The first apparatus to use this principle was one developed by Lawrence in America. This is called a cyclotron, and in it protons or deutrons are accelerated to enormous energies. When these particles are made to hit certain elements, the nuclei are bombarded, and neutrons ejected. These neutrons were used by Stone in California in the treatment of cancer. This treatment, however, was abandoned in 1943 because of the severe late reactions obtained and it has not been resumed. It is interesting, however, to note that neutrons are absorbed much more readily by fat than by other tissues, and possibly some therapeutic application will be found for them. Another product of the cyclotron, fast protons, will shortly be tried in medicine. These particles produce very little effect in the tissues until they reach a certain depth, where their release of energy is very great. The application of this property to therapy of deep tumours is obvious.

Another device for accelerating particles is the betatron. This is an ingenious machine which gives electrons very high energies without the use of correspondingly high voltages. The electrons are accelerated by making them travel in a circle within the field of a large electro magnet. It is much less cumbersome than the cyclotron which may weigh more than 1,000 tons.

A betatron is operating at the University of Saskatchewan. Its weight is only 5 tons, and it produces x-rays of energy of 25,000,000 volts. The distribution of dosage in the tissues from this machine is interesting. The dose rises from about 15% on the skin to 100% from 3 to 5 cm. deep. Following this the percentage depth dose falls off very slowly. With x-rays of even higher voltage the maximum dose would fall at greater depths. This machine is at present being used in the actual treatment of advanced malignant cases. It is easy, by the use of several crossfiring x-ray beams to attain homogeneous irradiation of deep seated tumours without producing any appreciable affect on the skin. A further advantage is that for a given tumour dose, the integral dose, that is, the total radiation absorbed by the patient, is much smaller than with conventional x-rays. Little or nothing is known of the biological effects of these rays. It is just possible that they may have a greater selective effect on cancer cells than ordinary x-rays, although this is improbable since their biological effect is caused by ionization in the tissues, as with conventional x-rays.

CONCLUSION

It must be remembered that radiotherapy is a young science, with probably a great future in front of it. We must look to physicists for further advances. The fields of radioactive isotopes and supervoltage therapy are being opened to us with amazing rapidity. It is over 50 years since the discoveries of Roentgen and Becquerel. The first 40 years were spent in the developing and harnessing these rays to medical use. The last ten years have seen surprising new discoveries in nuclear physics, the application of which to medicine are only now being investigated.

BERYLLIUM GRANULOMATOSIS

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A NUMBER of cases of beryllium poisoning have been reported in the medical literature of both Great Britain and North America during the last few years. It is interesting to note that this is an industrial and public health hazard which appeared a few years ago and will soon be passed as a new substance is about to be used in fluorescent lighting which will eliminate beryllium and its compounds.

CASE REPORT

H.I., male, aged 29, was referred to one of us (J.G.) on August 30, 1946, because of raised, red, tender scars on the forehead (Fig. 1). He was in a disgruntled frame of mind and felt that his original cuts had been passed along to resident hospital staff and therefore inexpertly handled. The hospital entry of May 6 records that he had been hit with a broken fluorescent bulb, receiving a three-sided cut on the right forehead. A vessel was tied off with catgut and 2% novocaine was injected. The cut was washed with green soap and water and six plastic sutures were used. Sulfa powder and elastoplast dressing were applied. On May 9, the sutures were removed and sulfa powder and elastoplast dressing reapplied. On May 13, the wound was washed with alcohol.

This would seem to indicate better than average emergency care and should have resulted in an excellent scar. On presentation in August, however the scars were epithelialized, but soft, red, tender and raised. The patient grudgingly wondered if the powder used on the inside of the light bulbs might not have something to do with the unsatisfactory nature of the scars and volunteered the information that finger cuts stitched previously had healed well.

The scars were excised and revised under local anæsthesia on September 13 and healing was uneventful with an excellent result. The pathologist reported tuberculous-like granulation tissue. The patient was informed of this but insisted that his health was good and he had just passed an examination for a $10,000 life insurance policy. The conclusion was reached that the forehead lesion was some sort of a granuloma due to the fluorescent powder. He was re-examined on March 17, 1947, when his health was good and the scars were cosmetically excellent.

Pathological report.—Sections (Figs. 2 and 3) consist of a piece of skin and subcutaneous tissue. The surface is covered by an atrophic layer of stratified squamous epithelium showing a thin layer of keratinization of the surface and pigmentation of the basal layer. There are sebaceous glands and hair follicles present.

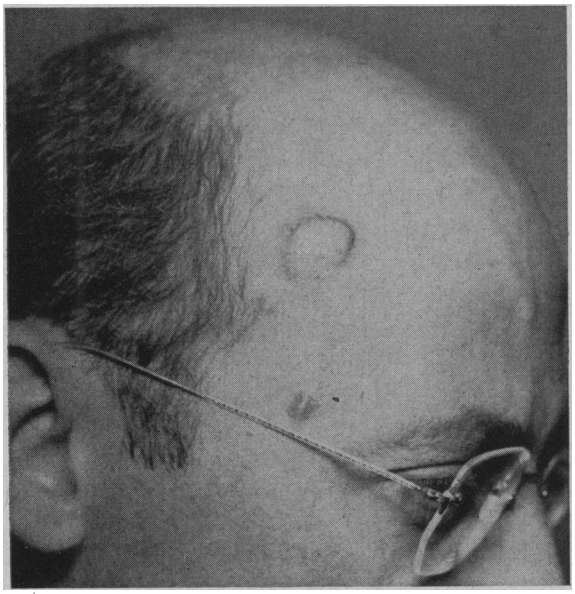


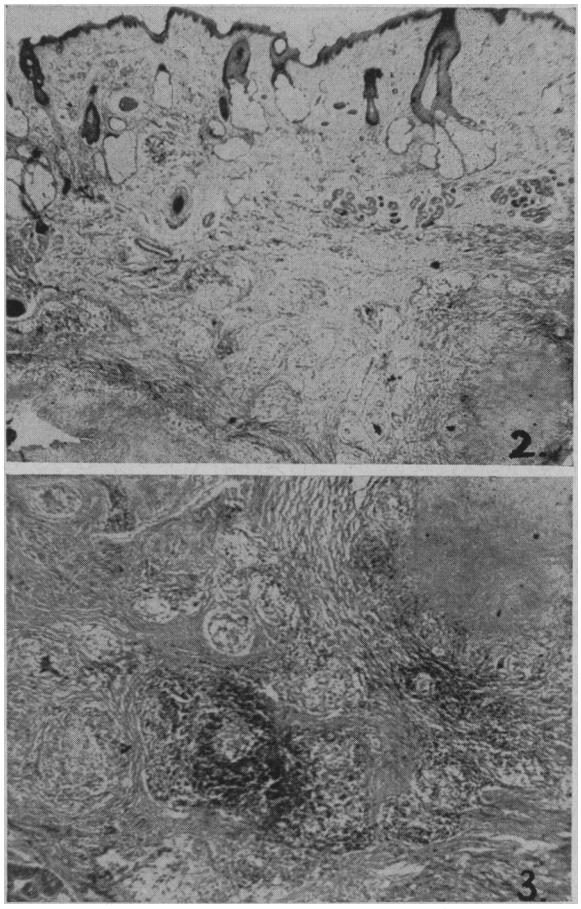
Fig. 1.—The beryllium granulomata, as seen on August 30, 1946, resulting from a cut with a fluorescent light bulb.

Throughout the corium and subcutaneous tissue there are multiple tubercle arrangements of epithelioid cells, in some areas isolated and in others confluent. About these areas there is a varying degree of lymphocytic and plasma cell infiltration, some of the tubercles show multinucleated giant cells, resembling the Langhans type. In the larger confluent areas there is central necrosis that becomes homogeneous and eosinophilic and contains karyorrhectic nuclei. In some others there is a heavy infiltration of polymorphonuclear eosinophiles and some neutrophiles. In other places the necrotic coagulum is fenestrated and gives the appearance of vacuoles at the site of dissolved-out cells. The lesion nowhere involves the papillary zone of the corium but is widespread throughout the reticular zone and extends into the subcutaneous fat. The first diagnosis on this case was a granuloma of the skin of tuberculosis etiology. Stained sections for tubercle bacilli were negative.

In the light of further history and present day knowledge, this conforms to the type of skin granuloma reported as resulting from a type of reaction to beryllium.

Coakley, Shapiro and Robertson,[1] in reporting a similar case, described four types of cutaneous lesions. (1) Contact dermatitis, where the dust of beryllium sulphate, fluoride or oxyfluoride comes in contact with the skin over a period of time. (2) Ulcers due to implantation of beryllium sulphate crystals in a laceration. (3) Cutaneous lesions in patients with pulmonary granulomatosis. (4) Subcutaneous granuloma in cuts made by broken fluorescent lamps, the lesions appearing like sarcoidosis of the skin.

A case is cited of a male sixteen years of age with a history of being cut on the cheek two years previously with glass from a broken fluorescent lamp. The wounds were sutured at time of accident mainly to control hæmorrhage.



Figs. 2 and 3.—Photomicrographs of different magnification showing the "sarcoid" bodies, giant cells of the Langhan's type and general similarity to tuberculous tissue.

Several months later a painful nodule appeared in one wound with intermittent discharge: radiation therapy was used to no avail, and complete general investigation was negative. Finally a wide thorough excision was carried out, after which complete healing occurred. Histological structure of the section was similar to Boeck's sarcoid.

Van Orstrand, Hughes, De Nardi and Carmody[2] report on 170 cases in the Cleveland area over a period of four years, which mani-

fested themselves as dermatitis, chronic skin ulcer and inflammatory changes in the respiratory tract. Some gave naso-pharyngeal symptoms and others progressed to diffuse pneumonitis. There were five deaths in the series. Most cases suffering from pulmonary disease were or had been within three years, workers in beryllium-producing plants. Most cases suffering from dermatitis were found to be chronically exposed to the metal and/or its salts. They make suggestions for prevention, such as safety clothing—masks—adequate ventilation, and properly protected equipment.

Doane[3] reports a case of hand laceration caused by glass from a broken fluorescent lamp. The wound was closed followed by poor healing with a minimal amount of pus discharged periodically from which no growth was obtained. The wound was reopened and search made for a foreign body, but none was found; after closure granulation tissue reappeared, repeated probing and cauterization had no beneficial effect; x-ray radiation was tried unsuccessfully the wound repeatedly breaking down for about a year. Finally wide and thorough excision was followed by healing.

The *British Medical Journal*[4] reports the case of a patient aged 36 engaged in industrial work in contact with beryllium oxide for one year from December, 1941 to December, 1942. In 1945 he complained of a cough and showed loss of weight and died in a London hospital November 4, 1945, from some form of pneumonitis. Necropsy findings showed death due to beryllium poisoning.

From the transactions of the eleventh annual meeting of the Industrial Hygiene Foundation[5] Gardiner reports two clearly different pulmonary lesions due to beryllium and its compounds. (1) The acute type usually clearing in a few days, or it may be primarily fatal; no infectious agent is to be found. (2) A chronic type which may end in death from cachexia or dyspnœa and heart failure. The onset of this may occur as long as three years after exposure. X-ray reveals nodules in the lung uniformly distributed and there may be miliary stippling or lesions may be up to 5 mm. in diameter.

Differential diagnosis from silicosis may be difficult; lack of bone involvement differentiates it from Boeck's sarcoid. It has been named beryllium granulomatosis. Beryllium evidently acts in conjunction with an as yet unknown factor to initiate the pathological process. At autopsy spectroscopic analysis yields one to five micrograms of beryllium per six to seven grams of dry lung tissue.

Brown[6] reviewing the literature in 1946 stated that more than 200 cases had been reported up to that time. The common manifestations appear to be dermatitis and inflammation of the respiratory tract. Eruption on skin appears in most cases to disappear on cessation of exposure. Chronic ulcer resulted from crystals of beryllium within the skin; this healed eight to ten days after thorough excision and curettage of the fibrous base. A large percentage of the cases reviewed had pneumonitis, showing symptoms of cough, occasional blood-stained sputum, burning substernal pain, dyspnœa, cyanosis, abnormal taste and increasing fatigue.

Dutra[7] writing of the pathology of these lesions states that they resemble to some extent those of Boeck's sarcoid—acute diffuse interstitial fibrosis; only rarely are giant cells found at the centre of the lesion and these differ from sarcoid in the great variation in the number of nuclei (4 to 30). Typical epithelioid cells are seldom a part of the granuloma, most have either fibrinoid material or granular necrotic eosinophilic debris at their centres. Moderate numbers of lymphocytes are found even within the central granular debris. There is diffuse intraseptal fibrosis of a type not seen in sarcoid.

A statement[8] from The Medical Advisory Committee of the American Medical Association is to the effect that there is no danger from lamps when they are intact; it is after the destruction of old lamps that lacerations have been reported which were slow in healing, showed swelling and in some cases required surgical treatment. Breathing dust from broken lamps on isolated occasions is not serious but the continuous exposure to it may be. This report includes the following instructions *re* the disposal of worn out lamps. (*a*) Lamps should be broken out of doors in a proper disposal area or under a ventilated hood or in a waste container. (*b*) The operator must use a proper respirator. (*c*) The ultimate disposal of the remains must be such that the public are not exposed to powders or broken glass coated with them. A certain significant

amount of mercury vapour may be found in the surrounding air during breakage.

There were three scientific exhibits on this subject at the recent meeting of the American Medical Association in Atlantic City. H. S. Van Orstrand, Joseph M. de Nardi and Morris G. Carmody presented a nine year study of the toxic manifestations in workers exposed to beryllium and its compounds in over 400 cases. Among this group of cases were all known types of reactions to the compounds including dermatitis, granulomatosis, acute and chronic pulmonary symptoms conjunctivitis and ulcer. Robert E. Kehoe, F. R. Dutra, J. Cholak and E. J. Largent presented the results of work on experimental animals related mainly to pulmonary manifestations, they also found that some of the relatively insoluble compounds given intravenously produced malignant tumours. Raphael Pomeranz, Harry A. Brodkin and Harrison S. Martland, Jr., presented eighty 8 by 10 transparencies demonstrating radiologic, and gross microscopic pathologic studies of four autopsy cases of beryllium poisoning. They demonstrated comparative histologic studies with other pneumoconiosis, silicosis and sarcoidosis. The radiological aspects of the disease are well covered by Pascucci[9] and Wilson.[10]

Machle, Beyer and Gregorius[11] define berylliosis as a general disease characterized clinically by pulmonary insufficiency and with the major changes in the lung. They too describe the characteristic lesion as a granuloma, like that seen in sarcoidosis, and point to the acute and chronic types. Vorwald[12] also recognizes these two distinct types and says the pathological aspects are confined principally to the lungs and trachea. Royston[13] describes a case presenting clinically as bronchiolitis. The x-ray changes were miliary in character and completely cleared in eight weeks without residual fibrosis. Nichol and Domingues[14] present an analysis of the disease in considerable detail with excellent illustrations of the sarcoid bodies. These were taken from excised skin wounds in patients who, already suffering from pulmonary berylliosis, sustained cuts from broken fluorescent light bulbs with the resultant characteristic pattern of indolent granulomatosis. Their spectroscopic analysis of these lesions showed that they contained beryllium while examination of other scars from the same patients contained no beryllium. They postulate no connection between the skin lesions and the previously present pulmonary condition.

The United States Public Health Service announced in their release F.S.A.-571 dated May 6, 1949, "The major manufacturers of fluorescent lights have stated that after June 30, 1949, they will no longer use beryllium phosphor in the manufacture of fluorescent lights". This release also reads "although precautions should be taken against breathing the dust from broken fluorescent lights, there is no record of any person suffering injury from breathing dust from the occasional breakage of a lamp, despite the millions of lights in use". The committee also repeated its original statement "cuts do not cause any general sickness or spread further in the body".

CONCLUSIONS

1. Various beryllium phosphors were introduced in the middle thirties in the making of certain alloys and were used in increasing amounts in the production of fluorescent light bulbs.

2. An industrial and public health hazard has resulted producing granulomatous lesions of the skin and lungs.

3. A case is reported of a typical skin lesion resulting from a broken fluorescent light.

4. With the withdrawal of beryllium from such manufacturing processes, the hazard should pass.

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RÉSUMÉ

Les auteurs rapportent un cas de coupure faite sur une ampoule contenant du béryllium. Cette plaie prit plusieurs mois à guérir et on dut faire une exérèse de la cicatrice qui demeurait douloureuse et rouge. Ils en profitent pour faire une revue de la littérature traitant ce sujet. Le béryllium peut causer des lésions granulomateuses cutanées et pulmonaires, qui ressemblent à la sarcoidose de Boeck. Actuellement le danger est pas mal passé car le beryllium ne fait plus partie de la fabrication des ampoules électriques fluorescentes. YVES PRÉVOST