4. Radio-phosphorus is of no value in the treatment of acute leukaemias or of monocytic leukaemia.

5. "Hodgkin's disease, lymphosarcoma, reticulum-cell sarcoma, and multiple myeloma do not respond as favourably to P³² as they do to x-radiation."

6. The limited evidence available suggests that radio-phosphorus is not likely to prove to be a satisfactory agent for the treatment of carcinoma of the breast, malignant melanoma, lympho-epithelioma, Ewing's tumour, or mycosis fungoides.

However, the work of Kenney (1942) suggests that further clinical trials of radio-phosphorus in lymphosarcoma are desirable.

It seems doubtful whether radio-phosphorus, in the form of *inorganic* phosphate, will stand the test of time even in the treatment of chronic myeloid leukaemia. In his report to the United Nations Atomic Energy Commission on Sept. 23, 1946, Dr. C. P. Rhoads, the Director of the Memorial Hospital, New York, discussed the treatment of chronic myeloid leukaemia and concluded that "a tendency in most institutions is to discard the use of radio-phosphorus and to stick to conventional x-ray as being somewhat safer and more predictable in its results and attended by less hazards to the patient, even though it does cause some illness in the course of treatment."

In conclusion, one can quote again from Dr. Rhoads's report: "To have expected inorganic elements to be picked up so selectively and concentrated so adequately by cancer tissue as compared to normal tissue was a very optimistic hope. I am not surprised that we are somewhat disappointed, but we have a vast field before us. We are beginning to study the selective pick-up by cancer of a vast variety of organic compounds which can be synthesized in the laboratories of organic chemistry to contain radioactive isotopes of a variety of elements. I am very hopeful."

A final aspect of the therapeutic application of radio-phosphorus is the possibility of development of beta-ray applicators using P³², perhaps incorporated in plastics. A report on human skin reactions produced by the external use of radio-phosphorus has been published recently by Low-Beer (1946). "The estimated number of roentgen equivalents dissipated in the first millimetre of tissue is 4.3 per hour per microcurie per square centimetre area." The maximum range of the beta-particles from P³² is approximately 8 mm. in water or unit-density tissue. It is stated that half-value layer measurements have shown that about 48% of the radiation is absorbed in the first millimetre of tissue. "The results of these studies suggest that the use of radioactive phosphorus in the local treatment of certain superficial skin diseases is reasonable."

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Sixteen years have been added to the average life span of Americans was one point made by Dr. James A. Crabtree, acting Surgeon-General of the U.S. Public Health Service, in a recent address. He said that in the problems of communicable disease control, emphasis was shifting from the diseases of early childhood to those of middle and old age. Americans were taking a great interest in public health figures as the result of Selective Service findings, which drew attention to various national health defects. The control of venereal disease was progressing, and the mortality rate had decreased from 15 deaths per 100,000 in 1939 to 10.7 in 1945.

PINK DISEASE: A REVIEW OF 65 CASES

BY

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Pink disease sprang into prominence in medical literature in the early years of the century and seems to have established itself in this country as a not very common but, nevertheless, regularly recurring member of the group of diseases incident to infancy and early childhood. I have reviewed the case histories of patients who attended my out-patient clinic at the Royal Manchester Children's Hospital during the 14 years from 1932 to 1945 to see if any further light can be thrown on the nature of this still somewhat puzzling ailment. During this period 65 infants and young children—27 males and 38 females—suffering from the disease came under my observation. I followed the progress of 48 of these from the time of their first attendance to the end of their illness. The remaining 17 I saw on only one or two occasions, but I ascertained the subsequent progress of 14; the other three I was unable to trace. Of the 62 children whose subsequent progress is known, 53 made a complete recovery and 9 died.

Incidence of the Disease

Year:	1932	1933	1934	1935	1936	1937	1938	1939	1940	1941	1942	1943	1944	1945
No. of cases	3	4	5	4	1	5	3	7	6	6	7	2	5	7

There was a fairly even distribution over the whole period. The drop in numbers in 1936 and 1943 can have no significance where such small numbers are concerned, unless other observers have noted a similar feature.

Month of Onset of the Disease

Month:	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
No. of cases	8	4	6	5	4	6	5	4	7	6	2	5

These figures embrace the whole period and show that there was no demonstrable variation in seasonal incidence. The impression that it is commoner during the winter months can, I think, be explained by the greater severity of the disease, due to intercurrent infection, during that period of the year.

Age of Onset

Age in Months:	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	25	38	50
No. of cases	1	4	3	6	6	9	2	8	7	0	4	2	1	1	2	2	1	1	3	1	1

The figures show a rapid increase from the age of 4 months (the earliest age at which the disease occurred) to the end of the first year, and thereafter a sharp decline. The two children who succumbed to the disease in their fourth and fifth years were quite outside the usual age period in this series. A calculation of the average age of onset in each year throughout the period shows no significant trend in the behaviour of the disease towards an earlier or later susceptible age of choice.

Average Duration for Each Year

Year:	1932	1933	1934	1935	1936	1937	1938	1939	1940	1941	1942	1943	1944	1945
Average duration in months	4.5	3.3	3.7	3.8	—	4.1	3.0	3.7	4.7	3.0	4.6	—	5.3	3.9

In 1936 only one case was seen (duration 3.5 months); two cases were seen in 1943, but the duration of the disease could not be determined sufficiently accurately for inclusion in this table.

The average duration in 46 infants recovering from the disease was four months. The shortest was six weeks, the longest nine months. Here, again, there is no demonstrable change in behaviour, and little to support the impression I had formed that the disease tends to strike at an earlier age and to run a more protracted but milder course in recent years.

Age of onset did not have any significant influence on the duration of the disease, though it may be remarked that all infants whose symptoms persisted for more than five months had the ailment before the end of their first year. The eighth month seems to be the most common, and from the point of view of duration and morbidity the most unfavourable, age at which to contract the disease. The patients came indiscriminately from the whole area (predominantly industrial) served by the hospital, and no pre-dilection for any particular region or district was detected. Nor could social or financial status be shown to have any obvious influence. No evidence remotely suggesting transmission of the disease from one child to another came to light, and the theory of dietetic deficiency or lack of balance received no support from a study of the case histories.

Symptoms

The disease develops insidiously and is usually well established when the infant is brought to hospital. No first-hand observations can therefore be made concerning the onset, beyond noting that there is seldom any history of previous ill-health or serious dietetic mismanagement. A study of the case notes and of the clinical course of the disease as it unfolds itself readily suggests a natural division of the symptoms into two groups: the basic symptoms, constant and persisting throughout the duration of the disease; and the inconstant and variable cutaneous manifestations. The troublesome and dangerous intercurrent infections to which infants suffering from this disease are particularly susceptible are always ready to take advantage of any carelessness in management. There are three basic symptoms: a profound change in temperament, muscular hypotonia, and tachycardia.

The hitherto thriving infant loses his normal contented disposition and gradually comes to present a picture of unhappiness far exceeding in intensity and duration the intermittent fractiousness of teething, to which process the symptoms of the disease are at first too readily ascribed. The unhappiness increases until, finally, he exhibits a continuous, miserable, peevish resentfulness or an active, militant fury against all the agencies of the external world and particularly its immediate representatives, his mother or the examining physician. Muscular hypotonia may be extreme. The art of walking if already attained is lost. The infant slumps spinelessly in his mother's arms, with his face buried in her shoulder. The hypotonia is most characteristically seen in the thigh muscles, which lie flaccidly on either side of the femur and may, in severe cases, have almost a semi-fluid consistency on palpation. A persistently rapid pulse rate of between 144 and 168, rising to 192 under the provocation of examination or other interference, completes the basic pattern of the disease.

Superimposed on this sustained picture of infantile distress, the cutaneous symptoms vary considerably in their time of onset, intensity, and duration. They include the vasomotor phenomena of the extremities, the rash, excessive perspiration, and the special manifestations affecting the buccal and conjunctival mucous membranes. The puffy, pink or bluish red, cold, clammy hands and feet and the sudaminal eruption on the trunk and limbs, criss-crossed by excoriation from the constant scratching, are the two most regularly appearing features. The rash may be transient and of only a few days' duration or may persist for

several weeks. In 12 of 32 infants whose history could be regarded as reliable the rash and swollen extremities were said to have been present from the onset. In the remaining 20 they appeared at varying periods from two to eight weeks after the onset. Profuse sweating is a commonly associated feature which exacerbates the rash and helps to give the moist, cold, flabby, almost reptilian feel to the infant's skin. Desquamation appears from two to three weeks later, and reflects, in the extent and depth of the exfoliation, the intensity of the rash.

Buccal irritation, which is often rather to be inferred from the infant's facial expression of profound disgust or distaste and his obstinate refusal of food and drink than from any obvious lesion of the mucous membrane, may be the cause of most intractable and distressing anorexia, which is overcome only by the exercise of much patient perseverance on the part of the child's attendants. Conjunctival irritation, resulting in photophobia but with no visible evidence of conjunctival inflammation, is the most inconstant of the cutaneous symptoms. It may be entirely absent, barely perceptible, or quite a leading feature of the disease. In two infants it was a most troublesome symptom, persisting for some weeks after the other signs and symptoms had subsided, but finally disappearing without any evidence of organic ocular disease.

In only one case, the child of 4 years, was there an opportunity of getting any subjective account of the symptoms. He complained that his back was always itching and his hands and feet were smarting; he also complained of vague pains in his arms and legs. The majority can give no verbal interpretation of their feelings, but contemplation of the intense erythema and swelling of the extremities to be seen in many sufferers and the exercise of a little imagination should provide a completely adequate explanation for the extreme state of misery to which they are reduced.

The intercurrent infections to which infants suffering from this disease are particularly prone comprise low-grade superficial skin infections; deeper ulcerations in the flexures of the hands and feet when desquamation takes the severe exfoliative form; ulcerative stomatitis, which in two infants culminated in sloughing of the gums, shedding of teeth, and septic bronchopneumonia; and respiratory infections, always badly tolerated owing to the hypotonic condition of the thoracic musculature.

Deaths

There were nine deaths in this series: one infant collapsed quite suddenly in hospital at the height of the disease (1935); one died from the effects of a severe skin infection and widespread furunculosis (1940); two died from septic bronchopneumonia secondary to ulcerative stomatitis (1939, 1940); and three died from acute respiratory infections (1933, 1937, 1938). The exact cause of death in two infants could not be ascertained. Post-mortem examinations performed on two of these infants did not throw any light on the pathology of the disease. This inordinately high death rate is almost entirely attributable to intercurrent infection and underlines the vast importance of most careful precautions against the incidence of these dangerous complications.

Treatment

The precise cause of the disease is as yet unknown and treatment has been symptomatic, with special emphasis on prevention of secondary infections. It is generally agreed that home nursing is the method of choice. The enhanced dangers of infection in hospital (unless strict cubicle nursing is feasible), the impossibility at present of nurses devoting the necessary time and attention to feeding and maintenance, and the increase in misery and impotent fury, and

the consequent increase in tachycardia, brought about by separation from familiar surroundings and perhaps frequent changes of attendants, all weigh heavily in favour of nursing the infant at home unless circumstances make this quite impossible. However exacting the task the mother should be persuaded to make the extra effort. It should be explained to her that in no disease is patient devotion to the interests of the child better rewarded in the end.

Intensive parenteral vitamin or liver therapy was not employed in this series. A high vitamin intake has been advised as a measure of protection against superimposed infection rather than from a predilection for any particular theory of causation. The main principles in management are: scrupulous attention to bodily hygiene, particularly when desquamation is in process; most careful segregation from any human source of nasopharyngeal or respiratory infection, and immense patience in feeding—all food should be boiled or cooked and served as cold as possible (sometimes the only way food or fluid will be taken at all), and food should not be forced into the mouth because of the danger of injury to the buccal mucous membrane and subsequent stomatitis.

The judicious use of sedatives and the local application of such soothing and cooling preparations or physiotherapeutic measures as seem to bring the greatest relief to the patient without causing maceration of the tissues must be a matter of individual experiment and ingenuity. There is no single royal road to success in easing the intense discomfort which is often the most harrowing feature of the disease.

Summary

A review of 65 cases of pink disease is presented. The progress in 62 was ascertained, 53 completely recovered, and nine were fatal.

The incidence, age of onset, and duration of the disease are given.

The symptoms are divided into two groups, and these are discussed.

Treatment and the prevention of secondary infections are dealt with, and the advantages of home nursing are emphasized.

PELLAGROUS ENCEPHALOPATHY

BY

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The following account deals with a deficiency syndrome which occurred among prisoners of war in Singapore. As the title indicates, the clinical manifestations suggested a brain lesion: the only pathological support for this contention was the naked-eye appearances of the brain and spinal cord at the necropsies on the fatal cases. No histological examination was possible. The syndrome occurred in the form of a comparatively small outbreak after large epidemics of vitamin B₁ deficiency resulting in neuritic and oedematous beriberi and Wernicke's encephalopathy, and later epidemics of B₁₂-complex deficiencies giving rise to angular stomatitis, glossitis, scrotal dermatitis, pellagra dermal lesions, retrobulbar neuritis, and the painful-feet syndrome. So far as I am aware, no such outbreak as this has been previously reported.

This neurological disorder was remarkable for the appearance of spastic paraplegia, and for the sake of description and recognition among the medical officers of the camp it was termed the "spastic syndrome." The initial illness varied in severity from a state of deep coma to some effects so slight as to be recognized only by the existence of extensor plantar responses. The residual symptoms similarly varied from a persistent spastic paraplegia so severe as to disable walking to a recovery so complete that no signs remained.

With the assistance of the ward medical officers who had charge of them I was able to keep a close watch on the first

group of cases to be admitted to hospital between August and November, 1942. Other cases arising later I saw at less frequent intervals, but the total number under close personal observation was 29. In January, 1944, I extracted from the hospital records data from 34 undoubted cases of this syndrome which were not included in my previous number. Under the prevailing circumstances it was impossible to see or arrange to see every case suspected of the condition, so that this report of 63 cases fails to embrace the total number figuring in the official camp statistics.

In this series there were 6 deaths. Four of these patients, after an insidious onset, deteriorated rapidly and died within 3, 8, 17, and 18 days of admission to hospital. Necropsies were performed by Capt. Lennox, R.A.M.C., and the naked-eye findings are included in the case reports. One patient died of pulmonary tuberculosis and no necropsy was carried out. The sixth died a year after onset with progressive mental deterioration; no changes were found in his brain comparable with those in the other cases.

The records I managed to keep with me and finally bring home in October, 1945, were of the briefest. As my notes on various diseases grew in number, so the records needed to be condensed still further to reduce their bulk, for there was the ever-present possibility of confiscation.

Fatal Cases

Case I

This patient, who was admitted on Aug. 31, 1942, had noticed for one week double vision, burning pains in the legs and left hand, general weakness, and difficulty in chewing his food. Mentally he was retarded, and was easily moved to laughter by unamusing remarks. There was general weakness of his limbs of moderate degree, most marked in the grip of the left hand. No changes in sensation were observed.

When I next saw him, eight days later, generalized rigidity of his limbs had developed and he was unable to sit up. His tendon reflexes were exaggerated and there was ill-sustained clonus at both ankles. The abdominal reflexes were weak, and the plantar reflex was extensor on the left side. He was given "marmite," 2 oz. (56.7 g.) daily, from then on.

Six days later he became incontinent of urine, and during the next few days he was mentally confused. By Sept. 16 his legs had become extended and his arms flexed rigidly across the chest. There was some weakness of the left facial muscles. His temperature rose to 101° F. (38.3° C.). The following day he became incontinent of stools consisting of blood and mucus, lapsed into unconsciousness, and died on Sept. 18.

At necropsy small translucent dots were to be seen scattered about the white matter of the frontal, parietal, and occipital regions of the cerebral hemispheres. These dots were 2-3 mm. in diameter and had the appearance of sago grains in milk. In the colon there was patchy erosion of the crests of the mucous membrane in the distal part of the sigmoid and rectum.

Case II

For a fortnight before his admission on Sept. 4, 1942, this patient had noticed dimness of vision, and for a week unsteadiness of gait and pain in the neck. On examination there was marked dulling of his mental faculties, with disorientation for time and place. Weakness and rigidity were present in all his limbs, with exaggerated tendon reflexes and extensor plantar responses. Other evidence of dietary deficiency was manifested by angular stomatitis, glossitis, and scrotal dermatitis. For three days he was given 1.7 ml. (1 ampoule) of "nicamide" (nicotinic acid diethylamide) intramuscularly and 1.7 ml. by mouth daily. For the next three days 3.4 ml. was given by mouth daily, and subsequently "marmite" 3 oz. (85 g.) daily.

Five days after admission he became incontinent of urine and faeces; he could not speak or swallow, but could understand simple requests and statements. Within the next two days he deteriorated rapidly; his legs became rigidly extended and his arms flexed across his chest. His face was expressionless and practically immobile. The blinking reflex was lost but some vision was present. He moaned continuously, so far as could be gathered because of pain in his limbs. This pitiful condition gave place to coma, in which he died on Sept. 21.

Changes in the cerebral hemispheres, identical with those in Case I, were found at necropsy.

Case III

This patient was admitted from another camp on March 22, 1943, in a stuporous condition, with a slip attached to his shirt bearing the words: "Fever. Choking feeling and failing vision." He could