This state of affairs continued for 17 days, during which time the dose of A.C.T.H. was gradually reduced from 40 mg. six-hourly to 15 mg. twice daily, as supplies were running out. Her temperature rose to 101° F. (38.3° C.) and she had a haemoptysis of 12 oz. (340 ml.). A fresh supply of A.C.T.H. was obtained and her condition improved, but the drug was running short by October 3, and was tailed off and discontinued on October 7. Three days later her temperature, which had been rising, reached 102° F. (38.9° C.); she had a haemoptysis of 16 oz. (450 ml.), and several smaller ones. Her condition became critical. Her pulse rate rose to 140 a minute, and her blood pressure fell from its normal level of 130/80 to 90/50. The bleeding from her lungs was stopped by two transfusions of 2 pints and 1 pint (1,140 and 570 ml.) of blood respectively, but she remained desperately ill.

The next day A.C.T.H. was again obtained and 30 mg. was given intramuscularly with a further pint (570 ml.) of fresh blood. Two hours later her general condition was better, her colour improved, and her pyrexia began to settle. The A.C.T.H. was continued in doses of 15 mg. six-hourly, and a week later, on October 19, her blood count showed the first sign of improvement; haemoglobin, 72%; red cells, 3,890,000; white cells, 3,000 (60% polymorphs); 60 nucleated red cells per c.mm.; platelets 10,000.

The figures of her blood count remained round about the same level and on November 6 A.C.T.H. was stopped. On this occasion after withdrawal of A.C.T.H. her temperature did not rise or her condition deteriorate and her blood count had remained substantially the same, although transfusions of 2 pints (1,140 ml.) were required every two to three weeks instead of weekly. Her bone marrow on November 9 appeared completely aplastic, but the drop in cells was mainly in the red-cell series, her white blood count being constant at 2,000–3,000 and her platelets 10,000–50,000 per c.mm. Her condition appeared to improve for a time, but remained precarious throughout. The haemorrhagic incidents became more frequent. She was admitted for a further transfusion, developed a cerebral haemorrhage, and died before any effect of a new supply of cortisone could take place. She died on December 28—that is, 139 days after the onset of her blood disorder.

Post-mortem examination revealed a pale and fatty bone marrow, the presence of petechial haemorrhages in most organs, and a cerebral haemorrhage on the right side. Bronchiectasis, fatty degeneration of the liver, and deposition of haemosiderin in the liver and spleen were found. No significant histological changes were present in the endocrine organs.

Discussion

It is the experience of several workers that marrow function usually returns spontaneously in about a week after discontinuing the offending drug (Hutt and Lee, 1953). We felt at first that both cortisone and A.C.T.H. were of no value in the management of this case, but, as the aplastic condition of her marrow persisted and she did not deteriorate clinically, we began to think that it might be having a life-saving effect. Coincidentally with the reduction in the dose of A.C.T.H. to an ineffective level she developed on two occasions a pyrexia and severe haemoptysis, and on the second was desperately ill. On both occasions when an effective dose of A.C.T.H. was restarted her general condition improved in a matter of hours.

We found no evidence that cortisone and A.C.T.H. had any effect in hastening recovery of normal marrow function. Sternal marrow puncture was not used throughout as a guide to the amount of regeneration, as daily blood counts showed no signs of recovery and the patient was having to endure many but inevitable needle pricks and discomforts. We felt, however, that we were giving cortisone and A.C.T.H. a proper trial, as they were not begun until 11 days after the onset of purpura and the discontinuation of carbimazole. We suggest that these drugs would have produced signs of regeneration of the marrow after a course lasting 72 days if they were capable of bringing about such an effect.

Summary

A fatal case of marrow aplasia secondary to carbimazole is reported. It is believed that this is the first recorded example due to this drug.

Cortisone and A.C.T.H. were given for 72 days, and on two occasions when the dose was reduced the patient immediately became extremely ill with pyrexia and haemoptysis. A third attempt at withdrawal of the drug was achieved without untoward effects, but only after the peripheral blood picture had shown some improvement over a period of 18 days.

It is believed that cortisone and A.C.T.H. kept this patient alive while they were being administered, but no evidence was found that either of them assisted in the regeneration of the marrow.

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PRURITUS AND ITS MANAGEMENT*

BY

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Pruritus implies the peculiar uncomfortable sensation of itching, which leads to the physical response of scratching but is not associated with any inflammatory changes of the skin. As with love, it is difficult to know where it is bred, in the skin or in the head; whether in the nerve endings or in the accelerated appreciation of the sensation. It may even originate in the cerebral cortex.

Whether one itches may depend on the degree of attention paid to somatic sensation. We know that if we are obliged to keep still at attention, within a few minutes an intolerable itch is likely to develop, often near one of the orifices.

Itching is very easily suggested. The sight of a head infested with crawling lice will induce in the novice a crawling itching feeling over the skin, which might even be localized to the same area.

The pleasurable element of itching is a matter of common experience. According to Jowett, Socrates dilates in his dialogues on the sensual pleasure of itching and scratching. The back scratcher of the Chinese, so finely carved in the shape of a hand or a claw, indicates the artistic appreciation of the instrument and equally the pleasure it gives when used.

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Allergic Reactions

The peripheral nerve endings are stimulated by the histamine-like and other substances (Feldberg, 1953) produced by allergic reactions. Itching also occurs as a manifestation of physical allergy to heat, cold, and friction. Allergy to roundworms and threadworms can occasionally lead to general itchiness as well as to anal and vulval pruritus. Allergies to foods may be responsible for a generalized or localized pruritus as a manifestation of a specific sensitivity. The itching over the face and elsewhere felt after the consumption of beverages is associated with reflex vasodilatation and may be cholinergic.

Pruritus is an early and valuable warning sign of allergy or of intolerance to many drugs—for example, to heavy metals, mepacrine. Other drugs, such as cocaine, owing to their cerebral action, may give rise to hallucinations of tiny living animals under the skin.

Diabetes and chronic renal insufficiency may present first as a pruritus. The fact that no instance of these diseases was noted in the series of 64 consecutive cases of pruritus (Table I) is no indication of the relative frequency of their occurrence, for the urinary findings lead the diabetic and nephritic patient to the general physician.

TABLE I.—Age Distribution of 64 Consecutive Cases of Generalized Pruritus Without Physical Signs, and the Significant Associations

Age	No. of Cases	Associations
0-19	2	Mother with anxiety state—overtreated .. 1 case Allergic, hay-fever, and asthma .. 1 "
20-39	15	Xerodermia (congenital) and cold .. 2 cases Xerodermia (congenital) .. 1 case Hodgkin's disease .. 1 " Pregnancy .. 3 cases Drug: atropine, codeine .. 1 case Cardiac insufficiency (severe mitral stenosis) 2 cases Obsessive .. 2 " Anxiety state .. 2 " Parasitophobia .. 1 case
40-59	13	Anaemia .. 1 case Cardiac insufficiency .. 2 cases Acquired xerodermia .. 1 case " ? thyroid insufficiency .. 1 " Anxiety .. 2 cases Depression—testicular atrophy .. 1 case Manic depressive .. 1 " Menopausal depression .. 1 " Parasitophobia .. 1 " Undetermined .. 2 cases
60-74	34	Anaemia .. 1 " Hypertension .. 3 cases Xerodermia (1 with anaemia, 1 with hypertension) .. 5 " Deficiency (gastrectomy) .. 1 case Cardiac insufficiency (right-sided) .. 1 " Cardiac insufficiency .. 3 cases Carcinoma—bronchus .. 1 case Reticulosarcoma .. 1 " Delusional .. 1 " Obsessional .. 10 cases Anxiety state .. 1 case

It will be noted in Table I that a congenital or acquired dry skin, a deficiency of iron, circulatory insufficiency, psychoneurotic or psychotic mental disorders, and malignancy occur in the age groups above 20 years.

The Deficiency Group

The nutritional disorders due to deficiencies of iron, vitamin A, vitamin-B₂ group, vitamin C, and other essential elements may lead to a loose hyperkeratosis, with a degree of atrophy causing discomfort, and an itching skin.

The associated diminution of sweat and sebum, with their emollient and plasticizing constituents, will also encourage the exposure of terminal nerve endings within the epidermis. Cold weather and friction of clothing will the more readily provoke the sensation of itching under these circumstances, and this also applies to the dry thin skin of old age (see Table II).

TABLE II.—Incidence of Dry Skin, Cardiac Insufficiency, and Hypertension

Age	No. of Cases	Dry Skin	Cardiac Insufficiency	Hypertension
20-39 ..	15	3	2	
40-59 ..	13	2	2	
60-74 ..	34	5	4	7

An example of this deficiency group was the case of a woman aged 43 with a three-years history of generalized itching and a haemoglobin of 45%. When the anaemia was successfully treated with iron and vitamin C her pruritus improved.

The menopause in both sexes may be associated with an itchy skin. In the female the itching and flushing occur together, and the itching is due either to alteration of the skin tension or to increased production of choline-like substances in the skin. The work of Grant *et al.* (1936) suggests that an undue sensitivity or reactivity to acetylcholine occurs in heat and exercise urticaria, and pruritus may be the first and only symptom of this sensitivity.

The alleviation of the itching by the administration of testosterone and/or oestrogen would, I believe, be more readily ascribed to a central effect, for the result of treatment is so rapid. However, testosterone is known to increase by as much as 50% the amount of oxygenated blood in the skin, and the effect of this on enzymic activity and nutrition of the skin is readily appreciated.

The skin may become anoxaemic as a result of circulatory insufficiency, and this may lead to pruritus.

Two examples of severe itching with much excoriation in young adults with well-developed mitral stenosis were observed, and cardiac insufficiency was seen in six other cases (see Table II).

A well-recognized but rare cause of pruritus is that associated with the reticuloses, particularly Hodgkin's disease. This simple itching in one patient aged 38 was present for a period of 16 months. She had a tiny gland above the clavicle which, when removed at a second attempt, showed the histology of Hodgkin's disease. It has been suggested that there is a sensitization to the malignant glandular tissue. Again, pruritus has been associated with carcinoma of the stomach and prostate. Cardon (1943) records the case of a man aged 89 with a generalized pruritus for three years. The haemoglobin was 43%. A large pyloric carcinoma was found; this was removed, with immediate relief of the itching.

A man of 65 years with generalized itching of three years' duration, not included in Table I, without change in the texture of the skin, was found to have rarified areas in the left scapula strongly suggestive of secondary carcinomatous deposits: biopsy of the scapula revealed an adenocarcinoma. Thus the possibility of a visceral cryptic carcinoma must be considered in a patient of mature age with pruritus, with or without any xerodermatous change in the skin.

The fibres transmitting the sensation of itching pass along the spinothalamic track and have cell stations in the thalamus. The character of itching, with its liability to spread, poor localization, and the production of tension, anger, and restlessness, is distinctive.

In reverse, mental fatigue, tension, and anxiety seem to be able to potentiate the cell station in the thalamus and to lower the threshold of sensation of itching, to encourage its intensity, and to facilitate its spread over the body.

Using histamine to excite itching by intracutaneous injection, Cormia (1952) was able to demonstrate that the threshold value was lowered in normal subjects towards the evening. It was also lowered by psychic trauma, and the itching then became more persistent. Reassurance restored the threshold value to normal.

Emotional Reaction

Thus with every pruritus, if at all sustained, there is an element of emotional reaction, and at the end of the scale are those cases of pruritus in which the emotional, psycho-neurotic, or psychotic status is the most important causative factor in the pruritus (see Table III).

TABLE III.—Incidence of Psychological Factors

Age	No. of Cases	Psychological Factors and Mental Disorders—i.e., Disorders of Reception and Interpretation
20-39	15	In 5 cases
40-59	13	" 6 "
60-74	34	" 12 "

One sign which is a guide to this group is the degree of excoriation that the patient presents. The deep biopsy scratch marks over the face, shoulders, and arms indicate the exaggerated psychological and physical response to the sensation of itching. The investigation of these cases has shown, besides the more common anxiety and tension states, patients with hysterical or obsessive personalities, with paranoia, delusions, or involutional depression. The hysterics use their dramatic ravelled skin to gain their unexpressed desire for comfort and relief from a situation which for them is an intolerable one, physically or emotionally.

One obsessive with severe pruritus was a man who had complained since joining the Army. In civilian life he had always worked hard, all day long. He was unable to do so while in the Army. A similar case was that of a man of 22 who excoriated his face to escape from nasty thoughts and compulsions.

Patients with acarophobia or parasitophobia will present excoriations on the skin, and are convinced that the rolled-up fragments of horn and epidermis which they bring for inspection are living animals which they have felt crawling under the skin and which are responsible for the itching.

A female schoolteacher aged 57, with a two-years history of itching which had begun on the chest and hands and had persisted around the hips, said that she saw flea-like bodies on her skin and thought that they came from the vagina. Other delusions and hallucinations may follow, when the prognosis, especially in the elderly case, is bad, and the patient may need institutional treatment.

If one is dealing with the hysteric and psychotic individual the treatment must be undertaken by a psychiatrist. On the other hand, most cases of psychogenic pruritus occur in those who are amenable to explanation by the practitioner or dermatologist and are capable of insight into the motivation of their disorder. Reassurance and a discussion of business or family worries is often all that is necessary in many cases of anxiety states and tensions. The family practitioner is well able to undertake this task and to offer suitable advice.

Treatment

Treatment with A.C.T.H. or cortisone is not advised for generalized pruritus without inflammatory changes in the skin. Occasionally, in the severe pruritus associated with the reticuloses, these hormones may be indicated and may be the sole means of controlling a most intractable itching.

The antihistamines are widely, perhaps too widely, applied locally to the skin and by mouth. An attempt to be logical in the use of the antihistamines to control generalized itching would include consideration of the aetiology of the pruritus. Thus, if associated with allergy of the mucous membranes to dust, animal hair, or pollen, then diphenhydramine hydrochloride would be valuable. It is recognized that the antihistamines are, in general, powerful sensitizers when applied to the skin and may rarely by mouth give rise to an urticaria or blood disorder—for example, leucopenia. In most cases, apart from serum sickness, the relief of itching is due, one suspects, to the powerful

anaesthetic, central depressant, and sedative effects of many of the antihistamines. They are unreliable therapeutic agents in the treatment of pruritus.

The use of sedatives is of value only in those cases of pruritus in which there is an important element of anxiety or tension. Small doses of barbiturate or chloral at night might then be helpful. To attempt to suppress itching by the use of sedatives, particularly in elderly patients, is likely to be a failure. Patients have been seen confused, drowsy, and incoherent, but scratching as vigorously as ever.

The principles of topical therapy are simple. When the skin is dry, hyperkeratotic, or atrophied it should be protected by a greasy application—for example, simple toilet lanolin over limited areas, or a mixture of wool alcohol, hard paraffin, soft paraffin, and liquid paraffin (unguentum alcoholum lanae, B.P.). When combined with water up to 50% it is more easily applied and more cooling. Another easily applied base contains emulsifying wax, soft white paraffin, and liquid paraffin (unguentum emulsificans, B.P.), to which varying amounts of water can be added to allow of easier spread.

The addition of small amounts of phenol $\frac{1}{4}\%$, menthol $\frac{1}{4}\%$, and of tar (liquor picis carbonis, 5 to 10%) may be indicated for short periods to satisfy a demand for active therapy in a patient with a prolonged distressing symptom. Bathing is restricted to avoid maceration and separation of horn, the alkaline irritant effect of soap, and the trauma of towelling. In the elderly, one bath a week is adequate, the emulsifying effect of the bran bag being relied on to cleanse the skin. The skin is partially dried by patting with smooth soft towels and then powdered.

When the texture of the skin is not abnormal the anti-pruritic agents mentioned above, incorporated in lotions or liniments for their cooling and decongestive effect, may give relief.

The underwear should be loose, of smooth cotton, and the bed warmed at night. Sheets should be smooth and a cradle ensures minimum contact with the body.

The diet should be a non-stimulating one. Tea and coffee are best taken cool and weak, and spices and meat extracts used with care.

Hypnosis

Finally, a word on the treatment of pruritus by suggestion while in the hypnotic state. There is no doubt that the symptom of itching in certain individuals can be kept in check by this method, and both in simple pruritus and in the pruritic dermatoses considerable relief has been obtained.

The best-known exponent of hypnotism (or in the use of animal magnetism, as he called it) was Mesmer, who, Gilbert Frankau (1948) recalls, was born in 1734, twelve years after the last witch was burnt at Leith. A century later Mesmer's activities were described as Satanic when the morality of the subjugation of one man's will to another's was discussed.

The dependence and relationship between the practitioner of hypnotism and his subject is one that can scarcely be described as healthy, particularly in a hysteric. However, there is no doubt that the method can be temporarily effective in pruritus associated with anxiety or tension states.

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The *Medical Journal of the South-West* is the new name of an old friend, the *Bristol Medico-Chirurgical Journal*, which first appeared in 1883. Under the National Health Service Bristol has become the focal point of the South-west Region, and it is considered that the new title will more accurately designate the field from which the *Journal* hopes to glean its sustenance.