

- role of hypoxia causing decreased serotonin synthesis. *J Psychiatry Neurosci* 2013; **38**(6): 423–6.
- 37** Riblet NB, Gottlieb DJ, Hoyt JE, Watts BV, Shiner B. An analysis of the relationship between chronic obstructive pulmonary disease, smoking and depression in an integrated healthcare system. *Gen Hosp Psychiatry* 2020; **64**: 72–9.
- 38** Orlando M, Ellicksen PL, Jinnett K. The temporal relationship between emotional distress and cigarette smoking during adolescence and young adulthood. *J Consult Clin Psychol* 2001; **69**(6): 959–70.
- 39** McGirr A, Séguin M, Renaud J, Benkelfat C, Alda M, Turecki G. Gender and risk factors for suicide: evidence for heterogeneity in predisposing mechanisms in a psychological autopsy study. *J Clin Psychiatry* 2006; **67**(10): 1612–7.
- 40** Petitti DB, Perlman JA, Sidney S. Noncontraceptive estrogens and mortality: long-term follow-up of women in the walnut creek study. *Obstet Gynecol* 1987; **70**(3): 289–93.
- 41** Schairer C, Adami H-O, Hoover R, Persson I. Cause-specific mortality in women receiving hormone replacement therapy. *Epidemiology* 1997; **8**(1): 59–65.
- 42** Owen-Smith A, Bennewith O, Donovan J, Evans J, Hawton K, Kapur N, et al. When you're in the hospital, you're in a sort of bubble." Understanding the high risk of self-harm and suicide following psychiatric discharge: a qualitative study. *Crisis* 2014; **35**(3): 154–60.
- 43** Jiang T, Gradus JL, Lash TL, Fox MP. Addressing measurement error in random forests using quantitative bias analysis. *Am J Epidemiol* [Epub ahead of print] 1 Feb 2021. Available from: <https://doi.org/10.1093/aje/kwab010>.



psychiatry in history

Meduna's Mixture: surreal ecstasy or perplexing abreaction

Jack Wellington Alexander Wellington and Grace Wellington

Carbon dioxide therapy, a precursor of the modern-day provocation of seizures via electrical induction, became a widely accepted practice by both psychiatrists and related healthcare professionals to better treat neuroses and psychoses.

Dr Ladislas J. Meduna, neuropathologist and Professor of Psychiatry at the University of Illinois College of Medicine in Chicago, invented the concoction, later dubbed 'Meduna's Mixture', in 1921. Its formula consisted of 30% carbon dioxide and 70% oxygen (collectively termed 'carbogen'). However, carbon dioxide concentrations would vary from 1.5 to 50%, at the discretion of the practising psychiatrist or psychologist experimenting in the fields of psychosis and schizophrenia management. To induce abreaction, a psychoanalytical axiom of catharsis allowing individuals to become aware of repressed emotions or traumatic experiences, Meduna would administer 20–30 breaths of the gas mixture, resulting in an intentional unconscious, altered state leading to convulsion within 1–3 min.

Meduna described patients' sensory phenomena as unclassifiable, as 'the patient is not "sleeping" in the physiological sense, nor is he in the state of consciousness' concerning true hypnagogic or visual hallucinations.¹ Accounts demonstrating such experiences recall apparitions of a 'bright light, like the sun' after 20 respirations, others describing out-of-body sensations as if 'out in space,' 'wonderful' and 'marvellous'.¹ However, Meduna admitted to preconvulsive events that did not follow experiences of 'celestial beauty and serenity' but were 'horrifying beyond description' and these individuals were advised not to receive further psychotherapeutic interventions owing to fear of similar reactions. These experiences from carbogen inhalation relate to the consequences of a drastic elevation of blood acidity via excess carbonic acid production, and the preconvulsive events of either intense feelings of euphoria or sensations of impending horror are a direct result of such changes in the patient's biochemistry. Patients undergoing such treatment, be it challenging for some or pleasant for others, would then become climated to future psychedelic therapies if required.

This form of convulsive therapy was thought to be useful for managing neuroses and relieving obsessive-compulsive disorder, allowing carbogen users to neglect repressed emotions and ideas while permitting a smoother transition to a more profound psychedelic state. Although Meduna paved the way for neuropsychiatrists and related clinicians regarding the development and practice of pharmacological convulsive therapy, administration of Meduna's Mixture was extensively abandoned owing to its ineffectiveness when compared with other forms of convulsive therapy. An example of such comparisons involves landmark work by Italian neurophysiologist Ugo Cerletti and psychiatrist Lucio Bini, who discovered electroconvulsive therapy in 1938.

The contributions Meduna has made to psychiatry have been historically significant and pivotal to the progression of managing difficult or treatment-resistant mental disorders via convulsive therapy. Although pharmacological forms of these therapies have been widely discarded in contemporary psychiatric practice, we must not forget how the application of Meduna's Mixture became instrumental in advancing psychiatric practice to this day.

Reference

1 Meduna LJ. *Carbon Dioxide Therapy*. Charles C. Thomas Publishing, 1950.

© The Author(s), 2021. Published by Cambridge University Press on behalf of the Royal College of Psychiatrists

The British Journal of Psychiatry (2021)
219, 447. doi: 10.1192/bjp.2021.28