relatives still remain the onerous responsibility, and the duty, of those doctors who choose to make the problem of cerebral neoplasia one of their primary interests. Moreover—and this is even more important—in our series of 700 unselected cases of cerebral neoplasm, although 466 were gliomata, there were 147 cases that were potentially curable by surgery; in other words, 21% of favourable cases. In cases of neoplasm of the brain the segregation of the favourable cases from those of glioma in the early stages is one of the main problems of differential diagnosis, and carelessness in the diagnosis and handling of the glioma cases will reflect unfavourably on the potentially curable group.

In a further group of cases we are already using the newer methods of diagnosis, such as with radioactive isotopes, and are experimenting with biochemical forms of treatment and deep *x*-ray therapy.


### Summary

Experience with 700 cerebral neoplasms, of which 466 were gliomata, is reviewed.

The majority of these new growths are highly malignant and lead to death within two years. Early diagnosis is important. The initial symptoms and signs are raised intracranial pressure, epilepsy, mental change, and neurological signs, though it is generally impossible to base a diagnosis solely on the clinical evidence. *X* rays, electroencephalography, and lumbar puncture are useful diagnostic aids, but when these fail air encephalography, ventriculography, or angiography will be necessary to decide if a space-occupying lesion is present.

Surgical methods of treatment are summarized and discussed. It is emphasized that subtemporal decompression should be avoided.

Of the 405 patients operated upon, 7 were cured, 23 were returned to a useful life for periods of two to five years, and 52 relieved of distressing symptoms such as severe pain and vomiting.


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REFERENCE

Bailey, P., and Cushing, H. W. (1926). *A Classification of the Tumours of the Glioma Group on a Histogenic Basis with a Correlated Study of Prognosis.* Lippincott, Philadelphia.

The "Mental Health Facilities and Needs of Australia" were the subject of a report drawn up by Dr. ALAN STOLLER, Melbourne psychiatrist, with the assistance of Mr. K. W. ARSCOTT. The report was undertaken at the instigation of the Commonwealth Government and published by it. Its scope included examination of mental hospitals and auxiliary services, mental deficiency programmes, psychiatric services, and State legislation. Dr. Stoller sums up his findings on the hospitals: "Mental hospitals are hopelessly overcrowded, poorly maintained, and short-staffed. . . . Diagnostic and treatment equipment and facilities are sorely lacking. The hospitals are in no position to develop out-patient, training, and educational programmes, and research is virtually unthinkable." The average overcrowding percentage was 20%—at the main mental hospital for Queensland the figure was 95%. Victoria had the best mental health facilities, with active voluntary bodies, and residential centres for defective children. New South Wales provided four psychiatric clinics through the school medical service; elsewhere help for retarded children was extremely limited and legislation for them incomplete, so that often the number of such children was unknown. Early in May the Commonwealth Government announced a £A.30m. capital works programme to improve mental health facilities throughout the country.

# BERYLLIOSIS: A CASE REPORT

BY

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The hazards of dermatitis and respiratory disease from handling beryllium compounds were known in Europe before the last war, and Marradi Fabroni (1935) suggested calling the lung disease berylliosis. Various syndromes caused by beryllium were seen in considerable numbers in the United States of America during the last war, and these have been reviewed by DeNardi *et al.* (1953). In Great Britain, beryllium has been used, though not in the same quantities as in America, in the fluorescent lamp industry and in the form of beryllium-copper alloys in the manufacture of electrical equipment and special springs. It is remarkable, therefore, that there has been only one published case of delayed pneumonitis in a beryllium worker in this country (Agate, 1948) and one case of beryllium granuloma of the skin in a fluorescent-light-tube worker (Lederer and Savage, 1954).

The delayed chemical pneumonitis first described by Hardy and Tabershaw (1946) is perhaps the most interesting and elusive manifestation of beryllium toxicity. It is a slowly progressive sarcoid-like change in the lungs and liver which may come on after a very short exposure to beryllium compounds and after a latent period which may vary from a few months to eleven years. The clinical features are the insidious onset of weight loss, weakness, dyspnoea, and cough, with occasional febrile periods. The prognosis is grave, as the mortality in 35 cases reported by DeNardi *et al.* (1953) was 35%, and many of the remainder were severely disabled by pulmonary fibrosis.

The only British case (Agate, 1948) occurred in a physicist working on the development of tubular fluorescent lamps who was exposed to small quantities of zinc beryllium manganese. His symptoms did not develop until three years after his last contact with beryllium.

Although the first cases were described in a fluorescent lamp factory, it has also been reported in a brass foundry making and finishing beryllium-copper alloys (Jackson, 1950), and even in people who lived near beryllium extraction plants. Hardy (1951) lists 11 different industries in which chronic beryllium poisoning has been found. The incidence of chronic berylliosis is fortunately low. DeNardi *et al.* (1953) report 8 cases among 3,027 workers in three beryllium extraction plants, though 6 cases were found in 310 workers in the brass foundry (Jackson, 1950).

The following case is reported to draw attention to the possibility of delayed chemical pneumonitis due to beryllium in an industry hitherto regarded as safe. The case also shows the combination of unusual skin granulomata with lung lesions and would appear to be due to beryllium-copper alloy.

### Case Record

A 25-year-old woman was referred to the skin department in August, 1954, for treatment of Raynaud's phenomenon of the fingers, from which she had suffered since the age of 10. It was noted that, as well as having cold blue fingers, she had numerous linear granulomatous papules on the fingers, palms, forearms, and legs (Fig. 1), and that she had a granulating wound on the dorsum of the left foot, which she

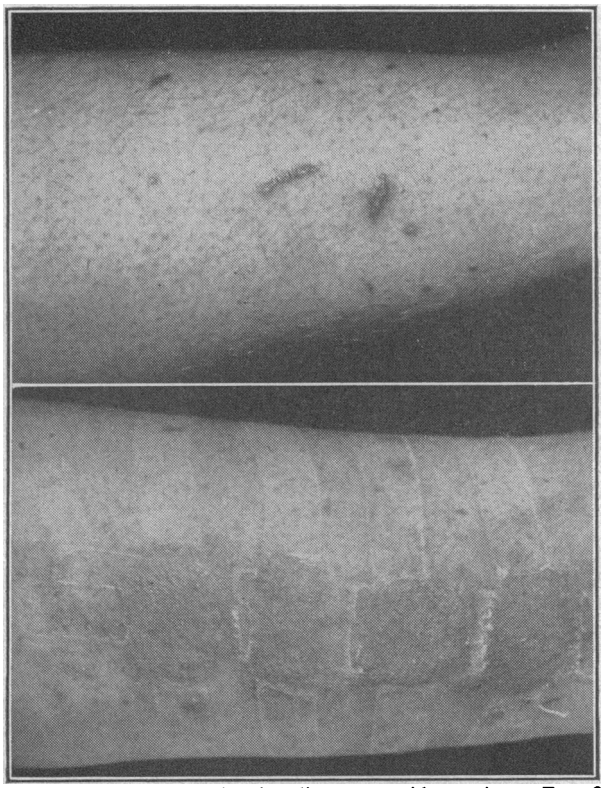

FIG. 1 (*Above*).—Leg showing linear sarcoid reaction. FIG. 2 (*Below*).—Patch tests with beryllium salts 48 hours after application.

stated she had cut at work four months previously and which had not healed. The granulomatous papules had appeared in the previous year. She also complained of a dry cough and increasing shortness of breath, which had so worried her that two weeks previously she had attended a mass radiography unit for a chest *x*-ray examination but no abnormality had been found. She had not lost weight, but had felt weak.

At the age of 10 she had had an attack of arthritis which had left some deformity of the right hand. Since the age of 10 she had had Raynaud's phenomenon of the fingers and toes. Her family history showed nothing relevant.

*Occupational History.*—For eight and a half years she had been employed by a firm of precious-metal smelters. For the first five years she was a backer in the rolling mill, handling gold, silver, and platinum sheets, and for the remaining three and a half years she operated a rotary shearing machine. This machine trimmed metal strip, a considerable quantity of which was 2% beryllium-copper alloy. She sustained frequent cuts and scratches on her hands, forearms, and legs from the sharp and jagged edges of the metal strip, and she could recall that the cut on her foot and several of the other linear granulomatous lesions had been caused by beryllium-copper strip. The machine which she operated was in a room by itself and she had no contact with fumes or dust from any other process. The shearing blade of the machine revolved only slowly, but fragments of the metal were occasionally thrown off.

On examination in August, 1954, she was not dyspnoeic at rest, but slight exertion produced rapid shallow breathing. Her fingers when cold were dusky blue and there was soft-tissue thickening around the right second and third metacarpo-phalangeal joints. On the back of the fingers and in the palms were numerous firm bluish-red papules, mainly aggregated in lines 0.5–1 cm. long. In the palms also were several superficial dry ulcers 2 mm. in diameter which resembled small chrome ulcers. On both forearms and on the lower part of the legs were more papules varying in colour from a yellowish brown on the forearms to a purplish blue on the legs, which showed acrocyanosis. On the limbs the papules had obviously occurred along scratch marks. On the dorsum of the left foot was a healing laceration which showed a granulomatous lupoid change in the scar. No skin lesions were found on the trunk or face. No abnormality could be found in the cardiovascular system, nor were any adventitious sounds heard in the chest. There was no lymph-node enlargement, and the liver and spleen were not palpable.

### Investigations

Histological examination of a papule from the left middle finger showed, in the dermis, numerous well-circumscribed nodules separated by dense fibrous tissue. The nodules consisted of foci of epithelioid cells, multinucleated giant cells, and small round cells. There was no caseation. Dark-ground and polarized-light examination of the section showed no foreign bodies. Histochemical staining for beryllium was negative. Mantoux test, 1/1,000 and 1/100—negative. The blood W.R. and Kahn test were negative. A blood count showed: Hb, 96%; white cells, 6,000 per c.mm. (polymorphs 60%, lymphocytes 30%, monocytes 8%, eosinophils 2%); E.S.R., 27 mm. in 1 hour; serum calcium, 9.8 mg. per 100 ml.; plasma proteins, total 7.3 g. per 100 ml. (albumin 4.8 g., globulin 2.5 g.). The E.C.G. was normal. Beryllium in urine, negative; beryllium in skin, negative.

Radiological examination of the hands and feet showed no abnormality. The lung fields showed a generalized very fine stippling; the picture was not the usual one seen in sarcoidosis, in which the stippling is usually dense and the hilar glands are more commonly involved. The evidence seemed to point to these changes being berylliosis rather than sarcoidosis, although differentiation is extremely difficult. Miniature radiographs of October, 1953, and August, 1954, did not demonstrate changes.

Skin patch tests were carried out with 1% and 2% solutions of beryllium sulphate and beryllium nitrate. In 48 hours a strongly positive eczematous reaction occurred beneath all four patches (Fig. 2). The inflammatory reaction was still present three weeks after the tests, and a skin biopsy was carried out from one area. There was a pronounced pseudo-tuberculous reaction in the dermis, made up of groups of concentric follicles. Each follicle was comprised of epithelioid cells, and most contained a multinucleated giant cell, some of these being very large with up to 50 nuclei. In one or two of the deeper follicles there was a necrotic centre. The epidermal changes were not significant. The follicles differed from the usual form of sarcoid in showing the central necrosis. No acid-fast bacilli could be found, nor optically active particles. Patch tests, using the same strength of solution carried out on 113 normal controls, were negative. One hundred of these patch tests were performed at St. John's Hospital for Diseases of the Skin (C. D. Calnan, 1955, personal communication).

*Respiratory Function Tests.*—Gaensler Timed Vital Capacity:— Total vital capacity, 2.19 litres, which is 75% of the predicted value for her age and weight; percentage of vital capacity expired in the first 0.75 second=75% (normal). Helium mixing:—The rate of diffusion of the helium was slightly abnormal; there was some slowing of diffusion even in the best-ventilated part, and a small volume into which diffusion was slower still.

*Progress.*—The patient's dyspnoea and cough has become more marked during the three months she has been under observation. For several days after the patch tests the dyspnoea appeared to get worse than usual and moist rales were heard over both lungs for the first time. These have since disappeared. She has been removed from contact with beryllium and has been found a sedentary job which is within her capabilities.

### Diagnosis

The presenting feature of sarcoid-like granulomata on skin damaged by beryllium-copper strip suggested at an early stage that at least the skin lesions were being produced by

beryllium, though lesions occurring as a Koebner phenomenon in sarcoidosis could not be excluded. The presence of small indolent ulcers clinically resembling chrome ulcers and previously described beryllium ulcers was, however, much in favour of berylliosis.

In 1953 DeNardi *et al.* reported the reliability of skin patch tests, which, they stated, showed an eczematous contact sensitivity in cases of berylliosis which had never shown any evidence of dermatitis. Patch tests were positive in 12 of their cases of chronic berylliosis, and results were negative in 5 other patients with various lung diseases, including sarcoidosis. The reliability of patch tests is also stressed by Van Ordstrand (1954), who states that, so far, he has no knowledge of a false-positive result. DeNardi *et al.* suggest four criteria upon which the diagnosis should be based: (1) history of exposure to beryllium; (2) clinical course of the pulmonary syndrome, including studies of pulmonary function; (3) radiographic evidence of granulomatosis of the lungs; and (4) patch tests.

The radiographic changes shown are those described by Wilson (1948) as stage I. He states that the earliest recognizable variation from the normal is a fine diffuse granularity presenting a fine sandpaper appearance, which under magnification of a reading-glass suggests a sandstorm. It is of interest that the miniature films taken by the mass radiography unit were incapable of showing this early positive change.

The patch tests were strongly positive, and it appeared that during the height of the skin reactions the lung lesions became temporarily more active. The initial change in the skin beneath the test patches appeared macroscopically to be an eczematous one, but a biopsy was not carried out immediately and there is no histological confirmation of this. Most significant, however, is the finding in the patch-test area three weeks later. Macroscopically the skin was still reddened and scaly and slight induration could be felt. Histologically, a sarcoid reaction was already present, and this extended deep into the corium. Histochemical staining to detect beryllium failed to demonstrate the metal in this tissue. Attempts to demonstrate beryllium in the urine and in skin papules from the forearm were also negative. Although unsatisfactory, there are a number of proved cases of berylliosis with similar negative findings (DeNardi *et al.*, 1953; Agate, 1948; Lederer and Savage, 1954).

## Discussion

This case provides additional evidence that it is beryllium itself rather than beryllium in association with silicates which is responsible for the sarcoid-like granulomata of the lungs and dermis. It also supports the theory that berylliosis is an acquired allergy. In favour of the allergy theory are the low incidence among workers exposed to beryllium, the long latent period, and the minute amounts of the metal necessary to produce the disease.

It is difficult to determine in the present case how the beryllium entered the body, since the metal chips from the shearing machine were quite large and not likely to be airborne. That sufficient entered the body to produce an eczematous hypersensitivity is proved by the positive patch tests. It is perhaps strange that the patient did not show a contact dermatitis when handling the beryllium alloy, but the explanation may lie in the fact that metallic beryllium is very insoluble and until it has undergone some change in the body does not produce a response. Aldridge *et al.* (1949) have shown that beryllium ions attach themselves rapidly to protein, and it is likely that a beryllium-protein compound acts as the sensitizing allergen for the skin.

Of great interest was the sarcoid-like change in the dermis three weeks after application of beryllium nitrate solution to the skin. This reaction has not previously been reported in berylliosis. Although sarcoid reactions can be produced in sarcoid patients by the injection of extracts of lymph nodes and by tubercle bacilli and their extracts, I have been unable to discover a previous description of a sarcoid reaction to substances applied to the skin. If the dermis responds to the presence of beryllium in this way, it is possible that the lung responds in the same way and the delayed chemical pneumonitis can thus be explained as an acquired hypersensitivity.

As has been stated, the prognosis of chronic berylliosis is poor and treatment has been disappointing, though there have been reports of benefit from the steroid hormones (Kennedy *et al.*, 1951). In the present case the symptoms are not disabling, and after removal from contact with beryllium the patient has been encouraged to continue working at a sedentary job within her physical capabilities.

## Summary

A girl trimming 2% beryllium-copper alloy strip for three and a half years developed sarcoid-like granulomata on her hands and forearms, which had been scratched by the metal strip. She was found to have a pulmonary granulomatosis clinically similar to delayed chemical pneumonitis due to beryllium.

The case fulfilled all the criteria for diagnosis of systemic berylliosis and, in particular, illustrated eczematous hypersensitivity to beryllium shown by positive patch tests, to high dilution of beryllium salts, and a delayed sarcoid reaction in the skin used for the patch tests.

My thanks are due to Dr. Marjorie Clifton, of the Department of Medicine, Sheffield University, who carried out the respiratory function tests; to Dr. P. L. Bidstrup, of the London Hospital, for the estimations of beryllium in the urine and skin; to Professor D. H. Collins for the pathological reports; to Dr. J. M. Barnes, of the Toxicology Research Station, for the histochemical examination of the skin sections; to Mr. R. Brook for the photographs; and, lastly, to the patient, who submitted most willingly to the lengthy investigations.

[A short report of this case has already been published in the *Proceedings of the Royal Society of Medicine*, 1955, **48**, 175.]

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Progress in the various branches of science needed for pest control is reviewed in the Pest Infestation Research Board report for 1954 (H.M.S.O., 3s.). The biology section is studying the population of pests associated with buildings, such as invest birds' nests or bat roosts; and also the populations found on stored materials, particularly those of the Khapra beetle—a serious pest in the maltings of Britain. The laboratory successfully fumigated Nelson's H.M.S. *Victory* with methyl bromide. No major change is reported in the work of the insecticide section, which has made considerable progress in studying the relative susceptibility of insects to insecticides. Paradichlorbenzene, in a test where Service uniforms were exposed to infestation for eight weeks, was found to kill all adult carpet beetles and 90% of the larvae; eggs hatched, but the young larvae died. 2% chlordane in refined kerosene painted in 3-in. (8-cm.) bands along the foot of walls, pipes, sinks, etc., and 5% chlordane in a non-inflammable oil on the outside walls, rid a 17-ward tuberculosis sanatorium of Pharaoh's ant at a cost of £75. Pit storage of grain is being tested throughout Africa and Cyprus; a gas-proof sheeting material is being tried out for this in collaboration with the Ministry of Supply.