BRITISH MEDICAL JOURNAL

LONDON, SATURDAY 9 MAY 1987

Hyposensitisation

Hyposensitisation for allergic disease was introduced at St Mary's Hospital, London, 75 years ago and continued largely as a treatment given by general practitioners until the Committee on the Safety of Medicines (CSM) last year effectively stopped this treatment in general practice.[1] The original workers, Noon and Freeman, observed 20 hay fever sufferers who had been treated with injections of boiled grass pollen extracts.[2,3] Their study was based on the false premise that pollen produced a toxin that caused the disease and that injections would induce antitoxin production. The report of "a distinct amelioration of symptoms" was enthusiastically received by doctors and patients desperate for any treatment of allergic diseases. With few exceptions the ensuing pharmaceutical investment in this treatment was not accompanied by good scientific assessment of efficacy. More recently the introduction of safe and effective drugs has pre-empted immunotherapy as a first line treatment for most allergic disorders. Furthermore, occasional severe adverse reactions and a few deaths led inevitably to the CSM action. Undoubtedly a critical review of immunotherapy was long overdue, but the recommendations have had important consequences for some allergic patients.

The CSM document treated hyposensitisation as a single treatment and did not look at the needs of specific patients with different allergic conditions, such as allergic rhinitis, extrinsic asthma, or insect venom hypersensitivity. Nevertheless, there is good evidence from double blind placebo controlled trials which shows that hyposensitisation works in bee and wasp venom hypersensitivity,[4] rag weed hayfever (not a problem in Britain),[5] and perhaps rhinitis induced by grass pollen.[6] Insect sting hypersensitivity is potentially fatal, and hyposensitisation is undoubtedly effective, although problems remain with this treatment.[7] Most patients with seasonal allergic symptoms are well controlled with the newer histamine 1 antagonists sometimes combined with topical corticosteroids. Using immunotherapy when oral and topical treatment produce little benefit is controversial, though sometimes worth while.[8] Apart from vaccines containing extracts of grass pollen, house dust mite, and insect venoms, there is little evidence that other preparations work in allergic disorders. These include antibiotics, for which the CSM Update stated that there is "convincing evidence of efficacy." There is no antibiotic vaccine available for hyposensitisation, which the CSM appears to have confused with "rush desensitisation."

Hyposensitisation for asthma requires special consideration. Sixteen of the 26 deaths from hyposensitisation reported to the CSM were in asthmatic patients. Over the same 29 years considered by the CSM over 25 000 patients with asthma have died because "medicine" failed them. While house dust mite hyposensitisation might have some benefit in childhood asthma,[9] evidence is conflicting in adults.[10] We should, therefore, await further trials before recommending it for general use.

The British experience of adverse reactions is different from that of the French. In France only 0·1% of 20 000 patients treated with immunotherapy had important complications. Asthma, rhinitis, and urticaria were the commonest reactions; anaphylactic shock occurred in only two patients, and both responded to adrenaline.[11] The difference may arise because in France treatment is given by specialists in clinical allergy, whereas in Britain hyposensitisation may be given by any doctor.

The CSM recommendation that has caused greatest controversy is that patients should be observed for two hours after each injection. Members of the British Society for Allergy and Clinical Immunology are unaware of any life threatening reaction occurring without warning after two hours; there is always clear indication very soon after the injection. If immunotherapy is considered in patients with asthma a measurement of ventilation such as peak flow should always be made before each injection. Because any potential benefit is small patients with lung function below half of the predicted normal should not be considered for immunotherapy.

Ignorance about treating anaphylactic reactions is widespread and reflects the poor training in clinical allergy in Britain. Many life threatening reactions are treated first with antihistamines and steroids rather than adrenaline. The primary treatment for severe anaphylaxis is 0·5 ml subcutaneous or intramuscular adrenaline 1 in 1000, and the dose may be repeated up to a total of 2 ml over 15 minutes if necessary.

We hope that the CSM Update will not stop research in immunotherapy in the country of its origin. Funding and ethical approval will be required for further studies. The outcome of the CSM recommendations is that immunotherapy will become, in the short term, a hospital treatment. There are too few physicians trained in clinical allergy and immunology who will be able to set up clinics for allergy sufferers. The Joint Committee on Higher Medical Training has been considering the need for properly trained physicians

in clinical allergy and immunology and has recently recognised a training course in internal medicine for this specialty. The National Health Service must face up to this problem as already many sufferers from allergy are resorting to fringe medicine.

In conclusion, careful control of hyposensitisation is required. Only insect venoms, grass pollens, and perhaps house dust mite vaccines should be used. The modern vaccines are potent, containing highly purified antigen, and therefore great care is required in using this treatment, particularly for patients with asthma. Full facilities for cardiopulmonary resuscitation must be immediately available, and patients must be carefully monitored before, during, and (at least for now) for two hours after injections. A review of hyposensitisation deaths along the lines of the British Thoracic Society investigation of asthma deaths would be valuable. Finally, medical training in clinical allergy and immunology should be urgently improved so that this specialty can be expanded in the National Health Service.

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Doctors and the death penalty: an international issue

One of the recent features in Britain has been the regular attempts in parliament to have capital punishment restored. It is an argument that has particular relevance for doctors. The introduction of execution by lethal injection in several states in the United States has caused concern among doctors, most of whom are disturbed that drugs and practices developed for treatment are being used to kill. Curran and Casscells concluded in 1980 that for doctors to participate in execution by lethal injection would be contrary to medical ethics.[1] But even when doctors are not giving the injections they may be required to determine the physical and mental fitness of prisoners for execution, provide technical advice, prescribe the drugs, supervise their administration, or examine the prisoner during the execution so that it can continue if he is not yet dead.[2] In 1977, for example, Oklahoma required doctors to supervise the execution process but dropped this requirement after several American state medical associations declared that direct participation by doctors in lethal injections was ethically unacceptable. In 1980 the American Medical Association as a whole adopted a resolution that stated that "a physician, as a member of a profession dedicated to the preservation of life when there is hope of doing so, should not be a participant in a legally authorised execution."

A recent report by Amnesty International on the death penalty in the US raises uncomfortable issues for doctors.[2] In one infamous case in 1977 the medical director of the Texas Department of Corrections checked that a convicted murderer's veins were suitable for injection, provided the medical technicians who gave the lethal dose with the drug, supervised them, and examined the man on several occasions to see if he was dead. The electrocution of a murderer in Alabama in 1983 needed three separate jolts of 1900 volts over 14 minutes before the supervising doctors could pronounce that the prisoner was dead. During the first jolt the electrode on the condemned man's leg burnt through and fell off. During the second jolt smoke and flames erupted from his left temple and leg. An execution by electrocution in Georgia in 1984 needed two shocks, and it took six minutes after the first charge for the body to cool enough before doctors could examine it. The prisoner took 23 breaths, and the two doctors stated that he was still alive. Ten minutes after the first charge the second and fatal charge was given. None of these examples provide much support for the argument that death by injection and electrocution represent a humane advance over death by hanging.

More important is the dilemma facing those doctors attending bungled executions: the person they examined was alive, but they were required by the state not to sustain his life. On the contrary, they were implicitly required to indicate to the executioner that the man required more trauma to complete the execution. This seems to be in conflict with medical ethics and to suggest that the doctors were doing more than what is permitted by the World Medical Association's 1981 declaration that "a physician's only role would be to certify death once the state had carried out the execution."

The Amnesty report also draws attention to the ethical dilemmas faced by psychiatrists looking after condemned but psychotic patients. It is a civilised ethical principle that insane prisoners should not be executed (although the reintroduction of capital punishment in the US has produced some appalling miscarriages of justice and ethical practice), but in some states this merely means that the psychiatrists are required to treat the mental illness so that with his mental health restored the condemned prisoner can be executed. Not surprisingly, the American Psychiatric Association has condemned this as "a perversion of medical ethics" and has opposed psychiatrists participating in capital punishment.[3]

Elsewhere in the world the death penalty has been discussed within professional associations. The Secretary General of the Brazil Medical Association recently argued that "the doctor's role is to alleviate pain and to prolong life... Doctors can never, under any circumstances, be in favour of the death penalty... Those who execute should assume full responsibility; doctors should have no part in this."[4] He went on to suggest that "this be policy of medical bodies world wide." In June 1986 the medical associations of the Nordic countries (Denmark, Finland, Iceland, Norway, and Sweden) resolved that it is "indefensible for any physician to participate in any act connected to and necessary for the administration of capital punishment." In Britain doctors have been silent recently on the death penalty,