Insulin coma therapy in schizophrenia

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In the 1930s three major physical treatments emerged in what was regarded as a revolution in psychiatry. Convulsive therapy persists to the present day. Leucotomy, the severing of pathways to the frontal cortex, is virtually obsolete though 12 000 such operations were reported in England and Wales between 1945 and 1954[1]. Deep insulin coma therapy (DICT) was regarded as the only specific treatment for schizophrenia from the late 1930s until it was discredited in the late 1950s. This account focuses on the history of DICT in England and Wales where in general it was given uncritical acceptance for over twenty years. The method had government approval and its exponents were professional leaders. It was extolled in psychiatric publications, especially those of the Royal Medico-Psychological Association (RMPA, forerunner of the Royal College of Psychiatrists).

The therapy was developed by Manfred Sakel at the University Neuropsychiatric Clinic in Vienna. He had graduated there in 1925 and then done a two year fellowship in internal medicine in Berlin. He next worked in a private psychiatric hospital in that city where he treated morphine addicts and found that small doses of insulin helped withdrawal. When he tried insulin in psychotic patients, like other experimenters he noted improvement. After animal experiments, allegedly in his own kitchen, he satisfied himself that hypoglycaemia could safely be reversed, thus permitting deeper levels of induced coma, a step that earlier workers had not taken. In 1933 he felt he was 'on the road to great discoveries' and returned to Vienna to work as a volunteer assistant in the University Clinic where he was allowed to practise his technique[2]. His theory was that insulin antagonized the neuronal effects of products of the adrenal system, these being the physiological cause of the patient's state. Between November 1934 and February 1935 he published thirteen reports claiming an improvement rate of over 88%[3].

His work attracted international attention and doctors from many countries came to study the treatment. In March 1936 the Board of Control for England and Wales sent a medical commissioner, Dr Isobel Wilson. The Board was the inspectorate and a quasi-judicial body overseeing mental hospitals; it was also, until 1948, responsible for mental health services[4]. In July 1936 His Majesty's Stationery Office published a 61-page booklet by Dr Wilson, *Hypoglycaemic Shock Treatment in Schizophrenia*[5], which received laudatory reviews in major medical journals and rapidly ran out of print.

As described in textbooks[6,7] DICT was extremely rigorous. It was administered in a separate unit, the patients staying together with the same doctors and nurses throughout. Comas were induced on five or six mornings a week. Typically, the third dose of insulin was 10–15 units with a daily increase of 5–10 units until the patient showed severe hypoglycaemia. Treatment continued until there was a satisfactory psychiatric response or until 50–60 comas had been induced. Experienced therapists let patients spend up to 15 minutes in 'deep coma' with hypotonia and absent corneal and pupillary reflexes. Clinicians noted gross variation between individuals in response to a given dose of insulin. Also, in the course of treatment a patient could show day-to-day variation in his reaction. Further there was an uncertain relationship between clinical signs and the blood glucose level. The hypoglycaemia made patients extremely restless and liable to major convulsions. Comas were terminated by administration of glucose via a nasal tube or intravenously. Patients required continuous nursing supervision for the rest of the day since they were liable to further hypoglycaemic 'after-shocks' and a doctor had to be immediately available. These circumstances necessitated high staffing levels. The morning treatment and afternoon recreational activities filled several weeks with close interaction and physical caring (e.g. the bathing and wiping of profusely sweating patients). This was quite unlike the conventional regimens in which staff tried to engage withdrawn or contrary individuals with whom they had difficulty empathizing. There was a mortality rate of about 1% as well as a liability to permanent brain damage. Most patients emerged from treatment grossly obese. All references, particularly the comments of doctors on the atmosphere in insulin units, describe tremendous enthusiasm.

DICT was adopted quickly and by 1938 it was established in 31 hospitals in England and Wales. The Board of Control monitored it and offered consultation with Dr Wilson to anyone wishing to use it or visit the Vienna Clinic[8]. This advice together with hospital inspections undoubtedly contributed to patient safety. Mainland European doctors trained in DICT, especially

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those fleeing Nazism, were employed to introduce it. The ensuing war years set back DICT in civilian hospitals with severe depletion of staff and serious sugar shortage. The post-war years saw restoration and expansion. In 1952 Dr Wilson wrote that 'a hospital of any size should have a unit' and that any closures were due to staff shortages. The journal of the RMPA (*Journal of Mental Science*) showed great interest in insulin therapy. It reported a 1937 meeting where Dr Pullar Strecker spoke on 'recent advances in insulin treatment' (he had visited Vienna in 1935 on behalf of the Scottish Board of Control[9]). In the next ten years it published 24 papers on DICT and in 1947 reported a major meeting on the topic. The principal speaker, Dr R K Freudenberg, described his ten years' experience of DICT[10]. He compared his results with a 1939 outcome study of untreated schizophrenics from the research unit at London's Maudsley Hospital[11]. This careful review of hospital records was intended as a baseline against which outcomes of new treatments could be measured. It is ironic that two of the Maudsley authors were to become uncritical supporters of DICT when its worth was challenged a quarter of a century later. In 1950 the RMPA's *Recent Progress in Psychiatry* devoted a chapter to the therapy[12]. It elegantly reviewed the published work, citing 104 references. A broad range of therapeutic strategies was described; for example, one group of therapists aimed at a one hour coma, another four hours. In some centres the therapy was combined with other therapeutic techniques. The most alarming reference, from France, described massive removal of cerebrospinal fluid and its replacement with air, along with induction of pyrexia[13].

This seeming professional consensus was publicly disrupted by a 1953 *Lancet* paper, 'The insulin myth'[14]. The young author, Dr Harold Bourne, had obtained psychiatric experience in the British Army and was at the time a junior doctor in a hospital for learning disabilities. He purported to show that there was no sound basis for the general opinion 'that insulin therapy counteracts the schizophrenic process'. He cited papers showing that diagnosis earlier in the disease was unreliable. However, the belief that DICT was more effective the earlier it was given led to treatment being started 'on a suspicion perhaps bolstered by a Rorschach [ink blot] or other test'. He discussed the non-specific effects. 'In most mental hospitals they are given, at a conservative estimate, 50–100 times as much medical and nursing care, measured by the clock as the general run of non-insulin treated patients . . . '. In many published papers there was a biased selection of patients which with concurrent administration of electro-convulsive therapy led to more obfuscation. The paper had been offered to the *Journal of Mental Science* a year earlier (H Bourne, personal communication). Many leading psychiatrists promptly sent condemnatory criticisms to *The Lancet*. Their tone was typified by remarks such as 'it is clinical experience that counts here, despite all figures to the contrary'. Only in 1957 was a controlled randomized study published, again in *The Lancet*, with careful admission and outcome criteria and separation of therapists and assessors. The non-insulin group received sodium amytal with recovery aided by dexamphetamine. The investigators found no significant difference at six months and concluded that insulin was not a specific therapeutic agent[15]. There was little criticism of these findings, though by this time DICT was superseded by the use of phenothiazines; it was soon abandoned.

The rise and fall of DICT follows closely a pattern described by McKinlay in his 'seven stages in the career of a medical innovation'[16]. Sakel's early papers represent the first or 'promising report' stage. Next is 'professional and organizational adoption' as exemplified by the Board of Control and RMPA support. In stage three the procedure is 'a good thing and ought to be available', from which it soon evolves to 'standard procedure'. The status of 'standard procedure' is privileged, and to question it invites retaliation from professional organizational interests. The procedure is secured by many observational studies. The objectivity of such studies can be seriously compromised as they often come from those with a vested interest in the enterprise. Stage five, 'randomized control trial', is difficult since the triallists are dealing not with an innovation but with a widely accepted procedure. The terminal stage of 'erosion and discreditation' usually occurs only when a new technique supersedes the old one.

The professional eminence of the main advocates of DICT is striking and its rejection did not affect their lustre. The most outstanding was Dr W Sargant, the champion of active physical treatments in Britain. With Dr Eliot Slater he produced *An Introduction to Physical Methods of Treatment in Psychiatry* which ran to five editions and was nearly thirty years in print. He was president of the Section of Psychiatry of the Royal Society of Medicine and Registrar of the RMPA. He pioneered general psychiatry at St Thomas' Hospital. His co-author Dr Slater had wider prominence, having been director of the MRC Psychiatric Genetics Unit and editor of the *British Journal of Psychiatry*. Professor Linford Rees, who authored the chapter on DICT in *Recent Advances*, later became a successful president of the Royal College of Psychiatrists. The leading 'hands-on' insulin therapist was Dr W Mayer-Gross, who had a most distinguished career in Germany before fleeing Nazism. He shared with Slater and Sir Martin Roth the authorship of *Clinical Psychiatry*, a standard textbook. The book advocated DICT and referred to Dr Mayer-Gross' extensive (10 year) experience; the 1960 edition refers to the 1957 controlled trial by Ackner but its advocacy is little changed[17]. Dr R K Freudenberg became an international authority on social psychiatry.

The prolonged use and advocacy of ineffective treatments is a commonplace of medical history and current practice. In the case of insulin treatment in schizophrenia a major difficulty lay in achieving a satisfactory definition of the disease. (As a gross instance an investigation published in 1972 showed that American psychiatrists were twice as likely to diagnose the condition as were British psychiatrists[18].) The support of the Board of Control must have been important in persuading cautious psychiatric hospital superintendents to use it. The 1930 Mental Treatment Act for the first time allowed admission to mental hospitals without compulsion, and it has been suggested that physical therapies were incautiously nurtured to give some meaning to the proffered 'treatment' under the Act[1].

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