food sensitivities which vary from patient to patient, and which are most likely to be allergic in origin.

Patients of both sexes have reported that they get migraine following sexual intercourse, and others seem to be sensitive to changes in atmospheric conditions and the weather. Convalescence after a febrile illness is at times associated with a lowered threshold to migraine.

Discussion

Migraine is a functional disorder of sudden onset, though the prodromal phase may be either of short or long duration. The disorders of function are complex, and so far it has not been possible to do more than form a working hypothesis based on circumstantial evidence to explain what happens in an attack. The evidence is derived from three main sources; clinical histories, metabolic studies, and the information provided by physiologists on the neuro-humoral and homeostatic mechanisms of the body.

The speed of onset of migraine, and the absence in most cases, of associated structural disorders or secondary elaborations, make it an excellent syndrome for the study of the response of individuals of a certain inborn constitution to the strain their lives and environment impose on them. The hypothesis is that the homeostatic control of the body breaks down at the onset of migraine, and this is usually followed by an enforced rest from activity, or by sleep, during which time the body has a chance to recover its functional balance, and the patient can return to normal health and activity. If this is true of migraine, it could also explain how the same factors operating in people of different constitutions give rise to related syndromes and disorders, some of which may be complicated by

secondary or morbid structural changes. For instance allergy and migraine tend to run in the same families (Bray, 1934).

In normal subjects there is little if any diurnal variation in weight. (See control in figure 9.) Premenstrual tension is the best under-

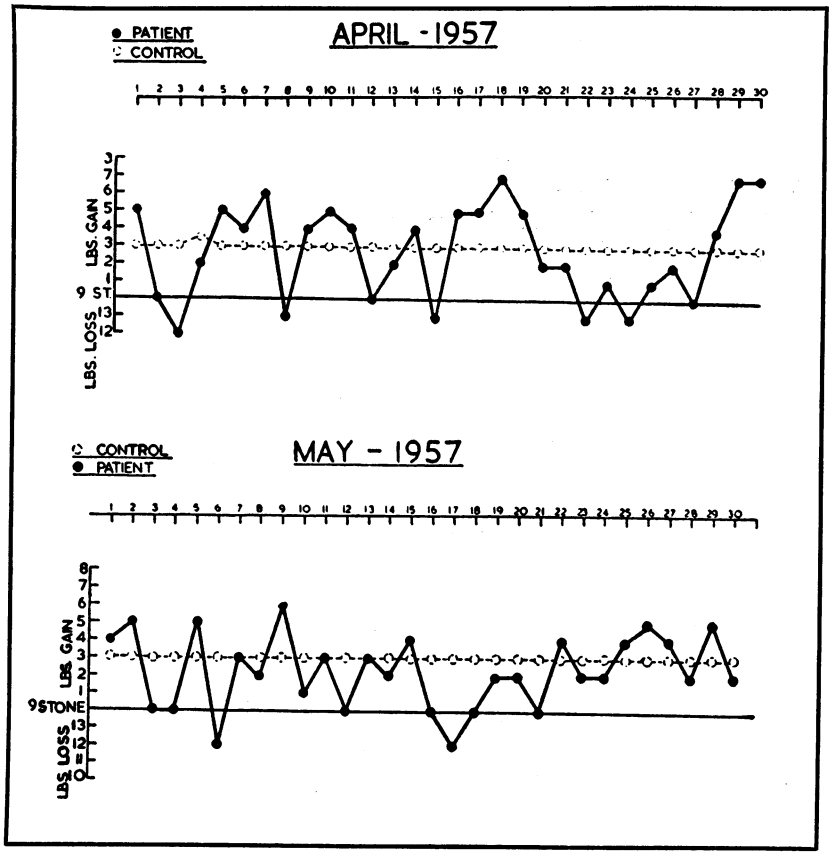

Figure 9
Showing weight changes in patient suffering from migraine compared with normal subject.

stood of the factors which may be associated with salt and water retention under physiological as opposed to morbid conditions. This has been fully described by Greene and Dalton (1953), who showed that a number of symptoms such as irritability, depression, lethargy, asthma, epilepsy, and rheumatism were manifested by patients who had premenstrual tension with weight changes. They thought that oestrogen preponderence over progesterone was responsible for this. At the same time Linford Rees (1953), discussing premenstrual tension from a psychiatric point of view, came to

a very similar conclusion over the part played by oestrogen preponderance. Further confirmation of this comes from a paper by Singh and Singh (1947), who precipitated migraine in patients liable to attack by injecting oestrogens, and who brought relief from migraine with progesterones. Thorn *et al.* (1938) produced water retention in dogs with injections of oestrogens.

However both sexes are liable to migraine with weight changes, and women may have attacks at any point in their menstrual cycles with diurnal weight swings continuing throughout.

As long ago as 1889, Wilson showed that in normal people more urine is passed during the day than night, and Stanbury (1951) found that the nocturnal output of water, potassium, chloride and sodium was about a third of that occurring during the day. Temporary upsets of sleep rhythms did not change this pattern, nor did posture or activity. He noted an oliguria and a high urinary specific gravity during sleep. Also during sleep, bicarbonate secretion was diminished and the PH. lowered. He showed that short periods of hyperventilation would cause a change of urinary secretion in the direction of the daytime pattern, and he did not think that the pituitary or the adrenal hormones were involved in this diurnal rhythm. Rosenbaum *et al.* (1952), stated that DOCA does not alter these diurnal rhythms, though cortisone could either suppress or reverse them. They thought it unlikely that endogenous cortisone was responsible for these diurnal changes. Besides having an unusual diurnal urinary secretory rhythm, there is evidence of a constitutional tendency in migraine patients towards instability of their fluid balance mechanisms. (Campbell, *et al.*, see diagrams 1 and 2.)

It is usual to prescribe thyroid for diseases which have an underlying pathological disorder of its structure. In migraine where there is no demonstrable disorder of structure, it is being given to restore functional balance to the body metabolism. Some of the factors which together or by themselves can provide the conditions for a breakdown in the physiological harmony of the body in migraine have already been mentioned under " Clinical Observations ".

Only comparatively small doses of thyroid have been used in treating migraine so far, and it remains for future research to determine the possible role of hormones generally in the treatment of migraine. Besides the clinical improvement thyroid brings about in these patients, and the changes resulting from its use in the daily variation of their weight, there is the paradoxical finding that many migraine patients while on thyroid show an increase of weight. In table I, patient No. 2 increased her weight from 11 st. 8 lbs to

12 st. 2 lbs, and patient No. 5 from 8 st. to 8 st. 6 lbs, besides the case already mentioned. This can be taken to suggest that with this treatment there is a better balanced metabolism. Further no patient has shown an increase in blood pressure while on thyroid, and in many it has fallen together with a fall in their blood cholesterol levels.

The case already described under "Thyrotophic Hormone" would suggest that a lack of circulating thyroid hormone was due not so much to a functional disorder of the thyroid gland, as to a failure of thyroid stimulating hormone from the anterior pituitary, or even further back in the hypothalamic areas regulating pituitary secretion.

The average blood cholesterol levels in patients suffering from frequent severe attacks of migraine is higher than normal, which might be expected if there were to be a lack of circulating thyroid for a significant period of time. Those patients having relatively infrequent attacks have blood cholesterol levels within normal limits.

Harris (1955), working with animals, showed that the T.S.H. and A.C.T.H. response to stress depended on the nature of the stimulus acting through the hypothalamus, and also on the reciprocal inhibitory properties of those hormones. It is suggested as a hypothesis that migraine patients respond to long-continued or repeated stress stimuli with a preponderance of A.C.T.H. activity over T.S.H. in the prodromal stages of an attack, when there is fluid retention together with an increase of blood Na concentration with a lowering of blood K (see figure 1). With the onset of the migraine attack there is a sudden reversal of these trends, before normal balance is restored.

There is evidence that the hypothalamus is sensitive to various environmental factors. Sexual functions are inhibited by malnutrition, during which there appears to be less gonadotrophin released from the anterior pituitary. The breeding rhythms of many wild and domesticated animals depend on the amount of light reaching the retina, and also on the day to day increase or decrease of daylight according to the season of the year. Many migraine patients are very sensitive to glare and flicker. In fact some patients who are suffering from frequent severe attacks of migraine may be so sensitive that they cannot bear to look at heavily striped material. Driving at night too, on busy highways can impose a heavy strain on them. Liveing quotes many examples of glare precipitating migraine, and he also gives instances of such sensory stimuli as noise or smell setting off attacks.

As far as is known there is no seasonal incidence of migraine,

and the syndrome is found in both hot and temperate climates.

Summary and Conclusion

Patients subject to frequent attacks of migraine have a constitutional instability of their salt and water balances, with retention occurring in the prodromal phase, and a diuresis during and after the onset of the main symptoms. These changes do not in themselves account for migraine, but they serve as indicators of the state of flux in the background metabolism, which is part of the migraine syndrome.

Evidence has been given to show that small doses of thyroid can modify the diurnal weight changes in migraine, with clinical improvement in the majority of cases. Thyroid deficiency in migraine is functional and fleeting in nature, and not an organically based condition. There is reason to believe that it is due to failure of stimulation of the thyroid gland through the hypothalamic pituitary pathway following previous excessive or prolonged stimulation. It is suggested that the fluid and salt retention is due to release of the A.C.T.H. mechanism after temporary T.S.H. insufficiency, and that migraine occurs because of a functional neuro-endocrine failure in homeostasis.

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Epidemiological Jottings

Dr Michael Linnett contributes this "jotting" about chickenpox and shingles:

"D.W., then aged four, went to stay with his cousins between 21 February and 24 March 1959. During this time his grandmother developed shingles having visited a shingles case, although it is not certain whether this was the original source of infection. D. left his cousins to stay with his grandmother on the 14 March, and stayed there until 27 March. He returned home to Corfe Castle on 27 March and developed chickenpox some 8 to 9 days later—that is to say on 5 or 6 April. His father developed shingles on 21 April, and my small daughter happened to be staying with D. at the time and developed chickenpox on or about 19 April.

"It is of interest, concerning chickenpox in general, that only this week I have seen a family from the West Indies (British born) who came over to this country a few months ago; two weeks ago the boy returned home from school with two day old chickenpox, and over this last week the mother, two sisters and an uncle all developed chickenpox; the mother with such severity that it seemed that she was developing encephalitis and she had to be admitted to the fever hospital and was desperately ill with it. The diagnosis of encephalitis was confirmed clinically but she also had a pneumonitis, from both of which she is now recovering (16.8.61)."