

The effects of laser radiation on living tissues are being studied in several centres. L. Goldman and his colleagues⁶ focused a laser beam on the skin. Exposure to a pulse of energy which evoked no more than a pricking sensation gave rise to an area of superficial coagulation necrosis sharply demarcated from the unirradiated surrounding tissue. For reasons not yet explained the area of necrosis in some experiments subsequently spread beyond the irradiated area. The same group of workers⁷ showed that laser energy is better absorbed by, and more destructive of, pigmented than non-pigmented tissues. A similar difference in susceptibility has been seen in pigmented and non-pigmented cells grown in tissue culture.⁸ M. S. Litwin and D. H. Glew⁹ have concluded that the main effects of irradiation with laser beams in the infra-red and optical-light wavelengths are those of the intense heat generated. They thought that more subtle and complicated effects might be expected from lasers producing emissions at shorter wavelengths and higher energies. They quoted evidence of the production of free radicals in laser-irradiated rodent skin and other biological materials, and suggested that the particle cloud near an irradiated target can be expected to be highly ionized. These observations suggest that laser irradiation may be carcinogenic, and they also provide a possible explanation of the spread of necrosis outside the irradiated area observed by Goldman and his colleagues.

What of the hope that lasers might be of value in the treatment of cancer? Carefully planned x -irradiation, with delivery of the correct dose to the cancerous tissue and minimal exposure of surrounding normal tissues, may be as successful as surgery in the treatment of strictly localized neoplasms. Where cancer has become disseminated throughout the body successful treatment depends on the exploitation of a difference in response between the tissues of which the cancer is composed and normal tissues. On this principle cancers derived from hormone-dependent organs have been treated with great success. But success with chemotherapeutic drugs without hormonal effect has been limited to causing remissions and symptomatic benefit: permanent cure has rarely been achieved. The fact that laser beams are easy to focus and are of very high energy could give them advantages over surgery or conventional radiotherapy in the treatment of localized cancer, but neither of these special properties confers advantages in the treatment of disseminated cancer. At present the main medical applications of lasers seem to be associated with micro-surgical techniques.

P. E. McGuff and his colleagues at Boston¹⁰⁻¹² studied the effects of laser beams on transplanted animal tumours and on human tumours transplanted to the hamster's cheek-pouch. After exposure to laser beams for 0.5-3.0 milliseconds the immediate damage appeared to be slight, but thereafter the

tumours regressed. Regression of the whole tumour took place even when only part of it was exposed to the laser beam. In attempting to explain the latter effect the authors suggested that the laser energy may inactivate an enzyme necessary for the metabolism of the tumour. A simpler explanation would be that the regression of the unirradiated tumour was merely a manifestation of the delayed effects of exposure to heat or of ionization in the region of the target area.⁸ Alternatively, it is possible that the antigenic nature of the tumour is subtly altered so that the host is stimulated to produce antibodies which then destroy both the laser-treated and untreated tumour. Such a mechanism has recently been suggested to explain the increased radiosensitivity of a tumour after a heavily irradiated autograft of the same tumour has been injected elsewhere into the same animal.¹³ J. P. Minton and A. S. Ketcham,¹⁴ from similar experiments to those of McGuff and his colleagues, concluded that tumour regression followed only when a certain ratio of laser energy to tumour size had been exceeded.

The skin is a moderately effective barrier to the laser beam, and for the treatment of human cancers other than those of the skin itself the tumour must first be surgically exposed. Reports of cases of human cancer treated with laser beams are now appearing.¹²⁻¹⁵ Regression of isolated nodules has been recorded, but no beneficial result has become apparent which could not have been achieved as easily by more conventional forms of treatment. The hopes for the future are mainly two. Firstly, laser beams of particular wavelengths may prove to have selectively destructive effects on tumour tissue; for instance, the higher absorption by pigmented cells leads one to hope that melanotic tumours will prove to be selectively sensitive. Secondly, laser treatment may strengthen the body's immunological attack on the tumour. Whether or not these hopes are fulfilled there can be no doubt that lasers are new precision tools being put in the hands of the medical profession.

Advances in Surgery for Otosclerosis

Any student of medical history must surely be fascinated by a study of the development of microsurgical procedures now being carried out on the human ear. Without in any way detracting from the imaginative and courageous attempts by J. Kessel¹ in 1876 to mobilize and three years later to extract the stapes, we must acknowledge that the renaissance in otological surgery is primarily related to the development of the operating binocular microscope—yet another example of the correlation between medical and technological progress. With the aid of this instrument the surgeon can work in a brightly lit field at magnifications of up to 40 times. These are essential facilities, for the area of the stapedial footplate is only about 3 sq. mm.

The most frequent cause of fixation of this minute ossicle in its labyrinthine window is otosclerosis. In middle age a focus of otosclerotic bone is probably present in one out of eight white women and one out of fifteen white men; the condition is uncommon in Negro and Chinese populations. However, for every eight patients with histological evidence of otosclerosis only one has clinical evidence of fixation of the footplate.² Increasing stiffness of the stapedia-vestibular joint causes deterioration of hearing. For lack of effective medical

¹ *Brit. med. J.*, 1963, **1**, 562.

² Maiman, T. H., *Phys. Rev. Letters*, 1960, **4**, 564.

³ — *Nature (Lond.)*, 1960, **187**, 493.

⁴ Schawlow, A. L., and Townes, C. H., *Phys. Rev.*, 1958, **112**, 1940.

⁵ — in *Quantum Electronics*, ed. C. H. Townes, p. 553. New York, 1960.

⁶ Goldman, L., Igelman, J. M., and Richfield, D. F., *Arch. Derm.*, 1964, **90**, 71.

⁷ — Blaney, D. J., Kindel, D. J., Richfield, D., and Franke, E. K., *Nature (Lond.)*, 1963, **197**, 912.

⁸ Helsper, J. T., Sharp, G. S., Williams, H. F., and Fister, H. W., *Cancer (Philad.)*, 1964, **17**, 1299.

⁹ Litwin, M. S., and Glew, D. H., *J. Amer. med. Ass.*, 1964, **187**, 842.

¹⁰ McGuff, P. E., Deterling, R. A., Gottlieb, L. S., Fahimi, H. D., and Bushnell, D., *Ann. Surg.*, 1964, **160**, 765.

¹¹ — Bushnell, D., Soroff, H. S., and Deterling, R. A., *Surg. Forum*, 1963, **14**, 143.

¹² — Deterling, R. A., Gottlieb, L. S., Fahimi, H. D., Bushnell, D., and Roeber, F., *Canad. med. Ass. J.*, 1964, **91**, 1089.

¹³ Haddow, A., and Alexander, P., *Lancet*, 1964, **1**, 452.

¹⁴ Minton, J. P., and Ketcham, A. S., *Amer. J. Surg.*, 1964, **108**, 845.

¹⁵ Goldman, L., and Wilson, R. G., *J. Amer. med. Ass.*, 1964, **189**, 773.

therapy surgical attempts to overcome the loss of hearing have followed three main pathways.

Towards the end of the nineteenth century pioneers such as Boucheron, Miot, Jack, and many others were performing transtympanic mobilization or extraction of the stapes. Without adequate illumination, magnification, or antibiotics these procedures must have been incredibly difficult for the surgeon and hazardous for the patient, who frequently developed post-operative labyrinthitis and meningitis, from which he died. Eventually both operations fell into disrepute and were abandoned. Not until G. L. Jenkins³ described in 1913 a method for by-passing the middle ear by means of an opening made into the lateral semicircular canal was interest once again aroused. In the following years many modifications of this procedure were developed in an attempt to prevent closure of the fenestra and onset of infection as well as to improve conduction of sound. By 1938 J. Lempert⁴ had perfected his one-stage fenestration operation. It was then universally adopted as the operation of choice for the surgical relief of otosclerosis.

In 1952 S. Rosen⁵ resurrected the mobilization operation, its great advantages being that the surgeon could usually avoid a "wet" mastoid cavity, while the patient had to endure a much shorter stay in hospital and less vertigo after the operation. But even the multiplicity of modifications in technique introduced by Rosen and other otologists rarely gave permanent improvement in hearing in more than 50% of cases. A new generation of otologists were now emerging, well trained in the techniques of microsurgery and experienced in both fenestration and mobilization operations. It was inevitable that interest should be reawakened into the possibilities of removing the ankylosed stapes and replacing it by some form of prosthesis. J. J. Shea⁶ in 1958 introduced an operation utilizing the same approach to the middle ear developed by Rosen but replacing the stapes by a vein graft-polyethylene strut prosthesis, thus completing the continuity of the ossicular chain. The long-term results of this operation in skilled hands have been dramatic. The current trend is towards stapedectomy by the Shea technique or one of the many modifications that have been developed throughout the world. Techniques have varied mainly in the type of prosthesis inserted after removal of the stapes. They include stainless steel wire and a plug of fat,⁷ wire and Gelfoam,⁸ and polyethylene strut with perichondrial graft.⁹ Whatever the method used it is now generally accepted that the best results obtained by stapedectomy equal those obtained by the fenestration operation.

If the patient with widespread obliterative otosclerosis is to benefit, extensive and traumatic manipulations with drill or pick will be required to free the stapedial footplate and surrounding otosclerotic bone. The danger of damage to the cochlea is considerable and may be as high as 4%.¹⁰ To minimize this risk Shea¹¹ introduced a new procedure utilizing a Teflon piston 0.8 mm. in diameter which is connected to the incus at one end and reaches down through a

small hole drilled, in the thickened footplate, into the vestibule. This method has proved so successful that Shea now employs it for most cases of otosclerosis needing surgical treatment. Teflon is one of the "self-lubricating" fluorocarbons and appears to be well tolerated in the middle-ear cleft. Experimental observations on cats have shown that Teflon pistons can remain in the middle ear for long periods without causing a local foreign-body reaction. A similar tolerance is shown to many other artificial substances now used as prosthesis, though local reactions may be greater than to Teflon.

At present the operation of choice for otosclerosis is undoubtedly stapedectomy by the Shea technique or one of the modifications of this method. In skilled hands worthwhile improvement in hearing can be expected in over 80% of cases, but 4% may lose their hearing completely in the operated ear. Advances in microsurgery of the middle ear have been rapid and dramatic during the past decade. The time would now appear ripe for a critical appraisal of the present position with particular regard to selection of cases, surgical technique, and the requirements for training otologists in these procedures.

Attack on Cancer

Just as an inflammatory reaction can arise in response to a great variety of agents, organic or inorganic, so it is becoming clear that many forms of cancer are responses to specific causes of some sort in the environment. And once causes can be identified they can be removed. The ever-present example of lung cancer due to cigarette-smoking is of outstanding significance as a cause of death. Others that have been in the news recently are industrial exposure to β -naphthylamine, causing bladder cancer,¹ and to gasworks effluents, causing cancer of the bladder and lung.^{2,3} Now the interesting observation is recorded in the annual report of the Imperial Cancer Research Fund that a strong statistical association has been found between melanomas of the skin and trauma.

The outstanding work being carried out by the Fund's research staff under the director, Dr. G. F. Marrian, F.R.S., has followed two main lines recently—namely, studies of viruses and of hormones. The isolation from cases of leukaemia of an organism thought at first to be a virus⁴ and later considered to be a mycoplasma⁵ was of uncommon interest, though what part, if any, it plays in the causation of the disease remains doubtful. No fewer than four viruses have been isolated from Burkitt's lymphoma, research into which is being hotly pursued by Dr. T. M. Bell and his colleagues at the East African Virus Research Laboratory, Entebbe. In addition those old friends the Rous-sarcoma and polyoma viruses are the subject of many experiments on animals. Meanwhile the reluctance of mice to follow man in the pernicious habit of cigarette-smoking is gradually being circumvented, and as a result in one case a malignant tumour of lung was produced by tobacco smoke.

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² Guild, S. R., *Ann. Otol. (St. Louis)*, 1944, 53, 246.

³ Jenkins, G. L., *Seventeenth International Congress of Medicine*, 1913, p. 609.

⁴ Lempert, J., *Arch. Otolaryng.*, 1938, 28, 42.

⁵ Rosen, S., *ibid.*, 1952, 56, 610.

⁶ Shea, J. J., jun., *Ann. Otol. (St. Louis)*, 1958, 67, 932.

⁷ Schuknecht, H. F., jun., Graham, A. B., and Costello, M. R., *Laryngoscope*, 1958, 68, 726.

⁸ House, H. P., *Arch. Otolaryng.*, 1960, 71, 312.

⁹ Goodhill, V., *Laryngoscope*, 1961, 71, 975.

¹⁰ Kaplan, J., and Shambaugh, G. E., *Arch. Otolaryng.*, 1961, 74, 522.

¹¹ Shea J. J., jun., *Rev. Laryng. (Bordeaux)*, 1962, 83, 1081.

¹ *Brit. med. J.*, 1965, 1, 329.

² *Ibid.*, 1965, 1, 876.

³ Doll, R., *et al.*, *Brit. J. industr. Med.*, 1965, 22, 1.

⁴ Negroni, G., *Brit. med. J.*, 1964, 1, 927.

⁵ Grist, N. R., and Fallon, R. J., *ibid.*, 1964, 2, 1263.

⁶ Atkins, H., *et al.*, *Lancet*, 1964, 2, 1133.