A REVIEW OF THE ROLES OF GLYCERINE AND CHLORAL HYDRATE IN 19TH CENTURY PHARMACOTHERAPY

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Introduction

Lyndall Gordon has proposed that Emily Dickinson (ED) suffered from epilepsy, a proximate cause of her reclusiveness (1). Although inessential to the main and dramatic story the book tells of the generational feud between 'the two houses', such a diagnosis would require a new interpretation of much of Dickinson's poetry – a task Gordon indeed has begun.

The hypothesis for epilepsy is based principally on finding the medication glycerine, which ED took with some frequency between 1851 and 1854 (prescribed by the eminent Harvard professor and co-founder of the Massachusetts General Hospital, Dr. James Jackson) in a list contained in a folder on Health and Medicine in the Jones Library, Amherst. The list is titled 'Medicinal Uses of Glycerine in the 19th Century', and was derived from a popular self-help text, *Health at Home or Hall's Family Doctor* (2). Among dozens of uses was a formula for epilepsy that called for 'half an oz. of hydrate of chloral and twenty five drops of essence of peppermint in four oz. of pure glycerine.' Gordon comments: "Glycerine has many uses, but one of the medical uses in those days was for epilepsy…. This use of glycerine in the treatment of epilepsy (as distinct from its use for TB) has gone unnoticed." (3)

This claim for glycerine is unsupported by the evidence. Glycerine, a sweet syrup obtained from fats or oils, was never identified as an active principle against epilepsy in any official pharmacopoeia, dispensatory or textbook on epilepsy written in the 19th Century that I could locate. Glycerine's uses included as a topical antiseptic, a demulcent and sweetener, an excipient, and solvent for other medications, and as a nutrient (thus its latter putative role in treatment of tuberculosis and diabetes).

The active ingredient in Hall's formula for epilepsy was chloral hydrate, first reported and used as a sleeping medication in 1869; it is acrid to the smell and taste, and irritating to the stomach; thus it requires to be given with various syrups and sweeteners to disguise the taste. Although mainly a hypnotic, chloral also had application against a range of convulsive disorders, which included tetanus, chorea, rabies, strychnine poisoning, toxemia of pregnancy, and alcoholic delirium tremens (I myself used the drug for the latter in the 1960s at Boston City Hospital).

The following provides the necessary documentation for both the drugs in Dr. Hall's formula; research was conducted at the British Library, the Wellcome Library, and the National Library of Medicine of the US National Institutes of Health.

Glycerine

In the various editions of the authoritative Dispensatory of the United States of America[1] we may find several statements:

- 'Glycerin possesses extensive powers as a solvent and is an excellent excipient for many medicinal substances…. Employed internally as a therapeutic agent, it is deemed alterative, nutrient, and demulcent…. Dr. JL Crawcour, of New Orleans, has used it with supposed advantage in phthisis *[tuberculosis]*, and prefers it to cod-liver oil. Dr. W. Lauder Lindsay made experiments with it, to determine its alterative and nutrient properties, and found it to increase the weight of the body. Some cases are cited by him, in which it appeared to act beneficially in tuberculosis and strumous affections *[scrofula, swellings often related to TB]'* (4).

- 'The uses of glycerin as a vehicle of other medicines have already been given. Employed *internally* as a therapeutic agent, it is deemed alterative, nutrient, and demulcent…. It sometimes appeared to act beneficially in tuberculous and strumous affections, forming a useful succedaneum for cod-liver oil, when the latter could not be borne by the stomach' (5).

- 'Its richness in carbon suggested its use as a medicinal food and especially as a substitute for cod-liver oil; but as in so many other instances, a little clinical experience showed the so-called scientific inductions to be untrue' (6).

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- 'Although at various times much lauded in tuberculous diseases and in diabetes, [glycerine] has entirely failed to gain the confidence of the profession, and is now very rarely employed' (7).

- 'Wasting Diseases: Cod liver oil, syrup of ginger, and mucilage of gum Arabic, each two oz; oil of cloves eight drops. Mix. Take a tablespoonful thrice daily; or Cod liver oil and glycerine each two oz, gum arabic two drams, oil of bitter almonds three drops, oil of cloves ten drops. Take a tablespoonful thrice daily. Take of citrate of ammonia iron and quinine ten grains, cod liver oil and glycerine each two oz. Mix. Dose a tablespoonful' (8). [2]

- 'Internally [glycerine] is nutrient and demulcent. It has been proposed as a substitute for Cod Liver Oil, but its nutrient properties are far inferior…. As an external remedy, however, it is highly valued, chiefly for its emollient and undrying properties…. It possesses great powers as a solvent, and is an excellent excipient for many substances' (9).

In none of these texts is glycerine ever mentioned as a medication to treat or prevent epilepsy.

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[1] The series ran from 1833 to 1955. Glycerine as an external remedy for skin diseases is first mentioned in the 1849 eighth edition.

[2] Hall recommended glycerine for consumption but in combination with iodides of potassium or iron or with morphine (8), p. 731.

(Additional evidence for glycerine's specific application in treatment of tuberculosis, based on its supposed nutritive effect, is given in my paper on ED's use of the medication (10). That ED obtained her prescriptions from a Boston druggist was less, I believe, a question of privacy as Gordon suggests, but that 'Glycerine could only be obtained from the better class of druggists'; that is, a lead-free preparation (see reference 48 in my paper). The apothecary in question, Joseph Burnett's, was but a five-minute walk from Dr. Jackson's office.)

Several textbooks on epilepsy of the time were consulted, searching for any mention of glycerine as a treatment for the disease. These included the text cited by Gordon, written by Edward Henry Sieveking (11).[3] In that edition, fifty-eight patients are presented; none received glycerine. In Sieveking's second edition are listed thirty-four different forumulae for treatment of epilepsy; none contained glycerine (12). William Alexander reviewed treatments for epilepsy going back to 1831. None included glycerine (13). Sir William Osler's magisterial textbook of medicine makes no mention of glycerine for epilepsy (14); neither does the practical textbook of medicine owned by ED's physician in her last years, O.F. Bigelow. In that text, foul-tasting cod-liver oil is recommended for consumption, playing the same nutritive role as glycerine (15).

Finally, Dr. Jackson's chapter on epilepsy in his 1855 'Letters to Young Physician Just Entering Upon Practice', makes no mention of glycerine as a remedy (16).

Chloral Hydrate

Although known for decades, chloral was first discovered to be a soporific in 1869, coming into wide medical use shortly after. William Whitty Hall lauded the new finding:

> THE NEW ANODYNE The medical world is delighted with the discovery of a new medicine, and the newspapers abound with advertisements, setting forth the peculiar advantages of each preparation, every man claiming that his own is the best. It is called CHLORAL HYDRATE. The object of taking this medicine is to promote sleep, and thus far, when administered pure and in a proper manner, it has advantages above all others known hitherto, whether in the form of Opium, Morphine, Laudanum, or Paregoric. This Chloral Hydrate is in white crystals; almost every liquid dissolves it; hence it is largely advertised in the shape of syrups, anodynes, and various fluid mixtures… (17).

Squire's 1871 Companion to the British Pharmacopoeia considered chloral 'an excellent hypnotic, producing sound and placid sleep', but also used against chorea, delirium tremens, 'nervous disturbances and restlessness' (18).

[3] Sieveking was acknowledged by Peter Squire in his 1864 'Companion': 'I am indebted to Dr. Sieveking for various suggestions as the Work has passed through the press' (preface, p. vii).

The 1880 edition of the Dispensatory of the United States of America discusses chloral's role against convulsions due to various causes, but relegates it to secondary status against classic epilepsy:

> Perhaps no medicine has come so rapidly into extensive use as that now under consideration…. It is simply as a soporific that chloral is most efficient and most employed…. In spasms chloral is often useful, though generally inadequate to the cure of the more violent and obstinate of these affections… (19).

The text mentions tetanus, hydrophobia, chorea and epilepsy, but, '[I]n the latter it is at best but an occasional palliative'. In another pharmacopoeia of the time, the unpleasant taste of chloral is stressed: 'Its taste even in a watery solution is somewhat acrid and bitter, causing a sense of burning in the throat and sometimes in the stomach also'. The text goes on to say that chloral 'has been used to mitigate the fits of *epilepsy* by giving it before their regular hour of recurrence, when they are periodical' (20). [Italics in original.]

Dr. Bigelow's textbook makes no mention of glycerine for epilepsy but advises:

> "Against idiopathic epilepsy the most powerful means [of treatment] consists in the simultaneous use of some tonic remedy (such as strychnine or arsenic) in a solution to be taken after meals; and of a mixture composed more or less like the following: -- [potassium iodide, potassium bromide, ammonium bromide, potassium bicarbonate, tincture calumbae [a palm root], distilled water] (21).

But for convulsions, the textbook advises chloral as an adjunct:

> For general usefulness in such cases no remedies can compare with the bromides of potassium and ammonium…. Quinine or belladonna may often be given simultaneously with great advantage…. Sometimes the action of the bromide seems to be favoured by combining it with moderate doses of digitalis…. Where sounder sleep is urgently necessary, chloral, either alone or in combination with bromide of potassium, should be given at bed-time (22).

Many texts advise the use of sweeteners with chloral. One prescribes orange juice and oil of peppermint: 'The taste of hydrate of chloral is quite unpleasant, but orange-juice completely covers it, and so does peppermint water or essence of peppermint' (23). Also mentioned are 'syrup of orange flowers', mint, orange, vanilla (24).

Squire's Companion to the British Pharmacopoeia of 1864 noted that glycerine 'is sometimes employed as a sweetening agent in the place of syrup' (9). In a later edition Squire mentions, 'Syrupus chloral', a concoction of chloral and syrup, and also with peppermint (25).

W.W. Hall advised that chloral 'should never be taken except dissolved in some liquid in proportion of twenty parts to a hundred; it is best taken in beef-tea, or syrup

of orange peel, or as an enema in gruel.' The proportion of chloral to 'some liquid' of one to five is similar to his chloral/glycerine proportion of one to eight (26).

The use of glycerine as a solvent for chloral is mentioned in at least one other text: 'Chloral is freely soluble in water, alcohol, ether, chloroform, glycerine…fixed oils and volatile oils' (27).

Medical textbooks of the time distinguished between epilepsy and convulsions, the former a recurrent, idiopathic ailment; the latter acute related to an acute event, such as tetanus, chorea, rabies, strychnine poisoning, toxemia of pregnancy, and alcoholic delirium tremens. Toxemia of pregnancy is due to severe elevation of blood pressure. Hirschhorn and Longsworth have suggested that ED's 's twice hours-long loss of consciousness in 1884 ('…unconscious for the first time in my life' [L907 to her Norcross cousins]) was related to acute hypertension (28). [See there also the relationship of hypertension to Bright's disease, O.F. Bigelow's diagnosis on the death certificate.] ED may have received various anti-convulsant medications following these episodes (29). Alexander mentioned a great variety of such medications – such as arsenic, zinc, picrotoxin, borax, antipyrin, cod-liver oil, curare, quinine, hyoscyamus, aniline, and quinine (30). At the end of her life, when she lapsed into coma, ED was prescribed a dose of chloroform, perhaps to still unremitting convulsions: 'In the *status epilepticus*, chloroform is *the* remedy *par excellence*' (31). [Italics in original.]

Conclusion

In all authoritative texts of the time reviewed, glycerine was never advised or mentioned for treatment of epilepsy. Glycerine found its use as a solvent for other medications, a topical antiseptic and emollient, a nutrient in consumption, and as a sweetener. Chloral hydrate, although principally used as a sleep medication, found use against a range of acute convulsive disorders; and to a degree against epilepsy. W.W. Hall's formula for epilepsy is entirely consistent with these uses.

It is true that practitioners of the 19th Century practiced polypharmacy, often ignoring expert opinion. It cannot be ruled out that someone, sometime, tried glycerine for epilepsy; this would, however, have had no authoritative basis or precedent. It is therefore most unlikely that this was the intent behind Harvard's Dr. James Jackson's use of glycerine for ED – prescribed at a time when she was losing weight, visiting physicians to find relief, coming only a few years after recovering from long episodes of cough. When ED wrote to her brother Austin in March 1854, just three months after her last prescription was filled, 'And if the cough troubles you follow my prescription, and it will soon get well' (L156, cited in (10)). She surely did not imply that Austin had epilepsy.

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