Anaemia may increase considerably as oedema decreases and plasma proteins rise. In this way severe anaemia may be unmasked.

Megaloblastic change was present in two cases. In six others there were bone-marrow abnormalities consisting of giant metamyelocytes and scanty red-cell precursors of intermediate type. Two of these had satisfactory haematological responses to crude liver extract or to vitamin B₁₂.

The possible relationship of this anaemia to protein deficiency, liver disease, and nutritional megaloblastic anaemia is discussed.

I thank Dr. Pauline Klenerman for giving me full access to her cases of kwashiorkor in African children, Dr. N. A. Rossiter for facilities to study Indian children under his care, and Dr. J. Parker, medical superintendent, for permission to publish these cases. Thanks are also due to Dr. J. Thomas, Director of Pathological Services, and his staff for their help with the biochemical estimations; and to Dr. Joan Scragg and the sisters for their assistance.

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The Minister of Education has issued a circular (272, 1954) about the precautions necessary to avoid food poisoning in the preparation and service of meals in school canteens. One of the objects of the Food and Drugs Amendment Bill at present before Parliament is to secure better hygienic conditions in places where food is prepared or served. The prevention of the contamination of food served in canteens depends, however, in large measure on the constant vigilance and the observance of hygienic practices by the canteen staffs. The Minister emphasizes that the risks of food poisoning are present wherever meals are prepared and served, and that there is no reason whatever to think that school canteens are more exposed to them than other forms of corporate meals. After briefly describing some typical examples of outbreaks of food poisoning in school canteens, the circular goes on to consider the prevention of food poisoning in schools under the following headings: Co-operation between medical, teaching, and kitchen staff; health of food handlers; hygienic conditions in the kitchen; the preparation and cooking of food; domestic animals and pests; milk supply; and notification of outbreaks of food poisoning to the medical officer of health. Under the last heading it is recommended that authorities should take steps to ensure that any outbreak of food poisoning is notified immediately, preferably by telephone, to the borough or district medical officer of health, so that he can begin his investigations and take precautionary measures without delay.

ADRENOCORTICAL FUNCTION IN BURNED PATIENTS

WITH SPECIAL REFERENCE TO A.C.T.H. AND
ADRENALINE TESTS

BY

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This paper is concerned with the activity of the adrenal cortex of burned patients, and in particular with a search for evidence of adrenocortical failure arising during the illness. The investigation is based on the spontaneous changes in the blood eosinophil count in burned patients, on the changes in the circulating eosinophils induced by injection of pituitary adrenocorticotrophic hormone (A.C.T.H.) or adrenaline, and on other findings.

In a previous paper (Sevitt, 1951) it was shown that a definite pattern of changes affects the number of blood eosinophils after burning (Fig. 1). Within a few hours their number is found either to be falling or to have fallen to low or zero values. This eosinopenia, which is accompanied by a neutrophil leucocytosis and commonly by some lymphopenia, is maintained for a variable number of days, after which the count begins to rise, to reach a peak value within the next few days. Evidence was produced which indicates that the eosinopenia after burning is a sensitive reflection of adrenocortical hyperactivity. This pattern of changes has been confirmed by Evans and Butterfield (1951) and by Wight *et al.* (1953).

FIG. 1.—Serial blood eosinophil counts during the first week after burning in three patients. In one patient the falling of the count soon after burning is seen, and this is followed by a period of eosinopenia, which is present in all three. The eosinopenia lasted 1, 5, and 7 days respectively in the three patients and was followed by a rise in the count.

This pattern of changes has been confirmed by Evans and Butterfield (1951) and by Wight *et al.* (1953).

The period of eosinopenia during which eosinophils are few or absent in the blood stream is maintained for varying periods in different patients and is terminated by the post-eosinopenic rise (Fig. 1). The duration of the periods of eosinopenia was estimated in 35 patients with an accuracy within $\pm \frac{1}{2}$ day. In Fig. 2 these periods are plotted against the skin area burned, which is expressed as a percentage of the total skin area. In patients with burns covering less than 10% of the body area the periods of eosinopenia are only one or two days, but are longer, usually three to five days, in those more extensively burned. The relationship between the eosinopenic period and the percentage area seems to be an exponential zone with its concavity facing to the left, rising steeply between four and six days after burning.

Several points, however, fall away from the correlation zone. On clinical evidence it was concluded that in those patients with a more prolonged period of eosinopenia—for example, Case 22—the percentage area burned underestimated the degree and duration of shock and stress. On the other hand, a period of eosinopenia appreciably shorter than that “expected” from the area burned may be due to one of three causes. Firstly, stress after burning may be less than expected

FIG. 2.—Relationship of the percentage body area burned to the duration of eosinopenia in 35 patients (see text). † = died. The numerals are case numbers.

from the area burned, and this may be reflected in physiological abatement of adrenocortical activity (Case 27); secondly, the eosinophils may become resistant to the action of adrenal steroids; and, thirdly, adrenocortical failure may be suspected (Case 29, see below).

Eosinophil Changes in Those Fatally Burned

Eighteen patients were investigated, including the eight previously reported (Sevitt, 1951). Eleven died during the period of eosinopenia, including one who died four hours after burning whilst the eosinophil count was falling. It is concluded that these patients died with hyperactive adrenal cortices. Their ages varied from 1½ to 77 years (five were younger than 12 years, four older than 75 years), nine were females, and the extent of body areas burned ranged from 30% to 80% in the different patients.

In the other seven patients post-burn eosinopenia was not present at the time of death (see Table). In two of them (Cases 29 and 30) adrenocortical failure may have occurred.

In Case 29, which was reported previously, there was a zero eosinopenia for only 1½ days after burning, indicating

adrenocortical hyperactivity during this period. After this a sudden hyperpyrexia and a rapid deterioration of the patient took place. At the same time the eosinophils returned “prematurely” to the blood stream and the patient died a few hours later. Biochemical changes in the heart blood removed immediately after death were consistent with acute adrenocortical failure, but previous oliguria complicated the picture. Case 30 is discussed later.

In the remaining five patients (see Table) there was no evidence of adrenocortical failure. One patient (Case 28) died three hours after burning without a fall in the eosinophils, but eosinopenia may have occurred had he lived long enough. Two (Cases 32 and 36) died a few days after normal periods of post-burn eosinopenia, and these indicated that adrenocortical hyperactivity was present at least for the duration of the eosinopenia. In Cases 44 and 49 the normal A.C.T.H. or adrenaline tests five and seven days before death (15 and 10 days respectively after burning) indicated normal stimutable reserves of the adrenal cortex at the time of the tests.

Stimulation of the Adrenal Cortex by A.C.T.H. and Adrenaline

An injection of A.C.T.H. or cortisone in normal persons produces a significant fall in the blood eosinophil count, but in patients with Addison's disease cortisone, but not A.C.T.H., produces this effect (Thorn *et al.*, 1947; Dougherty and White, 1947; Forsham *et al.*, 1948; Hills *et al.*, 1948; Prunty, 1950). A.C.T.H. therefore does not act directly on the peripheral organs, but its action is mediated through an increased glyco-corticoid secretion from the adrenal cortex.

The secretion of A.C.T.H. by the anterior pituitary is under hypothalamic control probably via an endocrine secreted by the hypothalamus into the hypophyseal portal blood supply (de Groot and Harris, 1950; Hume and Wittenstein, 1950). Hume and Wittenstein also showed that this hypothalamic-adrenocorticotrophic activity can be produced by nervous stimuli from an injured area and that this activation occurs through the spinal cord. This is obviously of significance in burns.

Intravenous adrenaline produces an increase of adrenocortical activity (Vogt, 1944), but this does not occur in the hypophysectomized animal (Long and Fry, 1945). From this and other work we may conclude that a small dose of adrenaline has little or no direct effect on the adrenal cortex, although this is not necessarily true of large doses, and that adrenaline produces its major effect on the adrenal cortex indirectly through the pituitary gland (Harris, 1951). The site of action of adrenaline is uncertain. It may be the adeno-hypophysis itself (McDermott *et al.*, 1950), but, if not, it is above this level, possibly in the hypothalamus. In future discussion the site of action of adrenaline will be referred to as the hypothalamic-pituitary or supra-adrenal level.

Seven Patients in Whom the Post-burn Eosinopenia Was Not Present at the Time of Death

Case No.	Sex and Age (Years)	Surface Area Burned	Interval Between Burning and Death	*Eosinophils	A.C.T.H. and Adrenaline Tests	Conclusion
29	F 9	42%	1½ days	Post-burn zero eosinopenia rising to 11, 99, and 127 a few hours before death (“premature” rise)		Adrenocortical hyperactivity after burning, possibly followed by adrenocortical failure
30	F 5½	49%	15 „	Post-burn eosinopenia 4½ days. Antemortem eosinopenia	A.C.T.H. test on 5th day = rise of 26%	Adrenocortical hyperactivity after burning and before death, ? temporary period of adrenocortical failure
28	M 80	40%	3 hours	257, 276, 268, at 1½, 2, and 2½ hours		None
32	F 36	50%	9 days	Post-burn eosinopenia 4½ days		Hyperactive adrenal cortices a few days before death
36	F 38	45%	8 „	Post-burn eosinopenia 5 days		
44	M 9	25%	20 „		Normal adrenaline test 15th day.	Normal functional reserves of adrenal cortices at times of death
49	F 2½	30%	17 „		Normal A.C.T.H. tests 8th and 10th days	

* Hours and days refer to period since burning; other numerals are eosinophils per c.mm. of blood.

A.C.T.H. and Adrenaline Tests on Burned Patients

If a lesion is present in the adrenal glands—for example, bilateral destruction by haemorrhage—neither A.C.T.H. nor adrenaline will depress the eosinophil count.

If a recent lesion is present at the hypothalamic-pituitary level in a patient with intact adrenal glands, an injection of a small amount of adrenaline will have no effect on the adrenal cortex and the eosinophil count will not fall. On the other hand, injected A.C.T.H. will stimulate the adrenal cortex and the eosinophil count will fall. Failure of adrenaline to lower the eosinophil count could reflect a disturbance at the supra-adrenal level; conversely, if an adequate eosinopenia is produced by a small dose of adrenaline the hypothalamic-pituitary adrenocortical mechanism may be considered intact.

A.C.T.H. and adrenaline tests were therefore performed on burned patients. The 21 patients tested were among the more severely burned and were all "shock" cases transfused with plasma or dextran. Twenty had burns involving 20% or more of the body surface, eight 30% or more.

The other factors involved in the interpretation of results are considered later.

Techniques of the Tests

One or two eosinophil counts on capillary blood were made one to 30 minutes before the injection, after which the counts were repeated hourly for four to six hours. The eosinophil counts were plotted against time after injection and the maximum change in the count was expressed as a percentage of the pre-injection level: a fall was given a negative value—for example, -60% —and a rise a positive value—for example, $+15\%$.

The B.P. solution of adrenaline, 1 in 1,000, was used and 0.3 ml. (≈ 0.3 mg.) was injected subcutaneously or intramuscularly.

The A.C.T.H. used (batch numbers J 16205, 27111, 27511, and 28112) was first shown to have the expected eosinopenic activity in normal adults and children. In five of the nine children tested the amount injected was 10 to 12.5 mg., in the remainder of the 14 patients tested 20 to 25 mg. was used.

It was not possible to standardize strictly the times of injection, but in two-thirds of the tests the drug was injected between 10 and 11 a.m., and in most of the remainder before 1 p.m. Abnormal results were repeated when possible.

Eosinophil counts were made by the direct "wet-field" method of Dunger (1910), using the eosin-acetone-water diluting fluid. The blood was diluted 1 in 20 in two pipettes and the cells in 0.65 c.mm. were enumerated in four Fuchs-Rosenthal fields.

Normal Eosinophil Response to A.C.T.H.

In normal people the blood eosinophils fall within an hour or so of injection and continue to fall during the next two to four hours, reaching their minimum level about three to five (usually four) hours after the injection (Fig. 3). Forsham *et al.* (1948), Prunty (1949), and others have shown that an injection of 25 mg. of A.C.T.H. produces an eosinophil depression of 50% or more, usually 60 to 90% four hours after injection, and this has been our experience.

Care was taken in interpreting results because it was thought that the blood level of eosinophils after the injection of A.C.T.H. or adrenaline could be influenced by factors unrelated to the injection. The first of these is the pre-injection level of the eosinophil count. If this is already low, adrenocortical hyperactivity may already be present, little or no additional activity may be produced by the injection, and a significant eosinopenia may not occur. Secondly, since some of the tests were performed during the post-eosinopenic rise of the eosinophil count, this spontaneous elevating effect might have antagonized the eosino-

phil-depressing effect of A.C.T.H. or adrenaline. Thirdly, in the diurnal variation of the blood eosinophils there is a morning fall in the count up to about 12 noon, after which the count rises. Therefore, in interpreting the present results, not only the maximum percentage fall in the count and the shape of the curve were considered, but also the possible influence of the above factors.

Normal results were obtained in 12 of the 14 tests with A.C.T.H., the eosinophils falling by 60% to 87% in 11 of them (Fig. 4), and in the twelfth a nearly normal fall of 46% was found. This is not considered significant, as four days later the response to adrenaline was normal. In all but three of the patients the tests were performed 10 days or less from the time of burning and one to five days from the end of the eosinopenic period—that is, during or soon after the post-eosinopenic rise.

Therefore, in these 12 patients, including one who died a week later, there was no evidence of adrenocortical failure of adrenal gland origin. Three of them, however, showed abnormal eosinophil reactions to adrenaline (see below).

FIG. 3.—Blood eosinophil responses following injections of A.C.T.H. and adrenaline in normal persons. Note that the eosinopenic response to 25 mg. of A.C.T.H. is quicker and more prolonged than that following the injection of 0.3 mg. of adrenaline.

FIG. 4.—Normal A.C.T.H. and adrenaline tests in severely burned patients. Each point is the result of one test. It is represented by a numeral which is the pre-injection value of the blood eosinophil count per c.mm. Its vertical position expresses the maximum percentage lowering of the count. The interrupted horizontal lines at -50% for A.C.T.H. and -40% for adrenaline represent the upper limits considered to be normal. The dotted vertical lines join the results of two or more tests on one patient. Fourteen of the A.C.T.H. tests were normal. These were done on 12 patients, one of whom subsequently died. Eleven of the adrenaline tests were normal, and these were done on nine patients, one of whom subsequently died. + = died.

Normal Eosinophil Response to Adrenaline

In normal people the shape of the eosinophil curve following adrenaline (Fig. 3) differs from the response to A.C.T.H. Usually little or no fall in the eosinophil count is found at an hour after injection; thereafter the count falls to reach its lowest level at two to three hours, and at four hours the count may be rising again. The adrenaline effect is usually slower and shorter than the effect of A.C.T.H. The maximum fall in the count varies between 45% and 70%.

Here it will be assumed that a lowering of the blood eosinophil count to 40% or more of the pre-injection level is normal, provided that the shape of the curve is within normal limits.

Normal curves were found in 9 patients (11 tests: Fig. 4) of the 12 patients tested, with maximum eosinophil depressions ranging from 47 to 70% (average 61%). Eight were tested within 15 days of burning, one of whom died from duodenal obstruction 20 days after burning and five days after the adrenaline test. Subsequent tests on one patient were also normal, as were the responses to A.C.T.H. in two others. Therefore, in these nine patients there was no evidence of adrenocortical failure. Indeed, the results indicated a normal function of the supra-adrenal adrenocortical pathway.

Abnormal Response to A.C.T.H.

Two of the 12 patients tested responded abnormally and one subsequently died.

Case 30

A girl of 5½ years, having burns involving 49% of the body area, was admitted shocked and with haemoconcentrations six hours after burning. She received 6 litres of intravenous plasma and 300 ml. of blood. Attacks of hyperpyrexia occurred on the first and ninth days after burning and slight jaundice on the fourth day. Her burns became colonized with *Ps. pyocyanea*.

Eosinopenia was present on admission and lasted just over four days, indicating hyperactivity of the adrenal cortex during this period. On the fifth day, during the post-eosinopenic rise of the eosinophil count, 12.5 mg. of A.C.T.H. was injected, but the eosinophil count never fell. Instead it rose from 108 per c.mm. before injection to a maximum level of 135 (+26%) at four hours after the injection (Fig. 5). Her blood pressure was normal (120/80) and normal blood glucose values (120 to 140 mg. per 100 ml.) were found. She became anaemic and was transfused. Her condition worsened, eosinopenia reappeared on the ninth day (eosinophils 12 per c.mm.), and was maintained until her death 15 days after burning, zero values being found during the last three days.

FIG. 5.—Case 30. Abnormal blood eosinophil reaction to an injection of 12.5 mg. of A.C.T.H. The eosinophil count does not fall after the injection, suggesting that adrenocortical failure is present.

At necropsy, purulent bronchitis was found. The adrenals were swollen and congested; histologically very little cortical lipid remained and small foci of haemorrhage were present. Such changes are common in fatally burned patients, particularly in children who die during the period of eosinopenia, and are largely due to intense adrenocortical hyperactivity (unpublished observations). However, many of the columns of the zona fasciculata were transformed into pseudo-acinous or pseudo-tubular structures by an aluminous exudate containing occasional polymorphs. These changes were noted by Rich (1944) in diphtheria and in meningococcal and other infections, and he suggested that they may explain the circulatory collapse. The lymph nodes of the lymph glands, tonsils, and the spleen showed central degenerative changes with oedema, cytoplasmic swelling, and rupture. These changes, which are commonly found after burning (Bardeen, 1898; Baker, 1945), also occur after the injection of A.C.T.H. and are probably due to adrenocortical steroids.

The abnormal response to the A.C.T.H. test during life and the pseudo-acinous degeneration of the adrenal cortex found at necropsy support a diagnosis of adrenocortical failure. However, the reappearance of eosinopenia on the ninth day after burning and the degeneration of lymphoid tissue found at necropsy do not support this view. If adrenocortical failure occurred it was a temporary phenomenon.

Case 52

A 6-year-old girl with burns involving 45% of her body was admitted shocked and with haemoconcentration one and a half hours after burning. She was transfused with dextran, plasma, and blood. Eosinopenia was found, and lasted three and a half days, indicating early adrenocortical hyperactivity. On the fifth day after burning, at the peak of the post-eosinopenic increase of eosinophils, 20 mg. of A.C.T.H. was injected. An unusual curve was obtained: the eosinophils did not fall from the pre-injection level of 287 per c.mm. for two and a half hours after the injection; at three and a half hours the count was falling sharply to a maximum depression of 49% at four hours, but at five hours the eosinophils had increased to more than their pre-injection level. Three days later the test was repeated, and this time the count rose hourly for five hours from the pre-injection level of 152 per c.mm. On the following (ninth) day a test showed a curve of nearly normal shape though the maximum fall was only 39%, but on the sixteenth day a normal curve was found (-73%). Biochemical investigations on the eighth and ninth days gave normal values for blood glucose (120 mg. per 100 ml.) and serum chloride (595 mg. per 100 ml.), but the serum sodium (285 mg. per 100 ml.) and the serum potassium (15.1 mg. per 100 ml.) were slightly low. On the seventeenth day the child excreted 1.2 mg. of 17-ketosteroids in the urine, probably normal for her age (King, 1951).

Clinically the child was never very seriously ill and she made a good recovery. If the abnormal eosinophil responses to A.C.T.H. on the fifth and eighth days indicate adrenocortical failure, then this was of short duration and of no clinical significance. On the other hand, the four A.C.T.H. injections may have excited a therapeutic effect.

Abnormal Responses to Adrenaline

Results of tests were abnormal in three patients, each of whom responded normally to A.C.T.H. Two were children in whom the abnormal responses were associated with a temporary abnormal mental state. When the children recovered mentally the adrenaline responses were found to be normal.

Case 31

A girl of 8 years with burns involving 47% of the body surface was admitted shocked and with haemoconcentration two hours after burning. Her transfusion with 6.2 litres of plasma and 1 litre of blood was probably excessive, as a temporary attack of pulmonary oedema occurred soon after. She became pyrexial—100–102° F. (37.8–38.9° C.). Meanwhile post-burn eosinopenia was found, and lasted 4.7 days. Her mental state and behaviour at this time became abnormal. She was confused, irritable, and querulous. Six days after burning, at the peak of the post-eosinopenic rise of the eosinophils, adrenaline failed to lower the eosinophil count significantly (-12%) (Fig. 6). This was confirmed two days later (-4%), and again on the 38th day after burning (-11%), although on the 15th day an A.C.T.H. injection produced a normal eosinophil response. Gradually,

FIG. 6.—Case 31. Abnormal blood eosinophil responses to adrenaline occurred on the 6th, 8th, and 38th days after burning, when little or no change in the eosinophil counts followed the injections. However, the response to the A.C.T.H. test on the 15th day was normal. During this time the child was mentally abnormal. An adrenaline test was normal on the 94th day, when the child's mental condition had returned to normal.

with careful nursing and feeding, blood transfusion, and successful skin cover by grafting, the child improved. Three months after burning, when she had once again become a likeable, normal, and intelligent child, an injection of adrenaline produced a normal eosinophil-depression curve (-45%).

Case 43

A girl of 9 years with burns involving 33% of the body area was admitted one and a half hours after burning, shocked and with haemoconcentration. She was transfused with 6 litres of plasma in the first 24 hours: a short-lived oliguria and oedema of unburned areas occurred.

FIG. 7.—Case 43. An abnormal blood eosinophil response to adrenaline ($+6\%$) occurred on the 8th day after burning, although the A.C.T.H. test was normal two days before. During this time the child was mentally abnormal. On the 14th day her mental condition was improving and a "borderline" normal result of -40% was found after adrenaline. Four months after burning, when she was again mentally normal, the eosinophil depression curve to adrenaline was normal (-77%).

The third patient with an abnormal response to adrenaline was a man in whom the A.C.T.H. response was normal. Clinically there were no unusual features, and it was not found possible to repeat the test.

Discussion

In a previous paper it was concluded that adrenocortical hyperactivity always occurs after significant burning (Sevitt, 1951). This was confirmed and extended in the present study, the main aim of which was to determine whether physiological failure of the adrenal cortex occurs in some patients. This was considered important, since "replacement" therapy with A.C.T.H. or cortisone may be indicated.

In 5 of the 54 patients studied there was evidence suggestive of adrenocortical failure. In one patient the evidence was based largely on a "premature" return of the blood eosinophils after a relatively short post-burn eosinopenia associated with clinical deterioration and, soon after, the death of the patient. In the absence of a post-mortem examination the evidence could not be conclusive. In two patients the eosinophil responses to A.C.T.H. were abnormal. One of them was not unduly ill, and the initial abnormal reactions to A.C.T.H. found within 10 days of burning were succeeded by a normal test a week later. In the other patient the abnormal reaction to A.C.T.H. and the pseudo-acinous change in the adrenal cortex found at necropsy support a diagnosis of adrenocortical failure, but the development of an ante-mortem eosinopenia and the finding of degenerative changes in the lymphoid tissue at necropsy indicate that the patient died with hyperactive adrenal cortices. If adrenocortical failure occurred in these two patients it was no more than a temporary phenomenon.

Nevertheless, two of these three patients died. The prognosis of severely burned patients with a tentative diagnosis of adrenocortical failure, based either on a premature rise

in the eosinophil count or on an abnormal eosinophil response to A.C.T.H., may be very serious. Therefore, in spite of the uncertainty whether or not adrenocortical failure occurred or was of clinical significance, it is suggested that such patients should be treated with cortisone as soon as the tentative evidence of adrenocortical failure is obtained.

Two children showed abnormal eosinophil reactions to adrenaline, associated with disturbed mental states: the reactions became normal when the mental conditions of the patients were either improving or had returned to normal. This association may be more than a coincidence. The cerebral changes may have involved not only the higher centres to produce mental disturbance but the lower centres, including the hypothalamic area or its central connexions, and so have interfered with the site of action of adrenaline. With recovery of the brain, adrenaline would again become eosinopenic. On the other hand, adrenaline tests performed on a child with a "true" encephalitis developing during the burn illness gave a normal result. Treatment with A.C.T.H. may be indicated in these patients.

Summary

A study of adrenocortical activity was made in 54 burned patients. It was largely based on the spontaneous changes in the eosinophil count found after burning, and, in 21 of the patients, upon the changes induced by a test dose of A.C.T.H. or adrenaline.

It is concluded that adrenocortical hyperactivity always occurs after significant burning. In 49 out of the 54 patients there was no evidence of subsequent adrenocortical failure, and these included 16 of the 18 patients who died.

In five patients, two of whom died, there was evidence of adrenocortical failure. In one a "premature" rise in the eosinophil count after burning was associated with clinical deterioration, and death soon occurred.

Twelve of the 14 patients tested with A.C.T.H. gave normal eosinophil depression curves, indicating normal stimutable reserves of the adrenal cortex. However, eosinopenia was not induced in a young girl tested on the fifth day after burning, suggesting that adrenocortical failure was present; but the spontaneous eosinopenia developing a few days later indicated that, if failure had occurred earlier, it was of short duration. She died 15 days after burning. In another child, not unduly ill, several abnormal reactions to A.C.T.H. were found within 10 days of burning, but on the sixteenth day the test was normal. She survived.

In nine out of twelve patients tested with adrenaline, normal eosinophil depression curves were obtained. The abnormal results found in two children indicated adrenocortical failure at the hypothalamic-pituitary level, since the A.C.T.H. tests were normal. The children were confused and irrational at the times of the abnormal reactions, but later, when normal adrenaline reactions were found, mental recovery had taken or was taking place. It is suggested that both the mental disturbance after burning and the persistence of circulating eosinophils after adrenaline were due to similar changes affecting the cerebral cortex and hypothalamus respectively.

I am in part-time employment of the Medical Research Council. The A.C.T.H. was made by Armour Laboratories and was obtained through the courtesy of the allocation committee of the Medical Research Council. Thanks are due to Messrs. R. Gill and C. Richardson, of the photographic department of the hospital, for photographing the figures, to various members of the

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THE ACHLORHYDRIC PATIENT WITH DYSPEPSIA

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Among those patients who are referred to hospital with a complaint of dyspepsia there remain after routine investigation an appreciable number in whom no satisfactory diagnosis is reached despite the fact that they give the impression of having organic disease. Such cases are usually labelled functional or nervous dyspepsia, or, if there is no free hydrochloric acid secreted in response to a test meal, achlorhydric dyspepsia. Gastroscopic examination will provide a satisfactory explanation of the symptoms in a large proportion of cases. Not only may small ulcers and ulcer scars which have been missed at a barium meal x-ray examination be discovered by this means, but it is also the most satisfactory method of confirming the presence of and differentiating gastritis. Where gastritis is found it is, however, impossible to give a reliable prognosis regarding the future comfort of the patient or to assess the possibilities of complications such as bleeding, ulceration, or the development of gastric carcinoma. As many patients have gastric changes without dyspepsia it is also impossible to be dogmatic on how much the patients' symptoms are attributable to the gastric condition.

Schindler (1947) has given a good working classification of chronic gastritis. He divides cases into four types—hypertrophic, superficial, and atrophic gastritis, and gastritis in the post-operative stomach.

Chronic hypertrophic gastritis seems to be a very rare condition in this country and is not to be confused with the simple hypertrophy with thick folds and prominent areae gastricae which is a normal variant and is the usual finding in patients with hyperchlorhydria and duodenal ulcer. In hypertrophic gastritis intra-

mucosal scarring has led to unevenness of the mucosal pattern, and there may even be pseudo-polypoid changes.

In chronic superficial gastritis there is uneven congestion of the mucosa and excess adherent mucus. Simple diffuse reddening of the mucosa is a physiological state, whereas a stippled or variegated appearance is pathological. Non-adherent mucus is a normal exudate and mucopus is usually swallowed sputum.

The atrophic group is characterized by thinning of the gastric folds, inability to distinguish the areae gastricae, and, when atrophy is marked, by the ability to see the intramucosal and submucosal vessels through the thinned mucosa (Fig. 1). There is often an element of inflammation, shown by congestion along the tips of the folds and by stippling of the mucosa. The appearance of gastric atrophy may be generalized or patchy, and a localized variety is not infrequently seen in the vicinity of ulcer scars. This latter is in reality a new thin mucosa or a stretched mucosa around a scar (Fig. 2).

FIG. 1.—Gastroscopic view of atrophic gastritis, showing visible submucosal vessels.

FIG. 2.—Gastroscopic view, showing atrophic gastritis with vessels more prominent in the vicinity of a healed gastric ulcer. Either a true adenoma is present or there is pseudo-polypoid change as a result of scarring. The folds towards the greater curve are normal.

Present Investigation

The case summaries of all patients attending the Gastroenterological Clinic, St. James's Hospital, London, during the years 1940–6 inclusive have been studied. Where a finding of achlorhydria on a first fractional test meal using gruel as the stimulant was recorded and where some address for the patient was given, the case reports have been abstracted. Certain groups have been followed up during 1952, giving minimum and maximum observation periods of five and twelve years.

These patients are almost without exception those with gastro-intestinal symptoms. It is well known that the