TABLE III.—Radiological Evaluation of Result of Treatment in Experimental and Control Groups. Comparison of X-ray Pictures of Stomach and Duodenum Taken Immediately Before Treatment, After Two and Four Weeks of Treatment, and Again Two Weeks After Cessation of Treatment

	Experimental Group (82 Patients)	Control Group (70 Patients)
Unchanged	36 (44%)	30 (43%)
Improved	28 (34%)	27 (39%)
Aggravated	5 (6%)	3 (4%)
Questionable	13 (16%)	10 (14%)

X-ray Examination.—The evaluation of the results of the treatment from a radiological point of view is based on examinations immediately before treatment, after two and four weeks of treatment, and again two weeks after discontinuation of treatment. Only obvious differences have been taken into consideration, especially diminution of niche and marked change in the deformation of the duodenal bulb or the pyloric canal. In cases of major haemorrhage the ulcer could not always be demonstrated, and thus the x-ray pictures from such patients could not contribute to the evaluation of the treatment. Table III shows the results of the x-ray examination. Also, no difference could be demonstrated radiologically between the experimental and the control group.

Summary and Conclusions

Eighty-two randomly chosen patients with gastric or duodenal ulcer have been treated with "anti-gizzard ulcer factors" (ether extract of calf's brain plus vitamin B₁₂). Seventy similarly chosen control patients were subjected to the same regimen with placebos substituted for "anti-gizzard ulcer factors." After a preliminary short follow-up period the results of the treatment were evaluated. Diminished pain and bleeding and comparison of repeated x-ray examinations were used as criteria. The experimental and the control groups did not differ at all in their response to treatment. "Anti-gizzard ulcer factors" were thus of no value in the treatment of gastric and duodenal ulcer in man.

Thanks are due to A/S Orthana Kemisk Fabrik, Copenhagen, for generous assistance in preparing and furnishing the preparations used in this study.

REFERENCES

- Cheney, G. (1938). *Amer. J. digest. Dis.*, 5, 104.
 — (1940). *Proc. Soc. exp. Biol. (N.Y.)*, 45, 190.
 — (1942). *Arch. intern. Med.*, 70, 532.
 Dam, H. (1934). *Nature (Lond.)*, 133, 909.
 — (1946). *Acta physiol. scand.*, 12, 189.
 — (1951). *Ann. Rev. Biochem.*, 20, 289.
 — (1954). *British Medical Journal*, 1, 1036.
 Noer, B., and Søndergaard, E. (1950). *Acta physiol. scand.*, 21, 315.
 — and Schönheyder, F. (1934). *Biochem. J.*, 28, 1355.
 — and Segal, H. L. (1945). *Acta physiol. scand.*, 10, 295.

The Atomic Energy Authority has lent to the Science Museum at South Kensington a large working model of the "B.E.P.O." atomic pile, the larger of the two pioneer piles set up at Harwell. This pile went into operation in July, 1948. It is used for research purposes, and for "cooking" radioactive isotopes for use in medical research and treatment, in agricultural research, and in industry. The model goes through a complete cycle of operations in five minutes, and shows the working of the control and shut-down rods which govern the heat output of the pile, and the movement of the hoist for loading uranium rods into the pile. The uranium rods are the pile's fuel, and during its operation some of the uranium is "burnt up," and the rods become contaminated by the products of combustion. The rods then have to be removed and processed to remove the fission products.

ERYTHRODERMIA WITH LIPOMELANIC RETICULUM-CELL HYPERPLASIA OF LYMPH NODES

(DERMATOPATHIC LYMPHADENITIS)

BY

R. C. NAIRN, M.D., Ph.D.

Senior Lecturer in the Department of Pathology, University
of Aberdeen

AND

T. E. ANDERSON, M.D.

Dermatologist, North-eastern Regional Hospital Board,
Scotland

The association of an unusual type of hyperplasia of the superficial lymph nodes with certain pruritic skin disorders, first fully discussed by Pautrier and Woringer (1937), has been amply confirmed by subsequent authors (Hurwitt, 1942; Soloff, 1942; Laipply, 1948; Obermayer and Fox, 1949; Laipply and White, 1951; Jarrett and Kellett, 1951; Wilson, 1954). There is substantial agreement that the lymph-node change is merely reactive, though there is some doubt whether the condition always remains benign: occasionally it has been found in association with leukaemia (Laipply and White, 1951) or mycosis fungoides (Bluefarb and Webster, 1950).

This syndrome is not a rarity, but its significance is still not generally recognized. The present paper is a clinico-pathological account of 13 further cases, with follow-up of from one to four years, and reaffirms the essentially benign reactive nature of the condition.

The following case reports have been classified in four groups according to the clinical diagnosis.

(a) Generalized Exfoliative Erythrodermia

Case 1.—Female, aged 74 on admission, November, 1951. The eruption had been present for a few months and there was a generalized lymphadenopathy of moderate degree. She gave a history of a previous attack in 1947 which developed at the beginning of a course of gold injections for arthritis. Psychogenic factors were marked. Biopsy of a lymph node from the groin showed pronounced reticulum-cell proliferation to form large pale-staining sheets, though the general architecture of the rest of the gland was well preserved. Eosinophils were numerous; abundant melanin, almost entirely intracellular, was scattered throughout the medulla. There was no lipoid or iron pigment. After a short course of A.C.T.H. the skin condition almost settled and the lymphadenopathy subsided. She was discharged in February, 1952, and her own doctor reports that the skin gave no further trouble. The patient died in the summer of 1952 of perforated appendicitis, peritonitis, and carcinoma of the ovary. At necropsy the skin was healed and there was no residual lymphadenopathy or evidence of reticulo-endothelial disease elsewhere.

Case 2.—Male, aged 51 on admission, August, 1952. The eruption, present for 11 months, had begun with pruritus and erythrodermia of the head and neck with rapid generalization. Exfoliation, beginning two months later, was associated with generalized alopecia. Psychogenic factors, profuse sweating, and a burning sensation in the skin were notable features. On admission there was moderate lymphadenopathy and the liver was enlarged 2 cm. below the costal margin. The peripheral blood picture was normal though the sternal marrow was very cellular (10% plasma cells). Biopsy of the skin showed a moderate infiltration of the

superficial dermis by lymphocytes, reticulum cells, neutrophils, eosinophils, and plasma cells. In the lymph nodes there was the characteristic reticulum-cell hyperplasia and infiltration by eosinophils and plasma cells, with deposition of melanin pigment and very little fat; iron pigment was present in small amount. Liver biopsy revealed slight fatty change and the presence of a few eosinophils and plasma cells in the portal tracts. The patient was in hospital for more than a year, during which time he developed polyradicular neuritis and thrombophlebitis of the legs and, later, superficial necrotic changes in the tips of his fingers. The response to general and local measures was slow; most benefit was obtained from A.C.T.H. He was discharged in September, 1953, with his skin condition settled apart from some excoriations of the legs. When seen in December, 1954, the skin condition had remained quiet and the lymphadenopathy had subsided. Biopsy of a node at this time showed no sign of the dermatopathic reaction.

Case 3.—Female, aged 68 on admission, August, 1952. The eruption had been present for five weeks and there was a history of a previous attack in 1942. Her skin showed patchy thickening in addition to the exfoliative erythrodermia and there was marked lymphadenopathy, especially in the epitrochlear nodes. Pruritus was intense and the psychogenic element was very marked. In October, 1952, a vesicobullous phase developed, followed by a thickened and deeply pigmented eruption over the whole integument except the face and the anterior aspect of the trunk. The liver was enlarged 2 cm. below the costal margin though liver-function tests were normal. There was persistent eosinophilia (15–23%) in the peripheral blood. Biopsy of the skin showed a moderate, largely round-celled though slightly pleomorphic infiltrate of the superficial dermis. A lymph node showed reticulum-cell hyperplasia, and slight eosinophil and plasma-cell infiltration. There was abundant melanin but no fat or iron pigment. In May, 1953, she was discharged with the skin condition quiet, though patchy pigmentation was present. This state of affairs persisted, apart from minor localized recurrences associated with emotional upsets, until October, when, according to her own doctor, she became markedly depressed and her skin condition relapsed. She developed oedema of the face, dyspnoea, and ultimately generalized oedema with stupor, and died in November, 1953, with pulmonary oedema. Permission for necropsy was not obtained.

Case 4.—Male, aged 76 on admission, December, 1952. An intensely pruritic exfoliative erythrodermia associated with marked lymphadenopathy had been present for six weeks. Eight per cent. of eosinophils was found in the peripheral blood, and the sternal marrow was normal. Biopsy of the skin showed mild parakeratosis, blurring of the stratum granulosum, and patchy atrophy of the stratum spinosum. There was an abundant, slightly pleomorphic, mononuclear infiltrate in the superficial dermis and a few foci of similar cells were seen near the vessels and glands. The usual reticulum-cell hyperplasia with a notable amount of lipid was found in a superficial lymph node. Melanin was scanty and iron pigment was absent. The skin condition settled slowly and the patient was discharged in June, 1953. He was still clear in December, 1954.

Case 5.—Female, aged 57 on admission, February, 1952. Exfoliative erythrodermia with marked pigmentation, pruritus, and superficial lymphadenopathy had been present for three weeks. Emotional and vasomotor lability was pronounced. The peripheral blood showed mild leucocytosis with eosinophilia up to 33%. The skin condition settled and she was discharged in June, 1952, but further emotional upset precipitated a relapse. She was readmitted in February, 1953, by which time her liver was palpably enlarged. Biopsy of the skin showed the histological features of erythrodermia. The characteristic reticulum-cell reaction and lipid and melanin deposits were found in a superficial lymph node, but there was no iron pigment. A liver biopsy showed many eosinophils in the vascular spaces and a few amongst the cells of the portal tracts; otherwise

there was no abnormality. Her condition improved and she was discharged in March, 1953, since when the erythrodermia has fluctuated; there was a further exfoliative attack in November, 1953. In November, 1954, apart from minimal changes, the skin condition had been inactive for eight months, although some lymphadenopathy had persisted. There was, however, no sign of the reticulum-cell reaction and no melanin in a lymph node taken at this time, though lipid was abundant.

Case 6.—Male, aged 50 on admission, November, 1950. Exfoliative erythrodermia, present for three months, settled with routine treatment in January, 1951. It was subsequently aggravated by contact irritants, and he was readmitted in July with widespread pruritic erythrodermia and axillary and inguinal lymphadenopathy. Eosinophilia was found in the peripheral blood and sternal marrow. The pruritus subsided and the erythrodermia cleared completely by August, 1951, when he was discharged. During the next three years there was only intermittent minor papulation of the face, neck, and flexures of the elbows, except for a slight relapse in January, 1954. Biopsy of the skin and superficial lymph nodes was carried out on three separate occasions during the observation period. In the skin there was a somewhat pleomorphic dermal cellular infiltrate; eosinophils were present in appreciable numbers. The lymph nodes all showed the characteristic reticulum-cell reaction; the amount of melanin was variable. A liver biopsy was normal. In November, 1954, papulation and enlargement of lymph nodes were minimal; biopsy of a node showed no sign of the dermatopathic reaction.

(b) Exfoliative Psoriasis

Case 7.—Female, aged 37 on admission, April, 1952. Psoriasis, present since 1939, had fluctuated in severity until March, 1952, when there was a severe flare-up during treatment. On admission she had extensive psoriasis of the scalp with scattered plaques over the trunk and extremities. Her right ankle was painful and swollen, though there was no radiological evidence of bony change. Slight pyrexia was present and the E.S.R. was 75 mm. in 1 hour (Westergren). "H.P.C." (3-hydroxy-2-phenylcinchoninic acid) therapy was followed by reduction of the ankle swelling, but it caused a vesicular skin reaction, which settled on withdrawal of the drug; the arthropathy then reappeared, this time in the right knee and left wrist. Another course of H.P.C. was tried, but further skin reaction necessitated its gradual replacement by cortisone. In June, 1952, despite the cortisone therapy, joint pains and stiffness increased, especially in the spine. The cortisone was stopped and A.C.T.H. tried instead, but the skin condition deteriorated to a generalized exfoliative erythrodermia accompanied by oedema of the eyelids and ankles. There was no conspicuous enlargement of the superficial lymph nodes. Stiffness gradually extended to most joints, and periarticular swelling and some osteoporosis developed. Further treatment by cortisone and also by mepacrine was ineffective. In October, 1952, the erythrodermia showed no improvement. Biopsy of a superficial lymph node showed sheets of reticulum cells and abundant melanin; lipid and iron pigment were absent. The patient's condition deteriorated and there was increasing pyrexia associated with cough and purulent sputum; enlargement of the liver was now detected. Later in the month she complained of chest pain, and within half an hour became comatose and died. Clinical pathological findings during her illness were not informative until the day before her death, when she was found to have complete agranulocytosis (total leucocyte count, 1,200 per c.mm.); one month before her death her leucocyte count had been normal. At necropsy the findings were those of an acute aleukaemic monocytic leukaemia and exfoliative arthropathic psoriasis.

Case 8.—Female, aged 61 on admission, October, 1952. Psoriasis had been generalized at the age of 16, but subsequently only a few chronic patches had been present until June, 1952, when she developed a generalized exfoliative

attack with intense pruritus. Lymphadenopathy was confined to the inguinal nodes. Biopsy of the skin showed the usual features of psoriasis with an occasional eosinophil in the dermal infiltrate. In an inguinal lymph node there were sheets of reticulum cells, many plasma cells and eosinophils, but no lipid or pigment. She was discharged, very much improved, in December, 1952, and two years later still showed only a few isolated patches of psoriasis and no lymphadenopathy.

Case 9.—Male, aged 51 on admission, November, 1952. Psoriasis had been present intermittently for 35 years, but despite treatment it had become generalized and exfoliative six weeks before admission. In hospital the psoriasis resolved with A.C.T.H. therapy, but superficial lymphadenopathy and hepatomegaly developed. Biopsy of a lymph node showed reticulum-cell sheets with lipid and abundant melanin. In a biopsy of liver there was mild fatty change and some increased cellularity of the portal tracts with minimal pleomorphism. He was discharged almost free of symptoms in February, 1953. In October, 1954, the psoriasis remained minimal though the liver was still enlarged.

Case 10.—Male, aged 55 on admission, April, 1953. This was an example of localized exfoliative psoriasis. A few plaques of psoriasis, mainly on the legs, had been present since 1949; one was at the site of a healed stasis ulcer of the left leg. On admission the psoriatic lesions of the legs were exfoliative and the regional nodes were enlarged. Biopsy of the skin confirmed the clinical diagnosis. A lymph node from the left groin showed reticulum-cell sheets and abundant melanin but no fat or iron pigment. The skin lesions resolved with routine measures and the patient was discharged in May, 1953.

(c) Besnier's Eczema on Ichthyosis

Case 11.—Female, aged 29 on admission, September, 1952. Ichthyosis with severe atopic dermatitis had been present since infancy and there was also a history of asthma. On admission there were widespread excoriations and generalized lymphadenopathy. Emotional lability was pronounced. Biopsy of a superficial lymph node showed reticulum-cell sheets, an abundant infiltration by eosinophils, but only minimal lipid and melanin; iron pigment was absent. Her condition improved and she was discharged a month after admission. When last seen in October, 1954, lichenification and pigmentation of the skin with excoriations were still present; the lymphadenopathy was unchanged.

Case 12.—Female, aged 40 on admission, May, 1953. Ichthyosis with minor atopic dermatitis had been present since infancy and she had had asthma for 10 years. The skin condition had deteriorated during the past three years and on admission was severe and generalized; lymphadenopathy was minimal. Emotional lability was a conspicuous feature. Biopsy of the skin showed a patchy, mainly perivascular, mononuclear infiltrate with slight cellular pleomorphism; the stratum corneum and stratum granulosum were well defined. In a lymph node from the groin there were reticulum-cell sheets with a moderate infiltrate of eosinophils, plasma cells, and lipid-laden cells: melanin and iron pigment were present in small amount. She improved with routine measures and was discharged in July, 1953. In November her skin condition remained controlled, showing only moderate lichenification with minimal scaling. The lymphadenopathy appeared to have subsided. Biopsy of an axillary node at this time revealed no sign of the dermatopathic reaction though there was some infiltration by eosinophils and plasma cells and an occasional particle of iron pigment. In October, 1954, her condition had remained quiet.

(d) Reticulosis

Case 13.—Male, aged 64 on admission, July, 1952. A pruritic skin condition with photosensitivity had been present for six months. On admission erythema with thickening of the skin was generalized apart from the legs and a few

small islands on the front of the chest; there was some exfoliation on the face. The axillary and inguinal nodes were moderately enlarged and the liver was palpable 2 cm. below the costal margin. The peripheral blood and sternal marrow were normal. Biopsy of the skin showed a diffuse, abundant infiltration of the dermis by mononuclear cells; pleomorphism, though present, was not conspicuous. Reticulum-cell sheets with moderate amounts of melanin and iron pigment and minimal lipid were found in a superficial lymph node. The condition was provisionally regarded as premycotic erythrodermia and he was given a course of urethane, which had to be stopped after five weeks because of nausea and vomiting. As the skin had improved vastly and the pruritus had disappeared he was discharged in September, 1952. However, he was readmitted six months later as the eruption had recurred with much scaling. Biopsy of the skin now showed considerably more pleomorphism of the dermal infiltrate. The histological appearances of another lymph node were the same as previously. Biopsy of liver showed minor increase in cellularity of the portal tracts, including a few eosinophils and plasma cells. Further treatment with urethane combined with R 48 (β -naphthyl-di-2-chloroethylamine) until July, 1953, largely controlled the skin condition for a further six weeks, when an acute relapse occurred with severe generalized lymphadenopathy. The peripheral blood showed a leucocytosis (12,700 per c.mm.) with up to 26% eosinophils. He developed extensive oedema and died in November, 1953. Permission for a necropsy was refused.

Clinical Review

The 13 cases described, all showing lymphadenopathy with the characteristic dermatopathic reaction in the nodes, have in common a pruritic skin disorder with exfoliation at some stage. Emotional instability, as emphasized by Jarrett and Kellett, was a feature of seven of our cases, and eosinophilia was found either in the peripheral blood or in the tissues, or both, in all but three psoriatic patients. Case 10 illustrates the fact that a generalized erythrodermia is not essential to the development of the lymph-node picture, since the lymphadenopathy here occurred in the drainage area of a purely localized lesion. Our series showed no sex preponderance (seven females and six males): this is in accord with the observations of Laipply and White, and suggests that the preponderance of males noted by Jarrett and Kellett may have been fortuitous. All the patients were adults, of ages ranging from 29 to 76; other workers have found much the same age distribution.

Pathological Review

Methods.—All tissues were fixed in formol acetate; the lymph nodes were transected as soon as possible, always within 24 hours, and one-half of each was transferred to Carnoy's fluid for paraffin sections. Haematoxylin and eosin staining was used routinely on all specimens. In addition, sections of the lymph nodes were stained for eosinophils (eosin and methylene blue), plasma cells (Unna-Pappenheim), melanin (blackening by Fontana's silver method and bleaching by Mayer's method), iron (Perles), and reticulin (Foot). Frozen sections were stained for fat (Sudan III). The skin sections were also stained for melanin, and the liver biopsies were examined by special stains when required.

Results.—The skin, examined histologically in nine cases, showed the usual features of the different diseases and nothing specifically characteristic of the dermatopathic syndrome.

The lymph nodes were variably enlarged, up to 3 cm. in length, and showed no outstanding macroscopic features to distinguish them from those with simple reactive hyperplasia or grave reticulosis.

The histological changes are summarized in Table I. Reticulum-cell hyperplasia was found in all cases: the reticulum cells occurred in pale-staining sheets in the medullary part of the gland, particularly in the outer part, so

TABLE I.—*Histological Features of Lymph Nodes*

Case	Hyperplasia			Eosino- phils	Plasma Cells	Lipoid	Melanin	Iron
	R	S	F					
1	+	+	—	+	—	—	++	—
2	+	—	—	++	++	±	+	—
3	+	—	+	±	+	±	++	—
4	+	—	—	+	++	—	±	—
5	+	+	+	+	±	+	±	—
6	+	—	+	+	+	—	++	—
7	+	+	—	±	+	—	++	—
8	+	—	+	+	+	—	—	—
9	+	+	+	—	—	+	++	—
10	+	+	—	—	±	—	++	—
11	+	—	+	++	—	±	±	—
12	+	+	+	+	+	±	±	—
13	+	+	—	—	—	±	—	±

R = Reticulum-cell sheets. S and F = Sinus and follicular hyperplasia respectively.

that they sometimes separated the follicles widely. In all but two cases there was also a minor degree of the more usual type of reactive lymphoid hyperplasia, either sinus or follicular in type, or both. Less constant features were infiltration by eosinophil leucocytes and plasma cells. Foam cells bearing sudanophil fat were found in moderate numbers in 7 out of 12 cases examined by frozen section; they occurred scattered throughout the medulla and especially in or around the sheets of reticulum cells. Melanin pigment, mainly intracellular, was found in all but two cases, and was abundant in six; it occurred anywhere in the medulla, and its deposition seemed to be related to the degree of pigmentation of the skin drained by the node. Iron pigment was found in three cases. Reticulin fibres were scanty in the areas of reticulum-cell hyperplasia; there was no increase of collagen.

The typical histological picture was not restricted to enlarged nodes, as it was often found in those of normal size removed at the same time. The presence of both melanin and lipoid together in a single node was noted in only six cases, and in only one were both present in abundance. Because of this we agree with Hurwitt and with Jarrett and Kellett that the term "dermatopathic lymphadenitis" for the reaction is preferable to the older term of "lipomelanitic reticulosis."

For practical reasons we have been unable to obtain much histological evidence about the fate of such glands. So far as can be judged, however, the picture seems to be reversible, since in most of our cases the lymphadenopathy had subsided when the skin condition cleared. In four cases a lymph-node biopsy at this time showed persistence of a little pigment or lipoid, but no sign of the dermatopathic reticulum-cell reaction. The lesion therefore should be regarded as a benign reactive change, and its recognition by histopathologists is of great importance. Unfamiliarity with the condition may lead to diagnosis of grave reticulosis or, at best, to guarded opinions.

Liver Biopsies.—We have not been able to find any previous report of the state of the liver during life in this

syndrome. Needle biopsies were performed in five of the present cases with mild hepatomegaly as it was thought desirable to exclude the possibility of a generalized reticulo-endothelial reaction. In none was there any evidence of reticulosis; four showed scanty leucocytic infiltration of the portal tracts and two of these livers were fatty.

Necropsies were performed on two of the four patients who died. One of these (Case 1) died of an unrelated cause and had no sign of generalized reticulosis *post mortem*. The other (Case 7) died of an acute leukaemia, but the question whether this termination was coincidental or not cannot be decided.

Control Observations

In an attempt to establish whether the lymph-node reaction could be found in conditions other than pruritic skin disorders with exfoliation we have investigated cases of pruritic and non-pruritic skin disorders without exfoliation by the methods already described. In addition, many routine lymph-node biopsies of patients without skin disease have been carried out for any evidence of similar changes; in a few of these the full range of staining techniques was used.

The control skin cases, seven in number, were chosen because of the close similarity to the first series; they were all pruritic and had some lymphadenopathy, though none had exfoliation. Their clinical and pathological features are summarized in Table II. The only consistent difference in the histological picture in the lymph nodes from that found in the main series was the absence of reticulum-cell hyperplasia. Some of the other features, apart from iron-pigment, were found in every case, though the changes were usually mild.

The lymph-node changes found in our main series of cases, with the exception of the reticulum-cell hyperplasia, are not specific to exfoliative pruritic skin disorders, or, for that matter, to any skin disorder. This has been made clear by control observations on nodes from routine biopsy and necropsy material from patients without skin disease. We have frequently been able to demonstrate small amounts of melanin or sudanophil lipoid in otherwise normal superficial nodes or in those showing only simple reactive hyperplasia: as the likely source of these substances is the skin, it is not surprising that their incidence and intensity in the lymph node be greater in pruritic skin disease. Moreover, it is well known that eosinophil or plasma-cell infiltration is a common finding in many other diseases. Reticulum-cell hyperplasia, on the other hand, appears to be a rarity apart from its association with exfoliative pruritic skin disease: we have found only one example of appreciable hyperplasia of this type in a control series of 100 patients in which 200 superficial or deep nodes, mostly showing simple reactive changes, were specially examined for this feature. We feel, therefore, that the presence within a superficial lymph node of reticulum-cell sheets, particularly if associated with a notable deposition of melanin or

TABLE II.—*Clinico-pathological Features of Non-exfoliative Cases*

Case	Age and Sex	Diagnosis	Duration (Years)	Other Features	Skin Histology	Lymph-node Histology
A	26 M	Besnier's eczema without ichthyosis	25	Asthma. Emotional lability	Conforms with diagnosis	Sinus and follicular hyperplasia
B	36 M	Psoriasis	15	Died of chronic nephritis. P.M. confirmation obtained	Typical	Mild sinus hyperplasia. Moderate amount of melanin
C	33 F	"	20	Treated syphilis	"	Sinus hyperplasia. Melanin scanty. A few eosinophils and plasma cells
D	58 M	Reticulosis	73	Blood eosinophilia. Hepatomegaly: liver biopsy—mild fatty change	Suggestive of early mycosis fungoides	Follicular hyperplasia. Many eosinophils and moderate amount of melanin
E	49 M	Prurigo	10	Intrinsic cerebral tumour	Erythrodermatous picture	Sinus hyperplasia. Melanin and lipoid in small amounts
F	44 M	"	1½	Blood eosinophilia. Emotional lability	Non-specific inflammation and eosinophilia	Sinus and follicular hyperplasia. A few eosinophils and small amounts of melanin and lipoid
G	56 M	Disseminated neuro-dermatitis	½	Emotional lability	Conforms with diagnosis	Sinus and follicular hyperplasia. Moderate lipoid and scanty eosinophils and plasma cells

lipoid, is almost pathognomonic of a dermatosis with exfoliation and pruritus in the skin drained by the node.

The single exception in the control series was found in a lymph node from the lymph drainage area of a malignant melanoma; it contained melanin but no recognizable tumour cells and there were sheets of reticulum cells in the melanotic areas. This isolated observation may be significant, though it could easily be coincidental, since we have not seen another example of this reaction in other equally melanotic nodes. Moreover, it will be recalled that reticulum-cell hyperplasia was absent from the melanotic nodes from our control cases with non-exfoliative skin disease.

Discussion

The present findings suggest that the dermatopathic syndrome is a specific entity in which chronic dermatosis with erythema, exfoliation, and pruritus is associated with hyperplasia of reticulum cells in the regional nodes: all our 13 cases with this skin picture have, without exception, exhibited the reticulum-cell reaction. The study has been made over the past four years, during which time we have probably seen most of the cases of severe dermatosis in the North-eastern Region of Scotland: a stable and well-defined community with a total population of nearly 500,000, of whom approximately 60% are in the age group concerned—that is, over 25 years. However, our figures for the prevalence of the syndrome in the area cannot be precise, since not every case manifesting these dermatological features in minor degree has been submitted to lymph-node biopsy. Nevertheless, it is felt that the study gives a useful idea of the prevalence of the overt case in this area.

The *pathogenesis* of the lymph-node reaction has not yet been elucidated, but certain observations are of interest. The common association with eosinophilia and emotional instability may well be significant as indicating possible allergic or neurogenic factors in the development of the syndrome (Jarrett and Kellett): our cases show the same relationship. We have found the characteristic lymph-node changes in association with several unrelated dermatoses, but the reticulum-cell sheets have occurred only in association with exfoliation. We have no good explanation to offer for this association: there may be some common responsible factor, or the reticulum-cell hyperplasia may be secondary to processes occurring in the exfoliating skin. The presence of melanin in the node may also play a part in the development of the reaction.

The *prognosis* of our cases depended upon the underlying dermatological condition and bore no relationship to the lymph-node picture. However, we are unable to affirm that the lymph-node hyperplasia does not on occasion result in malignant change, as two patients (Cases 7 and 13) died respectively of acute monocytic leukaemia and a grave reticulosis (probably mycosis fungoides). The association may be coincidental or the reticulosis may have caused the exfoliative skin condition. Nevertheless, the possibility that the neoplasia supervened on the reactive hyperplasia cannot be dismissed, since experimental studies (Gillman and Gillman, 1952; Richmond, 1954) have shown that reticulum-cell hyperplasia, artificially induced by such methods as injecting trypan blue into animals, may in fact go on to frank neoplasia.

The *treatment* of our cases has been by routine methods supplemented by A.C.T.H. alone in two cases (Nos. 2 and 9) and with the addition of cortisone in one case (No. 7). (Hormone therapy is fully reviewed in the M.R.C. Report (1954) and the *British Medical Journal* (1954).) The effect of A.C.T.H. was beneficial in Cases 2 and 9, but both hormones were disappointing in Case 7. This case (an example of exfoliative and arthropathic psoriasis) is of special interest, as it was the one in which leukaemia developed, apparently as a terminal event, since clinical and pathological investigations during the earlier part of the patient's illness showed no evidence of the disease. She had been exposed to long courses of powerful drugs other than the hormones, and we

have the uncomfortable feeling that the generalized reactive changes in the lymph nodes may have been affected adversely by the therapy.

Summary

Twenty cases of different clinical types of pruritic skin disease with varying degrees of lymphadenopathy have been studied clinically and pathologically during a four-year period. Seven of these cases had no exfoliation and showed only non-specific changes in the lymph nodes, under which term we have included the presence of small or moderate amounts of melanin and lipoid. The other 13 cases, however, all had an exfoliative phase and showed, in addition to the non-specific changes in the nodes, a characteristic proliferation of the reticulum cells. This change, which we have referred to as dermatopathic lymphadenitis, is almost pathognomonic of an exfoliative pruritic dermatosis.

The dermatopathic syndrome is a fairly well defined clinical entity, and its prevalence in overt form in the North-eastern Region of Scotland, with a population of nearly 500,000, can be roughly assessed from the knowledge that our 13 cases probably represent the sum total in that area over a four-year period.

The importance of the syndrome to the pathologist is that unfamiliarity with its manifestations may lead to confusion of the lymph-node picture with that of some grave reticulosis. However, the changes are merely reactive in nature and are essentially benign; they regressed when the skin condition settled, and the prognosis of the cases was that of the primary skin disease. Nevertheless, the possibility that the reactive hyperplasia may occasionally go on to frank neoplasia has not been excluded.

Our thanks are due to Professor J. S. Young for advice and helpful criticism.

REFERENCES

- Bluefarb, S. M., and Webster, J. R. (1950). *Arch. Derm. Syph. (Chicago)*, **61**, 830.
British Medical Journal, 1954, **2**, 1341.
 Gillman, J., and Gillman, T. (1952). *Cancer*, **5**, 792.
 Hurwitt, E. (1942). *J. invest. Derm.*, **5**, 197.
 Jarrett, A., and Kellett, H. S. (1951). *Brit. J. Derm.*, **63**, 343.
 Laipply, T. C. (1948). *Arch. intern. Med.*, **81**, 19.
 — and White, C. J. (1951). *Arch. Derm. Syph. (Chicago)*, **63**, 611.
 M.R.C. Report (1954). *British Medical Journal*, **2**, 1307.
 Obermayer, M. E., and Fox, E. T. (1949). *Arch. Derm. Syph. (Chicago)*, **60**, 609.
 Pautrier, L. M., and Woringer, F. (1937). *Ann. Derm. Syph. (Paris)*, **8**, 257.
 Richmond, H. G. (1954). Unpublished observations.
 Soloff, L. A. (1942). *J. Lab. clin. Med.*, **27**, 343.
 Wilson, H. T. H. (1954). *Arch. Derm. Syph. (Chicago)*, **69**, 577.

The ninth report and statement of accounts of the Joint Committee of the Order of St. John and the British Red Cross Society contains much interesting information about the excellent work being done for war casualties and for the population in general. The great bulk of the funds under the control of the Joint Committee is derived from the allocation of £6½m. from the Joint War Organization to cover expenditure for a period of roughly thirty years on the discharge of liabilities arising directly from the war of 1939–45; and the main, though not the sole, activity of the Joint Committee is the relief of ex-Service men and women disabled in the two world wars and their dependants. Since the end of the last war some £2m. of capital funds has been expended on the various activities of the several departments of the committee. Four institutions are administered direct by the Joint Committee; one—the rehabilitation centre at Headington Hill Hall, near Oxford—is maintained on behalf of the Ministry of Pensions and National Insurance, and eight others receive recognition and support. In the year ended June 30, 1954, assistance in one form or another was given by the emergency help and aftercare department to 81,000 men, women, or children.