shed is surrounded by a fluid-like oil coagulation is prevented. By watching the corpuscles under the microscope he has shown that they become flattened and irregular; they then lose their granules, or these retire to one part of the cell, leaving the rest clear. Such changes are better marked in the coarsely granular corpuscles than in the finely granular ones. He regards the shedding out of the fibrin ferment which accompanies these changes rather as a process of metabolism than of disintegration. I am inclined to adhere, however, to the old word disintegration, as what goes on is something different from what occurs in normal metabolic processes. As I pointed out some years ago, the disappearance of the granules from the cells inevitably suggests a comparison between the process and secretion, in which the shedding out of a ferment by secreting cells is accompanied by the disappearance of the granules which indicate the existence of its zymogen, or mother substance. This idea has since been verified by the discovery of the zymogen of fibrin ferment, and so strongly has the resemblance to secreting cells been recognised that some have gone so far as to speak of the coarsely granular or eosinophile cells as unicellular glands having a different origin and function from the neutrophile or finely granular cells which appear to be the principal phagocytes. Hankin⁸ has arrived at the conclusion that the alexines or protective proteids which confer bacteria-killing power on blood serum originate from the eosinophile cells, and this bears upon our present question because of the similarity, or it may be identity, between fibrin ferment and the alexines. There is, however, evidence that cells which are not eosinophile may yield fibrin ferment. The explosive cells in crustacean blood are hyaline, not eosinophile. (Hardy.) According to Sherrington, too, the eosinophile cells are not fibrino-plastic. I think it would be premature to lay down any definite rule as to which group of corpuscles fibrin ferment comes from; and further, seeing that substances which produce coagulation can be obtained from cells as diverse as those in the thymus, brain, liver, testis and kidney, it seems very probable that both kinds of leucocytes in the blood may give rise to fibrin ferment; they both consist of protoplasm, and the main proteid constituent of all protoplasm is nucleo-albumen.

During these lectures I have from time to time stepped aside from my subject proper in order to point out certain practical bearings which I considered to be of importance. I wish that I had had time, and still more the necessary experience, to have done so more fully. If, however, any grains of usefulness are scattered through what I have said, there is no doubt that others will pick them up and work out their practical side. In connexion with blood coagulation and thrombosis I need not stop to point out the immense importance of a correct knowledge of this subject to the pathologist, and I will content myself with two remarks only on its practical aspects. The first of these is to point out the great resemblance between the phenomena observed in the animals in the experiments described and those cases of pulmonary thrombosis which are occasionally seen in the human subject. One can hardly doubt that here we have to deal with poisoning by the same material. Professor Gerald Yeo was witnessing some of our experiments a few days since, and he described to me a case he had had in King's College Hospital.⁹ It was one of amputation of the breast for cancer, and the wound was perfectly aseptic; but ten days after the operation, without any warning, the patient died suddenly with great dyspnoea. Examination of the brain revealed no lesion, but at the necropsy a firm fibrinous clot was drawn like a tree with its branches from the pulmonary artery. The dyspnoea in this and similar cases points to the cause of death in the lungs themselves rather than in the respiratory centre; this difference is easily explicable on the ground that the dose of poison enters the circulation more slowly than in our experiments where it is injected. The second practical point which I wish to emphasise is a word of warning. When I have seen animals die in a few seconds, as though by a lightning flash, after a dose of five cubic centimetres of this poison, which could not have contained more than a few centigrammes of the material, I feel very loth to urge that any practical use of such substances should be made in the human subject, either for the stoppage of hæmorrhage or for the production of a clot in aneurysms. The cure would in such instances be worse than the disease.

⁸ Centralblatt für Bacteriologie und Parasitenkunde, Bd. xii., Nos. 22 and 23.

⁹ Many similar cases will be found in Sir J. Fayrer's Clinical and Pathological Observations in India.

A CASE OF ACROMEGALY.

By J. MACKIE WHYTE, M.A., M.B. EDIN., M.R.C.S. ENG.,
PATHOLOGIST TO THE DUNDEE ROYAL INFIRMARY.

THE subject of the following notes first came under the observation of Dr. Alexander Campbell and myself in September, 1890, on account of ingrowth of nails on both her great toes. My description was taken down at that time, but, as it has recently been verified and slightly added to, I shall speak of her as she is now, merely premising that no alteration of any importance has occurred during the past two years. She is a domestic servant, single, aged twenty-seven, and enjoyed good health, being strong and fit for her work till 1886. Her family history throws no light on the case. The mother is alive and healthy, of slight build, and below the medium size. The father died of paralysis five years ago, aged seventy. The maternal grandfather lived to be eighty years of age; the maternal grandmother died of "dropsy," aged fifty. The paternal grandparents died in old age. A sister and two brothers are alive and healthy; the youngest brother died of typhoid fever twelve years ago. From her personal history syphilis and alcoholism can be absolutely excluded, and her surroundings have always been favourable to health. Fig. 1, engraved from a photograph taken in 1884,

FIG. 1.

Engraved from a photograph taken in 1884 before onset of illness.*

shows her to have been then rather slim in build, with a bright expression, thin lips and other features, and small, well-shaped hands. About the time of onset of her present illness, namely in 1886, she was subject to certain depressing emotions. In that year she observed that she became more easily fatigued, and in the course of a few months great physical changes occurred. Menstruation, which had begun at fourteen and been normal hitherto, became scanty and in six months finally ceased. Her body became stouter, so that with her ordinary clothing breathing was greatly impeded. To get up from the kneeling posture she had sometimes to roll over on her side. Her face changed to such an extent that friends who had not seen her for some time failed to recognise her. The size of her gloves increased steadily from No. 6½ to No. 8, and her shoemaker was troubled with the difficulty of procuring "tops," remarking with somewhat ungallant candour that he had never known a woman to have so large a foot. The actual increase in the size is given as from No. 4 to No. 7. Profuse perspirations, violent headaches occipital and frontal, and a feeling of stiffness as if she was encased in starch were amongst her troubles. The various changes seem to have been coincident, although the muscular weakness first attracted her own attention. In spite of her physical disability she managed to keep her "places," being possessed

of an agreeable disposition and an indomitable spirit of independence.

Present condition.—Her general configuration is stout and clumsy; her expression when speaking is intelligent and cheerful, otherwise (see Fig. 2) heavy and dull. One is struck by the large size of her head and face, and also of her hands. Height, 5 ft. 4 in.; weight, 11 st.

Head and face.—The head is much larger than normal (see measurements below); the occipital protuberance is pronounced; the lambdoidal suture is well marked, but the other sutures and protuberances are not specially prominent, with the exception of the supra-orbital ridges, which give a receding aspect to the brow. The hair is abundant, dark-brown and of normal quality; the ears are normal in size, the tissue perhaps is thickened; the complexion is pale; there are shallow horizontal wrinkles on the forehead. The eyelids are heavy; the nose is straight and large, with a slight upward curve near the tip; the alæ are thick; the lips are thick, the lower one being heavy and hanging; the mucous membrane of the lips is normal; the lower jaw is large and the chin double; the angles of the inferior maxilla are more obtuse than normal; the lower teeth lie in normal relation to the upper; the teeth are very bad and have been so since she was sixteen years of age—there are small gaps between them. There is a small metal plate in the upper jaw

FIG. 2.

with four incisors and the left canine; this was put in eight years ago and suited; now it is loose and there is room for another tooth beside the right canine. The hard palate is flat and extensive; the soft palate and pharynx are flat and extensive in proportion. The tongue is broad (6 cm.) but not markedly thicker than it should be; it is slightly cracked and fissured and indented by the teeth at the edges; the patient feels as if it were uncomfortably big, especially when speaking. She has had this feeling since she had an inflamed sore-throat three years ago. The voice is rather husky; she was a fairly good singer, but now the voice has deteriorated in quality and also in range of pitch (being lower by two notes); the pomum Adami is not prominent; the thyroid gland is larger than usual, both lobes being easily felt.

Trunk.—The antero-posterior curvature in the dorso-cervical region with its concavity to the front is very marked; also in the upper dorsal region there is slight right lateral curvature. The patient is very quickly tired if she tries to hold her head erect. The ribs are broad, the costal cartilages and sternum are normal; the circumference at the nipples is thirty-five inches and a half on expiration and thirty-seven inches on moderate inspiration; the pelvic bones seem normal; the breasts are poorly developed and have always been so; the cardiac dulness is normal; there is a small area of dulness, the size

of a crown piece, behind the manubrium and the first left costal cartilage.

Upper extremities.—The clavicles are thick and long; the scapulæ and humeri seem normal; the arms are well-formed down to the wrists; the wrists, and especially the hands, are greatly enlarged; the hands are very inelegant (see Fig. 3), being thick and broad; fulness is specially developed in the hypothenar eminences; the markings on the skin are normal; the veins on the back are easily seen; the thickening seems to involve the bones as well as the subcutaneous tissue, the lower ends of the radius and ulna participating; the fingers have a stumpy appearance, not tapering, or only very slightly, as shown by measurement; the nails of the fingers are flattened out, slightly curved for-

FIG. 3.

wards in the terminal third and much broader in proportion to length than is normal; the thumbnail is an ellipse with the long axis transverse; the nails used to crack unpleasantly, the outer layer peeling off; there is no abnormality in consistence during the past two years.

Lower extremities.—The right knee is occasionally painful, especially after kneeling; a little crackling is felt in the joint on flexion; recently there was an attack of housemaid's knee on the left side; the bones and other tissues down to the ankles are increased in bulk; the feet are comparable to the hands in size and clumsiness (Fig. 4); there are no callosities

FIG. 4.

and there is a general thickening and enlargement. The big toes gave much trouble till operated on in 1890, through ingrowth of the nails; this, of course, was owing to the difficulty in getting large boots. The toes have a compressed appearance and would be square on section; the nails are like little ellipses with the long axis transverse and are embedded in the skin; there is a tendency to flat-footedness.

Muscular system.—This is to all appearance well developed; the grasp of the hands is very much less than normal; the muscles at the elbow and knee seem about normal; lifting heavy weights gives a sensation of strain in the upper dorsal

region and up the back of the neck; the general activity is greatly impaired; the gait is clumsy.

Nervous system.—The special senses are normal, with the exception of sight. Dr. M'Gillivray kindly examined her eyes for me, and he gives the following exhaustive report: "Nov. 14th, 1890.—The patient feels pain in the eyes, with frequent attacks of frontal headache; she complains of dimness of vision and great difficulty in reading, as the letters jumble up; she first noticed that her sight began to fail about a year after the onset of her present illness; up to that period her eyes had been perfectly well. There is slight hyperæmia of the palpebral conjunctiva and thickening of the eyelids in both eyes; there is no exophthalmos; the pupils are normal in size and react well to light and accommodation; the movements of the eyeballs are normal except for a jerky rotatory nystagmus when the patient tries to look to the right and left, but less marked in the former direction; pressure backwards on the eyeballs conveys no cushion-feeling to the fingers and causes no pain to the patient; tension is

normal. Vision: Right and left eye = $\frac{6}{9}$ c. + 1 D. cyl. = $\frac{6}{5}$.

She reads Jaeger 1 at eighteen centimetres with the right eye, and Jaeger 1 at twenty-one centimetres with the left, for a few seconds only. The range of accommodation is very limited. With the above correction the range of accommodation is improved. At twenty-five centimetres there is marked insufficiency of convergence; there is no diplopia; the fields of vision are normal, as also are colour and light sense. Ophthalmoscopic examination shows no abnormality. Feb. 10th, 1892.—The patient was re-examined. There is no alteration in the above symptoms except that the patient thinks the vision is improving and the headaches are less frequent and not so severe. Spectacles were not prescribed."

General sensibility.—The patient experiences a sensation of numbness in the fingers in the morning, lasting from ten to thirty minutes. The fingers feel dead, but do not change colour. The sensation of touch is then greatly impaired or lost. On the outer side of the right thigh from above the knee to near the hip she experiences occasionally a tingling sensation, especially if tired after standing. Slight pressure causes a painful feeling at those times, but firm rubbing gives relief. The sensation is not that of "sleeping." She cannot bear tight bands about the body. She has, as noted in the history, been a martyr to headaches, but these have been much less severe during the past year and generally yield to antipyrin. She can go to sleep at any time, day or night. Since the onset of her illness she has been very nervous, being easily startled and being then affected with palpitation and a breaking out of perspiration. There is no mental deterioration.

Skin &c.—The skin is rather coarse. In the region of the neck there is a large number of small warts, varying in size from that of a pinhead to that of a millet seed (they seem to be simply cutaneous); perspiration is constant, especially in the palms of the hands and the soles of the feet (it has become rather worse during the past year); the appetite is normal, but temporarily affected by headaches; thirst is great, but the urine is normal in quantity and is free from sugar and albumen; the pulse is 60, regular, and of fair strength; the heart, lungs and other organs are normal.

Measurements in centimetres.—Circumference of head, 57.5 cm.; occipito-frontal diameter, 18.5 cm.; bi-parietal, 15 cm.; bi-mastoid, 11.5 cm. Length of ear, 6 cm. From the roots of the hair to the tip of the nose, 13 cm., of which the nose measured 6 cm. Breadth of nose at alæ, 5 cm. Inferior maxilla from angle to angle, 21.5 cm.; length of ascending ramus, 3.2 cm. Circumference of neck at the thyroid isthmus, 36.5 cm.; length of the sternum, 21 cm. Circumference between umbilicus and xiphoid, 80 cm. Distance between anterior superior spines, 28 cm. The clavicle of the right arm, 15.5 cm.; tip of acromion to point of the mid-finger, 67 cm.; circumference of arm at top, 31 cm.; at middle, 29 cm.; above elbow, 26 cm.; at elbow, 28 cm.; circumference at mid-forearm, 23 cm.; at wrist, 18 cm.; length of hand from lower wrist-crease to tip of mid-finger, 18.5 cm.; circumference at metacarpo-phalangeal joints, 23 cm.; thumb length, 6.4 cm.; circumference, 8 cm.; index circumference at root, 7.8 cm.; at first joint, 7.8 cm.; at second joint, 6.8 cm. Right lower limb: Length of femur, 45 cm.; vertical diameter of patella, 6.5 cm.; transverse diameter, 7.3 cm.; circumference of knee, 37 cm.; of calf, 37 cm.; length of tibia, 35 cm.; circumference round malleoli, 26 cm.; over heel and front of ankle, 32.5 cm.; at first metacarpo-phalangeal joint, 23.5 cm.; length of foot, 25.5 cm.; circumference of great toe at root, 9 cm.; at nail, 9.5 cm.

Remarks.—The case is clearly one of acromegaly, typical

in its onset and its present aspect. The diagnosis could be made with positive certainty from the history alone, the alterations in fit of gloves, boots and tooth-plate being conclusive. This patient is not so extreme a case as are many that have been described, the absence of prognathism to any great extent being of importance in allowing a natural expression to remain. The comparatively short duration of the malady and the present arrest of its progress are worthy of attention in this respect. It is easy to see how this disease remained unrecognised till Pierre Marie pointed out the features which distinguish it. Such a patient as the above goes on long enough satisfied with her friend's diagnosis that she is getting stout &c., simply taking medical advice on one or two common symptoms. Further, there is a misleading symmetry about the enlargements in most cases. The tongue, for example, is absolutely large and is indented by the teeth, but it lies fairly easily in the very capacious mouth. The facial part of the head is in proportion to the cranial, and the neck and trunk are correspondingly stout. The hands and feet again, whilst large, both absolutely and relatively, in comparison to the rest of the limbs, are, as Marie said in his original paper, in themselves regularly formed. Still, an attentive examination of their shape, especially the want of proportion between breadth and length and the "sausage" look of the fingers, makes one see that they would be unnatural even to a giantess. As the total number of cases of acromegaly as yet described is under fifty, I hope that the above record will have a certain value.

Airlie-place, Dundee.

THE CHOLERA EPIDEMIC IN RUSSIA.

BY FRANK CLEMOW, M.D. EDIN. &c.

NO. II.—IN THE CAUCASUS.

GEOGRAPHICALLY the great mountain chain of the Caucasus is generally considered to be the dividing line between Asia and Europe; but administratively the whole of the Caucasus, including a considerable portion of the steppe lying to the north of the mountain chain, is included in Asiatic Russia. In the last article the cholera epidemic was traced throughout the Central Asian provinces and Siberia from its first introduction to Russian soil at Kaachka. In the present it is proposed to deal with it in the Caucasus in a similar manner. The Caucasus occupying the stretch of country between the Black and the Caspian Seas has a superficial area but little smaller than that of France or Spain. It is continuous on the north with the country of the Don Cossacks, from which it is separated by two small rivers; whilst on the south another river—the Araks—forms the natural boundary between this part of Russia and Persia. The country is further clearly divided into two parts, not only by an administrative division, but by marked geographical differences, which played an important part in affecting the relative intensity of the cholera epidemic in the two districts during the past summer. The Northern Caucasus is, for the most part, a flat but fertile steppe, watered by few and sluggish streams, and in part by artificial irrigation canals; but at its southern edge, as it approaches the mountainous region of the Southern Caucasus, the character of the country changes. It becomes sub-mountainous, with rapid streams flowing into the channels of the rivers Terek and Kuban. The Terek flows into the Caspian Sea, the Kuban into the Black Sea; neither receives any tributary from its northern bank, both being fed entirely by the mountain streams from the south. The Southern Caucasus, or Transcaucasia, is in many respects in marked contrast with the northern division of the country. Briefly, it consists of a series of immense mountain chains, culminating in the peaks of Elbruz and Kazbek, and watered by innumerable rushing streams, which mostly unite to form the channels of the River Kura, flowing eastward into the Caspian Sea, and of the River Rion, which empties itself into the Black Sea. That elevation has an important influence in modifying the intensity of a cholera epidemic has been very generally admitted, and is to a great extent supported by the behaviour of the present epidemic in the two divisions of the Caucasus. In general terms the flat, low-lying plains of the Northern Caucasus were very much more severely visited than the high and mountainous regions of Transcaucasia. This is clearly seen from the figures given below. In the three northern provinces, out of every 100,000 inhabitants 2390 were attacked by the disease, whilst in the southern only 1831 suffered,