conjunctivitis, and the discharge contained *C. diphtheriae*. The virulence of the organism was not determined.

Case 7.—Admitted to the military hospital suffering from impetigo of the chin of fourteen days' duration. Ten days later he developed bilateral purulent conjunctivitis. White membrane was seen on the edge and inside of the lower eyelids two days later. Swabs from eyes and skin showed the presence of *C. diphtheriae* (gravis). The patient was afebrile. At the isolation hospital 60,000 units of antitoxin were given and local treatment was applied to the eyes. Skin and eyes cleared up completely in about four weeks.

Case 8.—This man had impetigo of the face and neck, and two weeks after admission to the military hospital he developed rhinitis. A nasal swab was reported positive for *C. diphtheriae*, but the organisms were avirulent. After transfer to the isolation hospital skin swabs contained virulent *C. diphtheriae* (gravis type I), but throat and nose swabs were negative. The skin condition improved rapidly after the injection of 10,000 units of antitoxin.

Case 9.—Admitted to the military hospital with sycosis barbae. Three weeks later virulent *C. diphtheriae* (gravis type I) were isolated from the skin.

Case 10.—A case of impetigo of the face, neck, and left ear which developed a yellowish-white membrane on the skin behind the left ear one month after admission to the military hospital. A swab from this membrane was found to contain avirulent *C. diphtheriae*. At the isolation hospital only diphtheroids were found in swabs from the skin until one month later, when virulent mitis organisms were reported, presumably due to cross-infection. The skin healed in three weeks.

Case 11.—Admitted to the military hospital with seborrhoea capitis. Three weeks later conjunctivitis developed and virulent *C. diphtheriae* (gravis) were found in the purulent discharge. Swabs taken at the isolation hospital were negative, and the conjunctivitis soon cleared up. 20,000 units of antitoxin were given.

Case 12.—Eleven weeks after admission to the military hospital for treatment of impetigo this patient developed a mild purulent conjunctivitis. The discharge contained avirulent *C. diphtheriae*. At the isolation hospital eye swabs were negative, but throat and nose swabs were positive on two occasions within a week of admission.

Case 13.—Admitted to the military hospital as a case of impetigo, this patient was swabbed and found to have *C. diphtheriae* (gravis) on the skin, but the organism proved to be avirulent.

Case 14.—This man had impetigo of the chin and face three weeks before and a sore throat two days before admission to the military hospital. Throat and skin swabs contained virulent *C. diphtheriae*. The skin persisted positive after the patient had been transferred to the isolation hospital, but swabs from the throat and nose were negative.

Case 15.—This man had impetigo for one month before admission to the military hospital. Five days after admission he complained of sore eyes, and his left eyelid was found to be scabbed. A swab from the eye contained virulent *C. diphtheriae*. At the isolation hospital throat and nose swabs contained virulent organisms of the same type as those found in the eye.

Case 16.—Admitted to the military hospital with sycosis barbae of nine months' duration, this man two months later developed purulent conjunctivitis, and *C. diphtheriae* was found in a swab from the eye. The organism proved to be avirulent.

Case 17.—Five days after admission to the military hospital for treatment of impetigo of the face a blister appeared on one knuckle of this man's right hand. A slough developed, and was found to be infected with virulent *C. diphtheriae*. The infection persisted after transfer of the patient to the isolation hospital, and on two occasions virulent organisms were found in the throat and nose without clinical evidence of infection.

Case 18.—This man had impetigo for three weeks before admission to the military hospital. After two weeks' treatment only slight crusting remained. Following contact with cases which proved to be diphtheritic infections *C. diphtheriae* were found in throat and skin swabs.

Case 19.—After three months' treatment for impetigo in the military hospital a lesion thought to be keloid developed on the neck. A scraping from the skin contained virulent *C. diphtheriae* of gravis type. Swabs at the isolation hospital were all negative, and the skin healed quickly after diphtheria antitoxin had been given.

Commentary

General Features.—No toxæmias could be ascribed to the action of diphtheria bacilli in any of these cases. No paralysis ensued. Membrane was seen in three cases of cutaneous infection (in one of these the diphtheria bacillus isolated was avirulent) and in one conjunctival infection. In all the other cases the lesions had the usual characteristics of the skin condition originally diagnosed. The average length of stay in the military

hospital before transfer to the isolation hospital was four and a half weeks. The average in the latter hospital was six weeks.

Treatment.—In the isolation hospital diphtheria antitoxin was injected intramuscularly in every case. The other treatment was that usually given for the particular cutaneous or conjunctival infection.

Infectivity.—It is of interest to note that in addition to the 19 cases mentioned above there were admitted from the military hospital during the same period 18 other cases of diphtheria, including 7 of the staff. These 18 cases were faucial infections in all but one instance, the latter being a case of rhinitis.

Conclusion.—Recognition of cutaneous diphtheria among patients with a variety of skin infections suggests the need for more frequent bacteriological investigation of such cases.

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ACUTE ALEUKAEMIC MYELOID LEUKAEMIA

BY

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The occurrence of acute myeloid leukaemia in the aleukaemic phase during adult life is rare enough to make the following cases worth reporting.

Case I

A man 63 years old, a window-cleaner by trade, was admitted to the Royal Hospital on Sept. 13, 1942, with a history of a severe sore throat and difficulty in speaking for the past two weeks. These symptoms became progressively worse, and one week before admission he complained of severe malaise and generalized pains over the body; the temperature was then found to be 103° F. Five days before admission a haemorrhagic rash appeared on the legs and arms; this became purple after 48 hours. On the day of admission he complained of headache, shortness of breath, and stiffness of the neck. During the illness he became increasingly drowsy, but could be roused and was quite rational. He had been on a course of sulphanilamide (1 g. four-hourly) and vitamin C (150 mg. daily). Past and family history revealed no significant facts. Bowels and micturition had been normal; there was no loss of weight.

On admission the patient was very drowsy, but roused easily; temperature 102° F., pulse rate 94, and respiration rate 28 per minute. The legs showed a number of papulo-macular haemorrhagic spots with small yellow vesicular centres and irregular edges, located mainly over the shins; the size varied considerably, the largest being 1 cm. in diameter; there was no fading on pressure. The arms were covered with red indurated nodules larger than those observed on the legs, up to 2.5 cm. in diameter, chiefly localized around the elbow, resembling erythema nodosum and not showing the vesicular centre present in the leg lesions. There were also a few macular spots on the back and abdomen. The limbs presented cogwheel rigidity and the joints were very tender on movement. In spite of the increased respiration rate there was no clinical evidence of abnormalities in the respiratory system. Heart and vessels normal; blood pressure 120/70; spleen and liver not palpable; no glandular enlargement. Pupils and fundi normal; all reflexes normal; tongue and pharynx coated with dried mucus; breath fetid.

On the day after admission the patient developed herpes labialis, which later became haemorrhagic. Though remaining rational he became progressively more drowsy and dyspnoeic; the pulse rate rose to 120 and the respirations to 40 a minute. Death took place on Sept. 17.

The laboratory investigations carried out in the short period of time during which the patient was under observation showed: No abnormalities in the urine except a large amount of urobilin; haemoglobin, 62%; red cells, 3,940,000 per c.mm.; mean diameter of the red cells, 7 μ ; white cells, 2,800 per c.mm.—polymorphs 18%, eosinophils 1%, mononuclear cells 81%. Some of the mononuclear cells were typical lymphocytes, but the great majority were of primitive type; one normoblast was seen while counting 100 white cells; platelets in the films appeared to be very scanty.

At first sight the primitive cells were taken to belong to the lymphatic series; but on account of the presence of azur granules in the more immature forms it was decided to investigate the case more fully by means of sternal puncture and the peroxidase reaction. Sternal puncture, performed on Sept. 15, showed: primitive cells

(haemocytoblasts) 42.5%, myeloblasts 35.5%, premyelocytes 15%, myelocytes 0.5%, polymorphs 1.5%, lymphocytes 1.5%, monocytes 0.5%, basophils 1%, plasma cells 0.5%, normoblasts 1.5%. About 60% of the nucleated cells in the bone-marrow films showed the presence of peroxidase-positive granules. On Sept. 16 the white cells numbered 2,500 per c.mm., of which 85% gave positive peroxidase-stained granules. The differential count showed: haemocytoblasts 10%, myeloblasts 32%, premyelocytes 45%, myelocytes 3%, polymorphs 6%, lymphocytes 4%; two normoblasts were seen while counting 100 white cells.

Post-mortem examination on Sept. 17 revealed complete consolidation of the left lung, a few haemorrhages in the left parietal pleura and into the mesenteric fat, spleen slightly enlarged and soft, and bone marrow brownish pink in colour; no other macroscopic abnormalities. The previously described lesions of the skin of the limbs were still present but had become more purple, and those of the legs had lost the vesiculation in the centre.

Histological sections from the skin lesions showed infiltration of the corium with leucocytic cells surrounded by a zone of haemorrhage. The kidney, liver, and spleen contained a very few scattered foci of leucopoiesis. The lung showed the alveoli filled with fibrinous accumular exudate with little inflammatory reaction.

After the report on this case had been submitted for publication, a second case presenting similar haematological features was seen by one of us (B. L. D. V.).

Case II

A man 41 years old, who had been complaining of lassitude for two to three months and severe headache for the last fortnight, presented the following blood picture when first seen: haemoglobin, 34%; red cells, 1,640,000 per c.mm.; white cells, 10,200 per c.mm.—haemocytoblasts 16%, myeloblasts 42%, myelocytes 2%, polymorphs 14%, lymphocytes 25%, monocytes 1%. Except for marked pallor nothing abnormal could be detected on general examination: spleen and liver were not palpable, and there was no glandular enlargement. Sternal puncture showed a picture very similar to that of the peripheral blood, possibly through the marrow sample being heavily contaminated with peripheral blood. The primitive immature cells were almost identical with those observed in the previous case, and were correctly diagnosed only by means of the peroxidase stain.

White cell counts during the patient's stay in hospital showed variations between 6,800 and 18,600 per c.mm. He was given a large blood transfusion when his red cells reached the level of about 1,000,000 per c.mm., and was sent home, his general condition being much improved. When last seen his white cells had risen to a level of 50,000 per c.mm. with over 80% of very primitive mononuclear forms.

This case also, although not strictly comparable to the first because of the rise in white cells following the transfusion, when first seen in the aleukaemic phase presented a blood picture hardly distinguishable from that of lymphatic leukaemia without the aid of the peroxidase stain.

Conclusion

Both these cases are of interest in showing the "hiatus leukaemicus" of Naegeli, consisting of the presence in the peripheral blood of primitive cells and mature forms with few or no intermediate stages. The acuteness of the leukaemic process coupled with a very low white cell count as found in Case I is an uncommon feature. The bone marrow showed definite and marked leukaemic change, but other organs presented little leukaemic infiltration. The low white cell count may have been due either to the minimal leukaemic involvement throughout the body or to the destruction of the immature circulating cells by the spleen, itself not yet involved in the process.

It is worth noting that in both cases the peroxidase stain was essential for the correct classification of the immature cells, which might at first sight have been thought to belong to the lymphatic order.

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S. M. Feinberg and others (*Ann. intern. Med.*, 1943, 18, 311), recording 8 cases of allergic reaction to injected liver extract, suggest that this type of allergy is not uncommon. Their tests indicated that it is neither a species specificity nor an organ specificity involving the usual protein antigen. They believe that the allergic response is to "a special fraction of an organ (liver) not bound with the ordinary protein fractions but associated with the anti-anaemia fraction."

THE DIETARY FACTOR IN REPRODUCTION AND LACTATION

BY

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Any investigation into the causes of high infant mortality must take account of nutritional factors. Direct proof of the extent of their influence on human beings is hard to obtain, but by means of experiments on small animals, in which environment and diet are strictly controlled, it is possible to obtain valuable information regarding the effects of a deficient diet on breeding performance, and the possibilities of remedying the deficiencies by means of suitable supplements.

A recent breeding experiment on rats carried out at this Institute has given results which seem to be of considerable practical importance at the present time. This was a long-term experiment in which the females, mated at 100 days of age after being on their experimental diets from weaning, were carried through three successive matings. The object was to determine the effect on reproduction in rats of supplementing a poor human dietary by additions of inorganic calcium and vitamin B₁, given separately and in conjunction; to test the effect of dried yeast as a source of vitamin B₁ and other factors; and further to test the influence during the breeding period of an increased milk intake along with these supplements.

The basal diet was that employed in the growth tests on rats recently reported (*Journal*, 1943, 1, 161), and represents the average diet of households spending from 3s. to 7s. per head weekly on food. This diet contains milk equivalent to a weekly intake of 3 pints per person, and from the date of mating each group of rats was subdivided, half the animals, both male and female, receiving thereafter a doubled supply of milk.

Table I gives a brief summary of the results of the breeding test, combining the figures for three matings and rejecting animals which failed to produce three litters within six months. It is our practice to reduce all larger litters to 8 on the day after birth—a fact to be remembered in regard to the number of rats reared per litter.

TABLE I.—Showing Breeding Results for Three Consecutive Matings

Group	Dietary Supplements	Litters Born and Litters of 8 Reared	Aver. No. Born Alive per Litter	Aver. No. Born Dead per Litter	Aver. No. Reared per Litter Born	Aver. Weaning Wt. per Rat (Litters of 8) (g.)	Weights of Does	
							At First Mating (g.)	After Third Lactation* (g.)
IIA	—	24/4	6.9	0.8	5.4	33.6	185	228
II	Milk	30/14	8.8	0.5	6.3	39.1	186	255
IVA	Ca	27/13	8.6	0.3	6.9	35.1	202	239
IV	Ca + milk	21/14	9.2	0.5	7.4	40.5	196	273
IA	Aneurin	27/15	8.0	1.9	6.2	32.2	186	214
I	Aneurin + milk	27/14	8.7	0.4	6.8	38.7	185	243
IIIA	Ca + aneurin	33/17	7.9	0.6	6.5	36.5	193	258
III	Ca + aneurin + milk	27/18	9.9	0.4	7.1	41.9	186	268
VA	Ca + yeast	30/25	9.8	0.6	7.4	40.9	206	266
V	Ca + yeast + milk	33/23	9.8	0.8	7.0	45.8	209	302

* After rearing litters of 6 to 8.

Effect of Extra Milk

Comparison of the results for the various pair-groups shows at once the beneficial effects of the milk supplement. This is particularly evident in all groups in the weights of the young at weaning and in the weights of the does after lactation. The milk supplement has increased the average weight of each young rat in litters of 8 by approximately 5 to 5½ g., making an increase of 40 to 44 g. for the litter. At the same time the does, in spite of rearing this greater weight of young, have made a greater increase in their own weights. The milk groups show also in general a higher number of young born alive per litter, and a higher proportion of litters of 8 reared. This is especially marked in the basal group, in which the number of young per litter born alive is raised from 6.9 to 8.8 by