which, in the distant future, could eliminate the need for the driver to exercise any judgement. The conventional motor car will be with us at least until the end of the century and the vast numbers of persons who will be killed or permanently incapacitated can be confidently predicted—unless a new approach is made to the problem.


1 Department of the Environment, *Road Accidents 1970*, Table 6. London, H.M.S.O., 1972.
2 European Conference of Ministers of Transport, *Fourth Report on Trends in Road Accidents* (CM(72)10), 2 rue André Pascal, 75 Paris 16e. 1972.
3 Gissane, W., and Bull, J., *British Medical Journal*, 1973, **1**, 67.
4 Clayton, A. B., *Health Bulletin*, 1972, **30**, 277.


# Cannabis Debate Continued

Owing to its widespread illicit use an objective assessment of the type and degree of risk inherent in taking cannabis is of great importance. A report by H. Kolansky and W. T. Moore[1] provides new material for this debate. They present 13 detailed case histories of adults aged between 20 and 41 whom they had seen in the course of general psychiatric practice. These patients had all been smoking cannabis fairly heavily over a longish period. The clinical picture was of a rather stereotyped pattern of symptoms, which included headache, reversal of sleep rhythm, difficulties in recent memory, loss of interest in life goals, and what the authors describe as "mental and physical sluggishness." That the symptoms began after the patients started the heavy cannabis use and then tended to fade out within 3 to 24 months of its cessation is put forward as prima facie evidence of a causal relationship. These same authors had previously come to a similar conclusion on the basis of 38 case studies of adolescent cannabis takers.[2]

The cannabis debate has at times been a little too hotly partisan, with the contestants twisting or selecting the evidence to support extreme views. It is much to be hoped, therefore, that Kolansky and Moore's interesting clinical observations will receive thorough consideration. Careful clinical documentation of a short series of cases is not the end point of a resarch process, but it is often the valuable first step to a definitive investigation, though the interpretation of the findings deserves some thought. It should particularly be noted that Kolansky and Moore's patients were only from that segment of cannabis users who find themselves in trouble. The authors recorded clinical impressions rather than the results of psychometric tests. And some of the social decompensation which is prominent in the case schedules may reflect the patient's purposeful rejection of social convention, with cannabis as the symptom rather than the cause of the rejection. Kolansky and Moore's suggestion that some of their patients suffered actual brain damage rather than physiological disturbance would find support in views expressed by A. M. G. Campbell and his colleagues.[3] They reported on a series of 10 cannabis smokers whose air encephalograms were interpreted as showing ventricular atrophy. A lively correspondence was sparked off, in which Professor James Bull[4] challenged the radiological evidence, Dr. D. J. Fink[5] questioned the basis of the research design, and the authors made a reasoned reply.[6] And, as with the report by Kolansky and Moore, an open verdict would again seem to be the only fair reading.

These two recent studies have to be viewed in the context of many reports and rumours that cannabis is a hazard to health. This literature has been usefully reviewed in a World Health Organization publication.[7] The evidence on which some suppositions have been based has on close scrutiny proved to be rather insubstantial, yet there are hints that do deserve to be taken seriously. Possible effects of cannabis on time perception and on car driving have been briefly discussed in these columns.[8] A recent report[9] suggests that cannabis may cause hormonal disturbances leading to gynaecomastia. This is perhaps a relatively trivial complication, but it nonetheless suggests we are dealing with a powerful and little understood chemical.


1 Kolansky, H., and Moore, W. T., *Journal of the American Medical Association*, 1972, **222**, 1.
2 Kolansky, H., and Moore, W. T., *Journal of the American Medical Association*, 1971, **216**, 486.
3 Campbell, A. M. G., Evans, M., Thomson, J. L. G., and Williams, M. J., *Lancet*, 1971, **2**, 1219.
4 Bull, J, *Lancet*, 1971, **2**, 1420.
5 Fink, D. J., *Lancet*, 1972, **1**, 143.
6 Campbell, A. M. G., Thomson, J. L. G., Evans, M., and Williams, M. J., *Lancet*, 1972, **1**, 202.
7 World Health Organization, *The Use of Cannabis*, 1971, Technical Report Series No. 478.
8 *British Medical Journal*, 1971, **2**, 293.
9 Harmon, J., and Aliapoulios, M. A., *New England Journal of Medicine*, 1972, **287**, 936.


# Treatment with Calcitonin

Though there is still uncertainty about the physiological role of calcitonin,[1] it has several important diagnostic and therapeutic uses. The finding of increased circulating levels of calcitonin is helpful in confirming a diagnosis of medullary carcinoma of the thyroid—a tumour of the parafollicular or C-cells, which normally produce this hormone.[2] It is sometimes necessary to stimulate calcitonin secretion by an infusion of calcium to produce detectable levels, but the sensitivity of the radioimmunoassay has been improved recently. Raised levels of calcitonin are also of value in predicting recurrence of the tumour.

Calcitonin is helpful in the treatment of Paget's disease of bone[3] and of hypercalcaemia.[4] Features of Paget's disease are bone deformity and pain, rapid bone turnover, an increase in serum alkaline phosphatase levels, and excessive excretion of hydroxyproline in the urine. Administration of porcine,[5] salmon,[6] or human calcitonin[4] has abolished the pain and reduced the skin temperature over the affected bones. This treatment reduces the number of osteoclasts. Biochemical indices of bone turnover also improve. The serum alkaline phosphatase and urinary hydroxyproline levels fall, and bone takes up less calcium. Calcitonin must be administered parenterally, but the optimal dose schedule for each preparation has yet to be established. For human calcitonin it probably lies between 0·5 mg daily as a single injection (equivalent to 50 Medical Research Council units) and the same dose once a week.[7] The commercially available porcine calcitonin should be given initially in a dosage of 0·5—2·0 M.R.C. units per kg body weight per day divided in two doses. Salmon calcitonin, which has a longer biological half-life, is effective in a single daily dose of about 50 M.R.C. units.[6] Long-term therapy with calcitonin poses the problem of antibody formation. So far none of the patients who have received 1 mg of human calcitonin daily for 4-18 months developed antibodies,[7] whereas several of

those treated with porcine calcitonin for periods of up to two years have been found to have circulating antibodies. Reports on the possible antigenicity of salmon calcitonin are awaited.

Side-effects of treatment are usually slight. They include nausea, flushing, tingling, and erythema and pruritus at the site of injection. Only rarely have they been so severe as to necessitate stopping treatment, but it is probably wise to skin-test allergic patients before treating them with preparations of animal hormones.

At present calcitonin therapy should be considered for patients with Paget's disease who have bone pain not controlled by simple analgesics; widespread disease, especially if complicated by high-output cardiac failure; progressive deformity; fractures, especially in weight-bearing bones; or compression of nerves by bony overgrowth.

Hypercalcaemia is often due to increased resorption of bone, and several workers have reported that calcitonin is a safe and effective method of lowering the serum calcium. It has been used sucessfully in patients with hypercalcaemia due to disseminated malignant disease,[8] hyperthyroidism,[5] hyperparathyroidism,[4] idiopathic hypercalcaemia of infancy,[9] and vitamin D intoxication in both children and adults.[4] Alternative methods of treatment of hypercalcaemia are also effective, particularly sodium phosphate, but this is best avoided if the kidneys are impaired; calcitonin is then the treatment of choice. Preliminary studies have shown some symptomatic and biochemical improvement in one patient with osteogenesis imperfecta tarda treated with salmon calcitonin,[6] but confirmation on further patients is required. Whether calcitonin will prove to be of value in the treatment of idiopathic osteoporosis is still uncertain. Reports of short-term studies in man are conflicting, and results of long-term trials are awaited.[1]

There is no doubt that calcitonin therapy represents an advance in the management of Paget's disease. It is also of value in the treatment of hypercalcaemia associated with increased bone resorption, particularly if renal disease is present.


[1] Foster, G. V., Byfield, P. G. H., and Gudmundsson, T. V., *Clinics in Endocrinology and Metabolism*, 1972, 1, 93.
[2] Cunliffe, W. J., *et al.*, *Lancet*, 1968, 2, 62.
[3] Woodhouse, N. J. Y., *et al.*, *Lancet*, 1971, 1, 1139.
[4] West, T. E. T., Joffe, M., Sinclair, L., and O'Riordan, J. L. H., *Lancet*, 1971, 1, 675.
[5] Bijvoet, O. L. M., Veer, J. V. der S., and Jansen, A. P., *Lancet*, 1968, 1, 876.
[6] Goldfield, E. B., Braiker, B. M., Prendergast, J. J., and Kolb, F. O., *Journal of the American Medical Association*, 1972, 221, 1127.
[7] Woodhouse, N. J. Y., *Clinics in Endocrinology and Metabolism*, 1972, 1, 125.
[8] Foster, G. V., *et al.*, *Lancet*, 1966, 1, 107.
[9] Milhaud, G., and Job., J. C., *Science*, 1966, 154, 794.


# Locally Advanced Breast Cancer

In Great Britain breast cancer remains the commonest malignant disease of women. In spite of intense propaganda on early diagnosis many women still present with advanced lesions. Often this means wide dissemination, with metastases to liver, lung, and especially bone. Palliative treatment depends mainly on hormone therapy, cytotoxic drugs, and radiotherapy for especially painful sites of secondary deposits. But from time to time patients present with locally advanced carcinoma of the breast. The features of the disease may include fixation to underlying muscle, infiltration or ulceration of the skin, satellite nodules, and fixed axillary lymph nodes, but without clinical or radiological evidence of widespread metastases. These women form a special group as regards treatment, since their eventual death is made all the more miserable by the ulceration, discharge, odour, and bleeding of the fungating primary tumour. The medical attendant will achieve much if he can at least ensure that she dies with the local disease under control.

Mastectomy alone in the advanced cases has a deservedly bad reputation for rapid local recrudescence of disease.[1] The conventional treatment advised for advanced local breast cancer is radiotherapy. Though the tumour mass may shrink remarkably and ulceration heal, local recurrence is unfortunately common.[2 3] P. Helman and M. B. Bennett[4] combined radiotherapy with intra-arterial cytotoxic therapy and noted worthwhile palliation with this rather elaborate technique.

Recently J. Sonneland[5] reported a rather unconventional method of dealing with this problem in a woman of 87 with a fungating carcinoma of the breast. The surface of the carcinoma was destroyed by means of zinc chloride paste fixative. Six applications were made over a ten-day period, after each of which a leathery dead peel was excised at the bedside. There was little discomfort, and at the end of this treatment underlying pectoral muscle was reached, biopsy of which showed no evidence of malignancy. A split-thickness skin graft was then applied, and the patient was given stilboestrol by mouth. She died 18 months later of an unrelated condition, and the careful necropsy failed to disclose any residual malignant disease. This technique of chemosurgery has been used over the centuries, and it is still difficult to assess its exact role or indeed its advantages, if any, over conventional excisional surgery, diathermy coagulation, or cryosurgery. However, this apparently first reported case of the use of chemosurgery in the primary treatment of ad-advanced breast carcinoma is encouraging enough to warrant further serious consideration.

A more conventional approach to this problem has been a combination of radiotherapy and mastectomy. E. D. Montague[6] found that simple mastectomy followed by radiotherapy was better than radiotherapy alone for local control of large tumours in pendulous breasts. However, when ulceration was present, in 13 out of 33 patients treated by simple mastectomy and radiotherapy the tumour recurred as against 16 out of 55 treated simply by radiotherapy. Recently T. A. M. Stoker and H. Ellis[7] have reported on 24 patients with stage III breast cancer treated during 1962-70 by supervoltage radiotherapy to a maximum tumour dose of approximately 6,000 rads followed 4 to 16 weeks later by either simple mastectomy (in four cases), simple mastectomy with axillary clearance (11 cases), or radical mastectomy in nine cases in which the pectoral muscle was involved. The wound underwent primary healing in every patient. Three patients have developed local recurrence of their tumours, two within two years of surgery, and both of these have been subsequently controlled by hormone therapy or endocrine surgery. One recurrence was associated with disseminated disease and occurred shortly before death. Seven patients are dead, and in 6 of these cases no local tumour was present at the time of death. One patient was lost to follow up at one year, at which time she was well, and the remaining 14 are alive with local disease at present controlled. The mean survival time of the seven patients who died was 13 months after operation. Twelve of the patients have survived three years or more after mastectomy, and three of these have no