This Week's Citation Classic® CC/NUMBER 5 FEBRUARY 1, 1988

Hudson J I, Pope H G, Jonas J M & Yurgelun-Todd D. Family history study of anorexia nervosa and bulimia. *Brit. J. Psychiat.* 142:133-8, 1983; and **Pope H G, Hudson J I, Jonas J M & Yurgelun-Todd D.** Bulimia treated with imipramine: a placebo-controlled, double-blind study. *Amer. J. Psychiat.* 140:554-8, 1983.
[Labs. for Psychiatric Research, Mailman Research Ctr., McLean Hosp., Belmont, and Dept. Psychiatry, Harvard Medical School, Boston, MA]

These studies tested the hypothesis that bulimia is closely related to major affective disorder. The first found high rates of affective disorder among the relatives of bulimic patients; the second showed that the antidepressant medication imipramine was an effective treatment for bulimia. [The *SCI®* and *SSCI®* indicate that these papers have been cited in over 100 and 135 publications, respectively.]

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These reports were part of a series of studies exploring the relationship between bulimia (compulsive binge eating) and major affective disorder (the mood disorders bipolar disorder and major depression). Like many studies, ours stemmed from a serendipitous observation: James I. Hudson, then a first-year psychiatric resident at McLean, read a report of reduced ion-pump activity in obesity[1] and decided to measure this activity in bulimia and anorexia nervosa. While negotiations to perform this assay dragged on (and ultimately fizzled), he interviewed bulimic patients for personal and family histories of psychopathology and evaluated their responses to the dexamethasone suppression test (DST)—a test of adrenal function that is often abnormal in depression. The first seven bulimic patients showed high rates of personal and familial affective disorder, and four had abnormal DSTs. At this point Hudson shared his data with Harrison G. Pope, Jr., an experienced researcher in biological psychiatry. Pope helped complete the pilot study,[2] in which we proposed that bulimia was a *forme fruste* of affective disorder, and spearheaded the effort to conduct antidepressant trials in bulimia.

Then followed a year of intense effort, during which we performed the family history and imipramine studies, as well as studies showing high rates of personal history of affective disorder[3] and abnormal DSTs[4] in bulimic patients. Our principal coworkers were Jeffrey M. Jonas, then a psychiatric resident, and Deborah Yurgelun-Todd, then a research assistant. Since none of us had funding, and all had full-time commitments, we operated on a shoestring budget and pirated time. For instance, to do the imipramine study, we purchased from our own pockets the imipramine tablets, lactose, and gelatin capsules. We then ground the tablets with mortar and pestle and filled by hand each imipramine and placebo capsule used in the study.

Why has this work been cited so frequently? Possibly it is because, like scientists before us in many fields, we proposed that nature might be simple—namely, that bulimia was caused by a specific, pharmacologically reversible, biological disturbance similar to or identical with that which causes major affective disorder. This hypothesis challenged the prevailing view that bulimia was a complex, multifactorial disorder, caused by intricate psychosocial factors, and treatable only with talking therapy. Thus, our work sparked heated debate: others were eager both to confirm and to refute our findings.

Perhaps because of this controversy, we had difficulty obtaining funding; four successive grant applications to the National Institute of Mental Health for studies of eating disorders, two of which involved the studies that became this *Citation Classic*, were turned down. Nevertheless, our findings have been widely replicated by other centers and by us.[5,6] Now, it is generally conceded that there is an association between bulimia and major affective disorder and that antidepressants are effective in the treatment of bulimia, although the nature of this association and the exact role of pharmacotherapy in bulimia remain hotly disputed.[5,6]

1. **DeLuise M, Blackburn G L & Flier J S.** Reduced activity of the red-cell sodium-potassium pump in human obesity. *N. Engl. J. Med.* 303:1017-22, 1980. (Cited 215 times.)
2. **Hudson J I, Laffer P S & Pope H G.** Bulimia related to affective disorder by family history and response to the dexamethasone suppression test. *Amer. J. Psychiat.* 139:685-8, 1983. (Cited 70 times.)
3. **Hudson J I, Pope H G, Jonas J M & Yurgelun-Todd D.** Phenomenologic relationship of eating disorders to major affective disorder. *Psychiat. Res.* 9:345-54, 1983. (Cited 35 times.)
4. **Hudson J I, Pope H G, Jonas J M, Laffer P S, Hudson M S & Melby J C.** Hypothalamic-pituitary-adrenal axis hyperactivity in bulimia. *Psychiat. Res.* 8:111-8, 1983. (Cited 55 times.)
5. **Pope H G & Hudson J I.** *New hope for binge eaters: advances in the understanding and treatment of bulimia.* New York: Harper & Row, 1984. 239 p.
6. ————. Is bulimia a heterogeneous disorder? Lessons from the history of medicine. *Int. J. Eating Disorder.* (In press.)

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