Th. Sect. 1924

"Diffuse leukaemic Erythrodermia."

by.

F. C. K. Austin.

M D
1924

Two cases of a somewhat rare nature which came under my observation at Charing Cross Hospital are characterised by certain features herein set forth.

Case. 1.

Name. James Stephens.

Age. 44 years.

Occupation.

Farm Labourer until outbreak of war.

1914. Enlisted as a trooper in the Royal North Devon Hussars.

1916. Proceeded to Salonika joining the 11th Welsh Regiment.

1917 Transferred to the 6th Royal Irish Rifles at Salonika.

1917 Same year transferred to Labour Corps because of an injury.

1917-19 occupied in looking after animals of 45th Remounts.

Place of Birth.

Lydford: Devon: Patient is unmarried.

Place of Residence. Ivy Cottage: Lydford Devon.

Date of Admission. 28-7-24.

" " Examination. 28-7-24.

Complaint. Irritable skin eruption.

Duration. 5 8/12 years.

History: Family.

1904 Father died of some urinary disease aged 68.

Mother alive and in good health

One sister died of Phthisis.

Five sisters alive and in good health.

Three brothers " " " "

Personal.

From the age of 21 Accustomed to drink on

An average one pint of beer daily: Very seldom touched whiskey.
Smoked 10 cigarettes daily prior to his illness.
He is now an abstainer and non smoker.
Surroundings at home.

Good home: Worked in the open air.
Surroundings at work in the Army.

Patient was employed at Salonika amongst mules and horses fenced around in open spaces: The work entailed exposure to the variable climatic conditions of a tropical country where intense heat prevailed in summer accompanied with clouds of dust. and in the winter great cold and rain.
Previous Illnesses and Accidents.

Patient can only recall an attack of rheumatism 20 years ago.
States he never contracted any venereal disease.
1917 Sustained a traumatic Synovitis of right knee.
Time and mode of origin and course of present Illness.

Patient remained in perfect health until 1917 when he sustained an injury to his right knee due to a kick from a mule. This necessitated his transfer to a labour corps upon recovery. where he was attached for duty with the 45th Remounts Salonika and worked amongst horses and mules under conditions when either mud or dust prevailed.
During midwinter 1918-19 patient first noticed the flexures of both hands had become dry, cracked and bleeding. He attributed his condition to the wet and exposure which his work subjected him.

These cracks were over the knuckles and joints of his hands where movement was most marked. His hands became as dry as parchment so that their movement was increasingly difficult and the normal creases of his hands became more evident and fresh cracks developed daily until both palms and backs of his hands were covered with bleeding fissures intensely sensitive and greatly aggravated by any movement. The condition extended at this time as far as the wrists only. About this time patient suffered the same trouble with both feet as far as the ankles and almost simultaneously his face began to peel in a manner resembling sunburn and was so painful that he was unable to shave. About march of the same year the face healed though it still remained red and sensitive though he was now able to shave. His hands and feet did not improve. During this period patient tried to continue his work and applied an ointment given him by the medical officer. Patient was ordered to the United Kingdom in April 1919 and sailed from Salonika in April arriving at Dover on May 6th 1919 and later in the same month was demobilised.

1919-20. He attended his local doctor in Devon for months during which time the eruption spread to the remainder of his body. He felt his whole body dry and burning just as his face had done when the eruption began there. The itching sensation was dreadful and his body began to peel as from sunburn. The amount of desquamation was very noticeable amongst the bedclothes where he lay.

Patient came to London on April 1921 to see.

Dr Sequeria and he was admitted to the London Hospital where he remained under treatment nine weeks. His condition became somewhat quiescent during his stay in hospital and he returned to his home on July 1921. A month later, however, the eruption became as evitable as before and the peeling recommenced: He was now admitted to the South Devon and East Cornwall Hospital Plymouth on August 1921 where he remained 10 weeks with some improvement.

He left hospital in Oct 1921 and again returned home but a few months later in December his trouble was again in full cry and he returned to the South Devon and Cornwall hospital where he remained from Dec. 1921 until Feb. 1922. No improvement was noticed and he returned home where his trouble continued unabated. He came to London in March 1922 and was admitted for the second time to the London Hospital, where he remained until May but no improvement ensued. At this time his eyes began to feel sore with a burning pain. The lower eyelids became everted until the engorged conjunctivae looked outwards. His eyes wept copiously. Patient returned to his home in May 1922 where for a time he was very ill and developed delerium.

On December 1924 he left home for Tavistock hospital where he remained until June 1924 and in July he came to Charing Cross hospital.

Various ointments were tried in the different hospitals without success and X. Ray exposures were made on several occasions at the London hospital without any good result.

State on Admission.

General facts.

Height 5' 7" : Weight 11st 10lbs. Well developed. Tempature. Normal.
Integumentary System.

The face resembles the peeling stage of sunburn. The skin of the face is smooth and red. The red of the lips blending with the unusual bright flush of the cheeks. Numerous small dry branny flakes show on both cheeks and most evident in the region of the forehead. The natural wrinkles of the face are not accentuated as they are elsewhere eg. hands and feet.

The upper eyelids. are markedly thickened and the eyelashes are coarse, short and stubby.

The lower eyelids. are markedly everted and the congested conjunctivae look outwards: They are glistening with moisture which overflows and accumulates around the lower lids in large drops.

The eyebrows. are practically denuded of hair and the skin thus uncovered appears scaly.

The head. is scantily covered with hair and the scalp shows active desquamation.

The chest. Abdomen and back. are smooth and not so dry as the rest of the body: They have a very mottled appearance.

The hair of the axillae and pubis is sparse. The areola and nipple of each breast is more deeply pigmented than normal.

The legs.

Signs of desquamation are more extensive here than elsewhere on the body. Large scales of dried epithelium whitish yellow in colour appear partially adherent though easily detached. Smooth areas are interspaced where scales have become separated.

Hands and feet are extremely dry and swollen. The natural creases are everywhere accentuated giving the extremities a striking appearance. There are fissures where the creases have split and they are most evident over the flexures of the hands and feet. The skin is thickened and corrugated looking. The nails are stained brown in colour and their convexity has increased both in the antero-posterior and lateral directions. The excessive dryness is partially allayed by the constant application of ointment but wherever this dries the stiffness and pain on movement returns and so also the fearful itching sensation which the desire to scratch becomes irrepressible.

In the pathological institute of the Barnet Gross Hospital Medical School. A piece of skin was excised and sectioned:

Microscopical Examination.

Most superficial zone: Well marked layer of hyperkeratinisation.

The papillae are distorted in shape and enlarged. Young soft fibrous tissue on both sides of the papillae Clumps of round cells (lymphocytes) everywhere in evidence.

The pars papillaris and reticulum are well infiltrated with these round cells.

A few plasma cells were observed.

Deeper down there was a coarse zone of fibrous tissue Vessels and glands retained their normal structure. Groups of round cells were seperate around the blood vessels and not around the nerves.

Haemopoietic System.

lymphatic Glands.

There are numerous lymphatic glands enlarged in the following situations.

Cervical region.

Several enlarged glands can be palpated on both sides of the neck behind the posterior border of the sterno-mastoid muscle. They are about the size of hazel nuts and are indurated, firm and elastic to the touch. They are not painful or tender on palpation and the glands are discrete and movable.

Axillary region.

Small glands can also be felt in both axillae.

Inguinal region.

The enlargement of this group of glands is much greater than in other regions. Those of the left side are more numerous than in the right inguinal region. They display the same characteristics as those described under the cervical region.

Ductless Glands.

There is no enlargement of the Thyroid gland, spleen or liver.

There is no tenderness elicited on percussion over the long bones.

In the laboratory of the Charing Cross Hospital Medical School I examined the blood.

Examination of the blood.

Erythrocytes. 4,416,000. Haemoglobin 70%. Colour Index 0.8.

Leucocytes. 41,300.

Differential white blood count on July 28th 1924.

Polynuclear neutrophiles.	21.7	Per. cent.
" eosinophiles.	1.7.	" "
Small lymphocytes	73	" "
Large "	—	
" hyaline cells	3.3	" "
Coarse granular basophilic cells	.3	" "

137 nucleated reds per cu. m.m.

Differential white blood count made on 5th August. 1924.

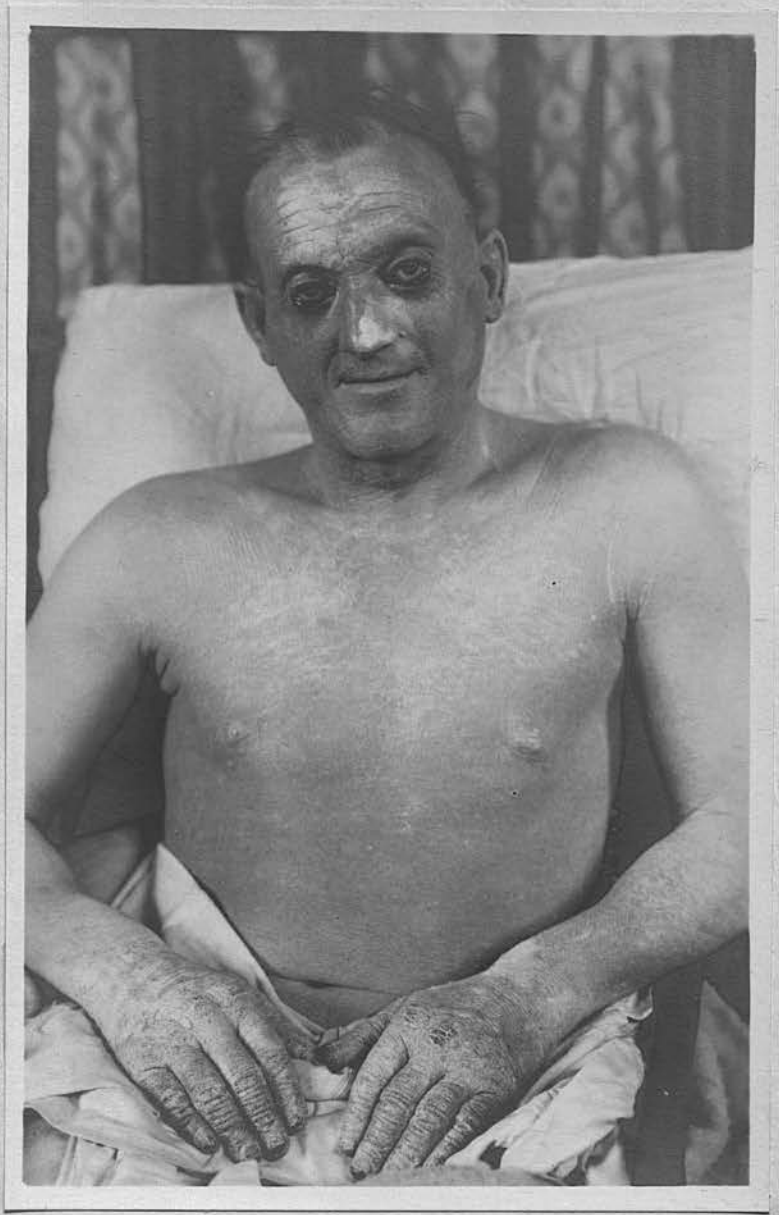
White blood count	43,000	
Polynuclear neutrophiles	18	per. cent
Small lymphocytes	74.5	" "
Large hyaline cells	3.0	" "
Eosinophiles.	4.0	" "
Basophiles	.5	" "

Examination of a lymphatic gland.
This gland was dissected out from the anterior part of the posterior triangle of the neck.
Macroscopic Appearances.
The capsule is thickened and fatty looking but otherwise normal.
Microscopic appearances.
Low power examination: shows marked thickening of the capsule with decided infiltration by lymphocytes. There is entire lack of definition of the gland substance. Absence of lymph sinuses.
The gland is a monotonous repitition of lymphocytes. Clear sinus spaces in each field appear to contain some indeterminate pink material.

High power examination.
lymphocytes everywhere.
Plasma cells and fibroblasts mixed with them.
The indeterminate pink material appears to be composed of large endothelial cells with minute nuclei and pale staining cytoplasm.

Other Systems examined.
Alimentary system.
Tongue clean and moist
Teeth fairly good condition.
Tonsils. Enlarged. Briefly left.
No history of any digestive disturbance.

Respiratory and circulatory have nothing to note.



J. Stevens.

Genito-urinary system.

Albumin and sugar not present.

Wassermann Reaction.

Negative.

Case. 2.

Name. Arthur Hill.

Age. 59 years.

Occupation. Valet at the Grand Hotel.

Place of birth Hartfield, Sussex: Patient is married.

Place of Residence. 143 Lavender Street, Clapham Junction.

Date of Admission. 13-8-24.

" " Examination 20-8-24.

Complaint. Irritable eruption of the skin.

Duration. Two years.

Family history.

Father died aged 74 cause Hemiplegia.

Mother died aged 48 cause unknown.

1 Brother died aged 68 from cancer of the throat

1 Brother died aged 11 from lung disease.

1 Sister died aged 66 from dropsy.

3 Sisters are alive and in good health.

Personal.

Patient has always had a comfortable home and good food. At one time he drank on an average one pint of beer daily. He has been an abstainer during the past few years. Smokes one ounce of St. Julien mixture daily.

Previous illnesses and accidents.
1884 fractured right thigh in the hunting field.
States he has never contracted Syphilis.
He has no children and his wife had no miscarriages.

General facts.

Temperature normal during stay in hospital.

Height 5 ft. 9" Weight 10 stone: lost 1 stone since onset.

Time and mode of origin and course of Present illness.

Patient was at work and in his usual health until 1922 when he first noticed his hands had become stiff, dry and cracked but there was no bleeding: This caused them to be painful on movement or on attempting to wash his hands. The only thing he could assign for his condition was his work as cadet which entailed constant pressing of cloths in which he was constantly dipping his hands into cold water, though he had been doing the same work for 30 years. He sought advice from his local doctor who treated his skin condition with various ointments over a period of 15 months without success. His fingers were itching intensely and the desire to scratch them was irrepressible: They were also swollen and covered with cracks. Very soon the itching spread to the remainder of his body leaving no part unaffected yet he noticed no alteration in the appearance of his skin which appeared normal except for the cracks on the hands. Towards the end of 1923 patient attended St. Johns' hospital Leicester Square as an outpatient.

but the treatment he received was unavailing: He attended this hospital for four months: He now noticed that his body everywhere had become very red in colour and he sought advice from this hotel doctor. He states that at this time he was ordered by him to rub on everywhere made his face burn and caused it to weep: He was in consequence sent to Charing Cross hospital where he was treated as an outpatient for 3 weeks whilst awaiting Admission: He was admitted on May 1924 and remained until July during which time his whole body was burning and itching and his face began to peel: He had starch poultices and a liniment applied during his stay in hospital.
Patient was re-admitted to Charing Cross hospital on 13-8-24.

State on Admission.

Integumentary System.

The face resembles. closely the severe peeling stage of sunburn. The skin of the face is for the most part smooth and yet unusually red especially the nose and cheeks: ~~Though~~ Numerous small dry flake like particles of desquamating skin show on both cheeks though this is most evident in the region of the forehead. The natural wrinkles of the face are not so accentuated as are seen elsewhere eg. hands feet, elbows and neck: There is little hair on the face and what there is to be seen is coarse and stubby around the chin: The sides of the face are completely denuded of hair.

The upper eyelids.

These are thickened and the eyelashes are sparse, short and coarse.

The lower eyelids are not swollen or everted nor is there any abnormal secretion. The eyebrows are coarse and sparse.

The Head.

The hair is very thin and many bald patches show where formerly he had a thick crop of hair. The scaly eruption is much more evident here than elsewhere. The patches of scurf are white and closely aggregated together form cakes of dried epidermis.

The ears are extremely prominent and of enormous size measuring almost four inches in length. They are so much swollen that the edge is as thick as a finger. The scales of the eruption are larger here than elsewhere on the face and situated chiefly along the edge of the ear and just outside the meatus. They are brownish in colour.

The neck looks dry and leathery in appearance and covered with brown scales which extend over the chest as far as the 2nd rib.

The chest, abdomen, back and legs.

The entire skin of these parts is smooth and not unduly dry but the most arresting characteristic lies in the colour. This is of a brick red description making the patient a typical "Homme rouge." The red of the legs is of a darker texture yet not a vestige of the wide area under description approaches the normal colour.

The hands and feet.

There is visible swelling of the parts. The dry skin is lax and intensely corrugated especially that of the hands. There are numerous cracks especially of the fingers. The desquamation on the dorsal aspects is well marked. The scales are large white and easily removed. The palmar aspect of the hands and the plantar of the feet are almost unaltered.

Portion of skin sectioned showed identical changes described in Case 1.

Haemopoietic System.

Lymphatic Glands.

There glands show very definite enlargement in the cervical, axillary and inguinal regions. They are indurated firm and elastic on palpation: They are quite painless and not tender to the touch and they are discrete.

Cervical region.

A few small enlarged glands could be palpated on the right side of the neck above the clavicle.

Axillary region.

A few small glands were palpated in the axillae.

Inguinal region.

There are half a dozen enlarged glands on both sides of a larger size than those of other regions.

Ductless Glands.

The thyroid, spleen and liver do not appear to be enlarged.

At the pathological institute of the Charing Cross Hospital Medical School.
Examination of a gland removed from the inguinal region was made.
Macroscopic appearances.

Capsule normal in appearance.

On section.

Rusty brown pigmentation seen.

Microscopical examination.

Identical with those seen in case 1. except that the infiltration of the capsule is more marked in this case.

At the Laboratory of the Charing Cross Hospital Medical School.
Examination of the Blood on July 25-8-24. was made.
Erythrocytes. 4,800,000. Haemoglobin 90%. Colour Index. .9.
Leucocytes. 13,800.

Differential white blood count.

Polymuclear neutrophiles.	13.00.	per. cent.
Small lymphocytes	82.50.	" "
Eosinophiles.	nil.	" "
Large lymphocytes.	1.50.	" "
Basophils.	.75	" "
Large hyaline.	1.75	" "
Lymphoblast.	.60	" "
Nucleated Reds.	nil	" "

Other Systems examined.

Alimentary System.

Tongue clean and moist.

Teeth Dentures both in upper and lower jaws.

Tonsils. Show no enlargement.

Digestion has always been good.

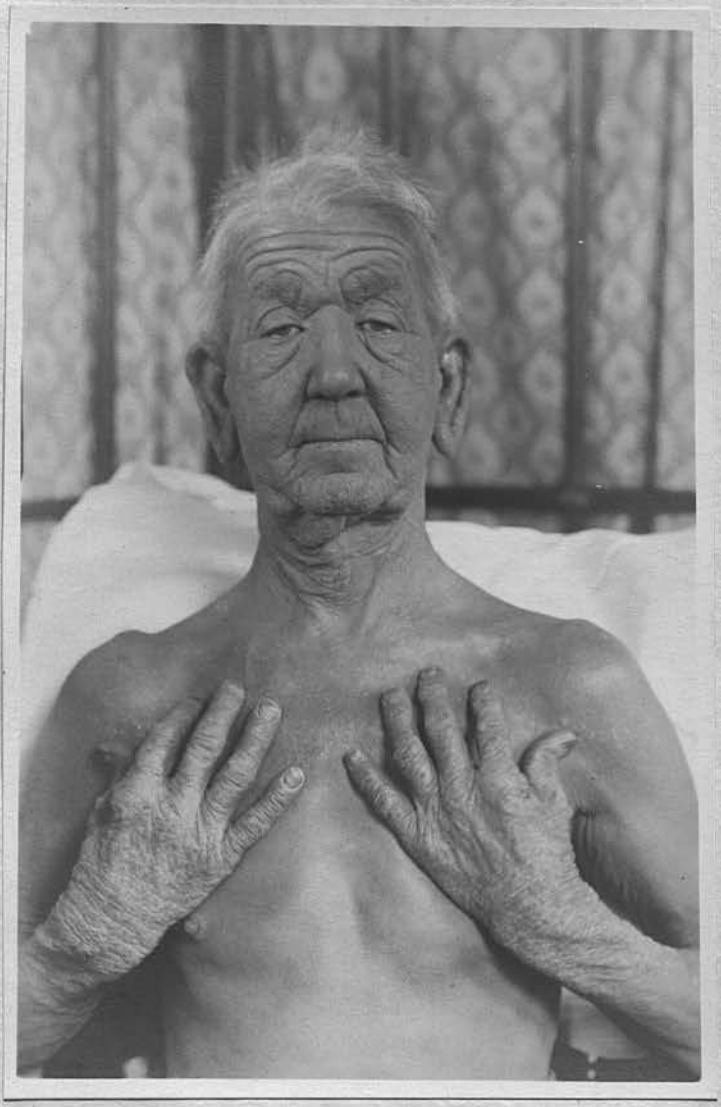
Genito-urinary System.

Urine Examination shows: no pathological constituent present.

Respiratory, Circulatory and Nervous Systems.

Nothing of import to note.

Wassermann Reaction found negative.



A. Hill.

Two additional cases described by Sequeira and Paulton under the heading of Lymphoblastic Erythrodermia (1) present characters strikingly similar to my own cases and their essential features are as follows.

Case 1.

William B. aged 60 years admitted to the London Hospital under the care of Dr Sequeira on Oct. 1st 1915. The family history was unimportant. In 1913 a "red patch" appeared on the shoulders and the eruption gradually spread over the whole body. On admission the patient was a characteristic "homme rouge". The skin everywhere being a brick red colour. The surface generally was smooth and some superficial oedema was present in the lower extremities where there was a slight scaling. The only parts of the skin which were approaching the normal colour were the orbital regions and the hands and feet. The eruption itched intensely and had done so from the onset.

Haemopoetic System.

The lymphatic glands in both cervical regions, the axillae and groins were enlarged, movable, painless and not tender. Radiographic examination failed to reveal any evidence of enlarged glands in the thorax: neither the liver nor the spleen was enlarged. The Wassermann reaction was negative.

Examination of the blood.

Red cells. 3,999,000. White blood cells 32,800. Hb. 70%.

Polymuclear neutrophiles. 16·5 per cent.

" eosinophiles. 6·5 " "

Small lymphocytes. 75 " "

large hyaline cells. 2.0. percent.

No section of the skin appears to have been made and apart from stating that some anomalies in a sectioned gland were found, no detailed description is given.

The urine was examined and found normal.

The disease showed itself extractable to treatment both by local applications and X. Rays.

Case. 2.

Mrs. J. aged 64 years. married late in life and had no children. She had always enjoyed good health until the onset of her present illness.

Family history.

Her father died young Cause unknown. One sister died aged 21 years of consumption. One brother died suddenly from haemorrhage from the lungs. One brother alive and well.

History of her illness.

From five to five and a half years ago patient began to be troubled with an itching of the skin chiefly on the trunk. This was mild at first but gradually got worse and became more generalised. About ten to twelve months later the skin started to get red first on the trunk and this likewise spread gradually all over the body and lastly appeared on the face and hands. For twelve months she had a great deal of suffering - her distress getting gradually worse. She had consulted several doctors and been in hospital without relief.

Integumentary System.

Patient was a stout, obese woman. The condition of the skin may be briefly described as a more or less generalised erythroderma with no specially distinctive features. The redness being most marked on face, trunk upper arms and thighs.

Face and head. The appearance of the face is best described by saying she looked somewhat like "a boiled lobster." The redness was most marked on the cheeks was uniform and there was no desquamation: Ears were congested and beginning to weep - the result of irritation from scratching.

The whole scalp was red, slightly scaly, infiltrated and intensely itchy. The hair was thin. Eyelids showed some blepharitis. The lips were a little blue in colour but otherwise the mucous membranes seemed normal.

Trunk. On the chest and back the erythroderma was fairly uniform, on the abdomen and lumber region somewhat punctate and scarlet in form in character. There was a moist intertrigo in the folds of the breasts.

Limbs. On the arms and legs the redness was less marked and only slight on the hands and feet.

Itching. This was intolerable and practically constant. As a consequence patient was very restless and got little sleep at night. Apart from the erythroderma and the altered blood picture nothing else was discovered.

Her appetite was exceptionally good. Her tongue clean. And she had absolutely no gastrointestinal symptoms of any kind. Bowels regular and motions normal. No enlarged glands were detected but patient was difficult to examine as she was very stout.

Urine normal. Temperature normal.

Haemopoietic System.

Red blood cells 3,720,000. White blood cells 23,000.

Haemoglobin 55.

Polymuclear neutrophile	29.5 per. cent.
Small lymphocytes	60.4 " "
large "	6
" hyaline	0.5. " "
Eosinophile	3.6 " "

No nucleated reds or basophiles found.

No report is given of any section of skin having been examined. Local and X-ray treatment proved ineffectual.

The earliest case I am able to trace in the literature on this subject is that described by Riehl in 1892 which he called leucaemia cutis (2). Apart from the clinical features, which are identical with those found in my case, he was able to confirm the accuracy of his observations during life by the result of post mortem examination which places his case in an unassailable position as that of a true leucaemia cutis. I therefore propose to include his case in some detail:

Riehl had under his care a female patient aged 57 suffering from lymphatic leucaemia. Her illness was first noticed in 1889 and began with an eczematous condition of the skin of the nape of the neck. It was accompanied,

by a good deal of irritation and in course of a few months became universal. There were enlarged glands in the cervical and inguinal regions.

On admission.

Lungs, heart and bones normal. Temperature 36°C. The integument everywhere bright red, in certain regions glossy, in others covered with slight branny scales and in others excoriated. Examination of the blood showed white blood cells in the proportion of 1 to 24 or 26 of the red corpuscles. Stained preparations revealed presence of lymphatic leucaemia. After remaining in hospital some time during which the skin underwent but little change she died. The autopsy confirmed the diagnosis. The bones showed no changes. Nowhere could any tumour of the skin be detected.

Microscopically.

The liver showed leukaemic infiltration around the interlobular vessels which were plugged with white blood cells. The spleen revealed similar changes of the follicles and around blood vessels. The lymph passages of the lymphatic glands were crowded with leucocytes and round celled infiltration was well marked in the neighbourhood of the capsule. As regards the skin leucaemic infiltration everywhere occupied the middle layers of the cutis. – Round cells with large nuclei, scanty protoplasm embedded in reticular tissue. The smallest groups were situate around the nerves. – The largest were diffused through corium. Towards the pars papillaris and the subcutaneous tissue the infiltration was less dense.

Here fusiform elements were recognisable. Connective tissue corpuscles in proliferation. - In the infiltration the lymph vessels distended with leucocytes was easily demonstrable by reason of their endothelial walls. The blood vessels also contained numerous leucocytes. In regions of the skin less affected, the infiltration was found chiefly round hair follicles - sweat glands and the larger blood vessels. In the neighbourhood of the leucaemic deposit oedema of the skin was well marked and the papillary layer resembled mucous tissue. Traversing the deposits coarse bundles of connective tissue were discernable. Where exudation was abundant numerous crusts covered the cutis.

"This case therefore was one of lymphatic leukaemia in which the skin was complicated. "The skin changes were undoubtedly directly connected with leukaemia. "The diagnosis was as firmly established by the histological characters of the skin as by the changes in the liver.

Sequeira and Panton challenge the diagnosis arrived at in Riehl's case and infer that he made a mistake in his differentiation between lymphocytes and myeloblasts and suggest that Riehl's case was one really of acute myeloid leukaemia. However the weight of evidence with which Riehl supports his case is too great to permit of this contention. He distinctly points out that microscopical examination showed leukaemic infiltration around the interlobular vessels of the liver and similar changes of the follicles.

and around the blood vessels of the spleen thereby making absolute his claim that he is dealing with a case of lymphatic leukaemia and not myeloid leukaemia.

The second earliest case is that described by Von Zumbusch (3) under the title of "Erythrodermia (pseudo) leukaemica" (Riehl). This case by its course and histological findings leaves no doubt in my mind that it is identical with my own cases and Von Zumbusch like Riehl had the opportunity of confirming his diagnosis by a post mortem examination in which the changes in the liver and spleen clearly denote the case to be one of lymphatic leukaemia.

Von Zumbusch in summing up his case draws attention to the absence of any change in the bone marrow and the minor infiltration changes in the internal organs from which he makes the important deduction that the disease is one primarily of the skin in which lymphoid tissue is known to be present.

Discussion.

Clinical Features.

From the following age table of patients described in this communication it is noteworthy that the age incidence 40

to 70 years corresponds closely to that at which Osler and McCrae (4) and Tidy (5) state that Chronic lymphatic leukaemia is most common:

Name of Patient.	J. Stevens.	A. Hill.	W.B.	Mrs. J.	Von. L's case.
Age " "	40.	59	60	64.	70.

Judging from the limited number of cases described in the literature the disease appears to be more common in males.

The disease develops insidiously and no metabolic, toxic or other cause can be said to account for its origin. On the whole the persons affected seem to be those who have previously enjoyed vigorous health.

There is no history of Syphilis and the Wassermann reactions are always negative.

The temperature throughout the disease is usually normal.

In the majority cases there is an intense pruritus and erythrodermia. The itching is general and of very long duration and un accompanied by any obvious change in the skin. This condition may last for several years. Eventually the face, trunk and limbs are involved in a diffuse scaly eruption which may have begun as a small patch. There is never any sign of tumour formation.

Erythroderma.

The whole surface becomes bright red. The skin is dry and accompanied by desquamation. The hair falls out all over the affected parts and the nails become separated. The itching everywhere is intensely aggravating. The lymphatic glands in all areas become enlarged and discrete.

The Skin.

All the above mentioned cases show the same type of skin affection that is "A diffuse infiltration of the skin with round cells. The skin being thickened, swollen and of a bright red colour."

This is in contradistinction to those described by Batty Shaw (6) and Pfeiffer (7) in which tumours of the skin were first noticed.

According to Naegeli. O. (8) Skin infiltration, such as has been proved by histological examination to be present in all my cases and those writers I have mentioned, is commoner with the aleukaemic blood picture than with typical leukaemia whereas it is very rare to find infiltration present in the skin in myeloid leukaemia.

Glands.

Glandular enlargements were found in all of the above mentioned cases. These were described chiefly in the cervical, inguinal and axillary regions. In one of my cases the tonsillar glands were also enlarged but in none of the cases was there any enlargement of the mediastinal glands even when X ray examination was carried out.

The enlargements were of the discrete type and never gave rise to pain nor did they show any tendency to break down or invade the overlying skin.

Microscopically.

Few observers appear to have histologically examined the glands: In my cases the infiltration of the capsule by lymphocyte cells and the crowding with lymphocytes of the gland substance were predominant and clearly defined the nature of the disease.

Blood changes.

The blood picture so far as the numbers of leucocytes is concerned would appear, according to the view taken by some writers, to contra-indicate these cases being accepted as those of lymphatic leukaemia and Sequeira and Panton deride the idea of a lower leucocyte count than 200,000 per. cubic millimetre and a lymphocytosis of less than

90 per. cent. being accepted in lymphatic leukaemia and since many other writers have insisted upon similar striking blood changes for the support of this diagnosis cases have been reported as aleukaemias to get over the difficulty of a leukaemia where only a qualitative and not a quantitative change in the blood has been found.

Naegli. O. however strongly emphasizes the fact that even in lymphatic leukaemia may we not infrequently expect to find a relatively low leucocyte count but stresses the great importance for care in all such cases to place reliance on the lymphocytosis disclosed upon making a differential leucocyte count since this will obviate the danger of wrongful deductions being arrived at in consequence of the initial error.

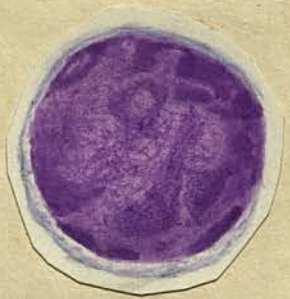
The following comparative table which I have drawn up includes those cases in my own series together with those of other writers referred to in my context.

Case.	J.S.	A.H.	W.B.	Mrs J.	Von Z.
Erythrocyte	4,416,000.	4,800,000.	3,999000.	3,720,000.	4,800,000.
Leucocytes	41,300.	13,800.	32,800.	23,000.	20,000.
Haemoglobin.	70 per cent	90 percent.	70 percent.	55 percent	90%.
Colour Index.	0·8	·9	·8	·7	·9.

Case.	J.S.	A.H.	W.B.	Mrsd.	Von Z.
Polynuclear neutrophiles.	21·7	13·00	16·5	29·5	26·0
" Eosinophiles.	1·7	Nil	6·5	3·6	0·9
" Mast cells.	-	-	-	-	0·2
Small lymphocytes	73	82·50	75·0	60·4	66·0.
Large "	-	1·50	-	6	6·2
" Hyaline.	3·3	1·75	2·0.	0·5	-
Basophils.	·3	·75	-	-	-
Lympho Masts.	-	·50	-	-	-
Large mononuclears.	-	-	-	-	·7

A leucocytosis of a moderate degree is common to all of them: The total number of leucocytes ranges from 13,000 to 41,000 per cubic millimetre. The relative proportion of the small lymphocytes range as high as 82·50 per cent. High lymphocytosis of this degree must are agreed indicates the leucocythaemic nature of the malady.

A further interesting feature is revealed upon subjecting these lymphocytes to the very high magnification of x 1000 times and comparing their appearances with that of the normal lymphocyte under a similar degree of magnification. It will be then seen that in the normal lymphocyte areas of isolated darkly staining cromatin arrange themselves around the periphery of the nucleus whereas in the lymphocytes from my cases these areas are nowhere to be seen



Normal Lymphocyte ×1000.

Lymphocyte from Patient ×1000.

Nor do they stand out in relief with the clearer centre as in the normal but instead the whole nucleus is more homogenous and comparable with the appearances seen in the cells of lymphatic leukaemia when so examined.

The changes in the red cells and haemoglobin are slight for I had an opportunity of comparing the red cell counts in the case of J.S. taken now after a period of five years with those taken when he was previously under observation and find the alteration almost negligible: My other case A.H. who has never previously been described and therefore no earlier blood counts are available for analysis yet considering his illness has lasted for two years the present red cell count would seem to bear this out.

Differential Diagnosis.

From other Erythrodermias.

The clinical features in these cases are in many ways analagous to those observed in other erythrodermias such as Mycosis Fungoides and Exfoliative Dermatitis: In the words of Bessnier (9) "In all cases of ambiguous pruritic dermatoses which are prolonged and rebellious to treatment the possibility of the disease being the premycosic stage of Mycosis fungoides should be borne in mind".

However the blood picture in the cases I have described is so distinctive as to render possible a diagnosis from other erythrodermias including that of Mycosis Fungoides.
Sequeira found after careful observation on the blood counts of a series of cases of Mycosis Fungoides (10) that "there was nothing abnormal in the blood in this disease."
Lymphodermia Perniciosa Kaposi (11)
I could serve no useful purpose entering into a discussion on the resemblances between my cases and his classical one since no differential blood count is available to enable a distinction being made.

From diseases in which glandular enlargement is a feature:
The most important of these to my mind are Syphilis; Hodgkin's disease; and lymphosarcoma.
Syphilis is clearly eliminated in my own cases since there was no history suggestive of it and the Wassermann reactions were negative.
Hodgkin's disease.
In Hodgkin's disease mild irregular pyrexia is usually a feature

of the disease: Variations in the numbers of the white cells is not especially characteristic: The lymphocytes only show a slight relative increase. Histologically there are striking differences between the structure of the glands in the two conditions.

Lymphosarcoma.

The wide area of glandular involvement found in my cases is in contrast to the more isolated involvement in lympho-sarcoma: The immediate outlook in lymphosarcoma is much more serious and rapidly fatal whereas my patients have been affected for six years in the case of J.S. and two years in the case of A.K.

From Acute lymphatic leukaemia.

The patient suffering from acute leukaemia is much younger and the progress downhill much more rapid.

Prognosis

The immediate prognosis as to life is undoubtedly good as the lengthy period following the onset of the disease that the majority of patients described have been under observation goes to show.

However the ultimate outlook is distinctly bad as it is in all leukaemias where recovery is practically unknown.

The administration of Arsenic appears to afford, temporarily at least, a beneficial action on the secondary anaemia when this by its presence calls for treatment.

X Ray where this has been tried may be said to provide no relief.

Conclusions.

The two cases described in this communication together with those quoted from the literature illustrate the rarest of cutaneous manifestations of leukaemia. The occurrence of nodular, tumour-like masses in the skin in lymphatic leukaemia is by no means rare but a diffuse erythrodermia is extremely uncommon. The blood picture in all the cases is of identical character, viz., some increase in the total number of leucocytes with a very well marked increase, both relative and absolute, in the number of lymphocytes. In all the cases, the lymphocytes were of the small variety, while the degree of anaemia has been very slight.

The cases which have been examined at autopsy have all shown the typical appearances of lymphadenosis, which term is preferable to lymphatic leukaemia as, in these cases, the

blood was not flooded with a huge number of white cells.

"The liver always showed the presence of peri-portal collections of lymphocytes and never any sign of diffuse myeloid metaplasia as is the case in myelosis.

"The glands showed only increase in number of lymphocytes without myeloid metaplasia but with some degree of infiltration of the fibrous capsule by lymphocytes.

"The changes in the spleen were confined to the region of the Malpighian bodies and did not involve the pulp as is always the case in the myeloses.

"These cases, thus, show all the typical appearances of chronic lymphadenosis but their genesis cannot be stated more definitely than has been done by innumerable writers in the past.

Sternberg (12) contended that the large celled type of lymphadenosis is a special morbid process and applied the term leuco-sarcomatosis to it, while the small celled form was regarded as being a true leukaemia on account of the absence of infiltration of the tissues and of atypical growth. "The present cases certainly belong to the second group both on account of the absence of infiltration and of the small type of

lymphocytes which were found.

It has been suggested that the total number of leucocytes is too low in these cases to enable a diagnosis of lymphatic leukaemia to be made with certainty, but if the disease be regarded as lymphadenosis, i.e. a proliferation of the cells of the lymphopoietic organs with a varying degree of change in the composition of the blood picture, there is no great difficulty in recognising the present cases as being aleukaemic lymph-adenoses i.e. cases with little escape of lymphocytes from the essential hyperplastic lymphopoietic organs.

The frequency of atypical manifestations in association with aleukaemic lymphadenosis has long been known. (Naegeli)

The age incidence of the cases is distinctly that of ordinary lymphatic leukaemia, the acute form of which is seen only in children while the chronic form affects almost entirely middle age.

The suggestion that the disease in these cases originates in the skin necessarily implies a belief in the infective nature of the leukaemias which is, of course, supported by the experimental work of Ellermann (13) on leucoses in fowls, which is a condition due to a filter-passing virus, but

its identity with the similar condition in man is far from certain.

The conception of leukaemia as a truly neoplastic process as supported by Banti (14) is difficult to reconcile with the histological appearances and with the great length of the history of these cases: if such a view were accepted, it would be necessary to regard the neoplastic process as a benign, not as a malignant one as was done by Banti.

Summary:

Two cases of chronic aleukaemic erythrodermia are described in detail and brought into comparison with others found in the literature. The rarity of the condition is pointed out and its identity with aleukaemic lymphadenosis is made clear.

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