pharmacological treatment of bulimia is well established, primarily the use of antidepressants, the effectiveness of medication in the treatment of anorexia nervosa is more uncertain. For example, the data evaluating the effectiveness of the selective serotonin reuptake inhibitor, fluoxetine, in prolonging time to relapse is not encouraging. Ninety three (93), recovered subjects were utilized in this two site (Toronto, Canada and New York, New York) study. Although survival rates within the study differed between the two sites (survival was greater in Canada; p=0.005), fluoxetine, overall, did not prolong time to relapse.

Despite these negative findings, results from a study with the atypical antipsychotic, olanzapine, suggest greater efficacy in treating anorexia nervosa with this drug. In a 13-week trial, 34 day-treatment patients with anorexia nervosa were given olanzapine and monitored for weight gain. It was reported that patients on olanzapine had a faster rate of weight gain as compared to those patients receiving day-treatment only (p=0.04). These results should be interpreted cautiously, notes Dr. Walsh. No medication is clearly effective for anorexia nervosa and that the best treatment remains caloric intake.

In the final address of the session, Annemarie van Elburg, MD, Reintveld Center for Eating Disorders, the Netherlands, compared and contrasted eating disorders in children and adolescents. In children, the most common eating disorders include food avoidance emotional disorder, functional dysphagia, pervasive refusal syndrome and early anorexia nervosa. Adolescents commonly present with the more classical eating disorders of anorexia nervosa, bulimia nervosa, eating disorder not otherwise specified and emetophobia. One central question is whether the age of onset of eating disorders is getting younger. Although, no clear biological underpinning has been identified, the anecdotal correlation between puberty and the onset of a full blown eating disorder suggests a neuroendocrinological trigger and provides an opportunity for future investigations.

Evaluating the Effectiveness of Your Medication Choice:

One significant issue facing patients currently on antidepressants is the loss of effect that may occur with chronic use of the drug, ie, the so called "poop-out" effect. Elaborating on this issue, Mark Zimmerman, MD, Brown University School of Medicine, Providence, RI, states, "When you see someone in your practice, and you put them on medication, and they respond, you are essentially seeing two types of individuals. Some are true drug responders. Some have responded to the non-specific effects of treatment. They are placebo responders." Despite their response to treatment, there are no available clinical indicators to differentiate between these two types of responders.

The fact that some individuals are placebo responders, may account for the majority of cases of relapse reported in medication continuation studies (Zimmerman M, Posternak MA, Ruggero CJ. *J Clin Psychopharmacology* 2007;27:177-81). One experimental design that is useful in parceling out the rate of relapse attributable to placebo responding is the "Extension Design". In this paradigm, active medication or placebo is initially assigned in a double-blind fashion. Responders to active medication or placebo then go on to the continuation phase of the study with no change in their treatment. That is, individuals assigned to the medication group remain on medication, while those given placebo continue to receive placebo. This design allows for the question, what percentage of relapse in patients on active medication can be attributable to an initial placebo response?

In order to calculate the percentage of relapse accounted for by placebo responding, four pieces of data are needed. In the acute phase of the experiment, the Response Rate to Medicine (RRM) and the Response

Rate to Placebo (RRP) are needed to complete this calculation. In addition, the relapse rate in people who responded to medication (RLM) and the relapse rate in people who responded to placebo (RLP) must be obtained from the continuation phase of the study. Once this data is collected, the rate of relapse that may be attributable to initial placebo responding can be estimated.

In a hypothetical study, 150 patients received medication, and 100 of them responded, (RRM=66%). These 100 medication responders were continued on medication in the continuation phase where 30 patients relapsed (RLM=30%). 150 patients received placebo and 50 of them responded. (RRP=33%) These 50 were continued on placebo in the continuation phase where 25 of them relapsed (RLP=50%)

First, an estimate of the rate at which patients displayed a placebo response despite receiving active medication (ePR) is calculated by dividing the RRP by the RRM.

ePR = RRP/RRM, in our case 33%/66% = 50% of medication responders are actually placebo responders

Second, how many patients treated with active drug in the continuation phase, who were responders in the acute phase, are presumptive placebo responders (PPR)? To get this figure, the number of patients receiving active medication in the continuation phase is multiplied by the placebo response rate calculated in the first step.

PPR = ePR * The number of PTs receiving active medication in continuation phase or 50% * 100 patients = 50 patients who are presumptive placebo responders.

The number of patients treated with active medication in the continuation phase who have responded, but are expected to relapse because they are presumptive placebo responders (eRLP) can then be calculated by multiplying the PPR by the RLP.

eRLP = PPR * RLP, or 50 * 50% or 25 patients

Finally, what percentage of relapse can be attributable to initial placebo responding? This final calculation is obtained by taking the number of presumptive placebo responders on active medication that have relapsed (ie,eRLP) and dividing by the total number of patients who relapsed on medication in the continuation phase.

eRLP / N 25/30, or 83%.

Thus the in this study, presumably 83% of the patients who relapsed after responding to medication and continuing on medication in the continuation phase actually relapsed because they were placebo responders.

Using this method, researchers and clinicians may more accurately determine who is truly responding to their choice of medication versus those who may merely be placebo responders and, thus, more likely to "poop-out" during the latter portion of their treatment.

Tamoxifen Treatment of Bipolar Disorder

Protein kinase C (PKC) is a family of enzymes involved in phosphorylation and cellular messaging. A growing body of evidence suggests that PKC inhibition may be a possible mechanism to treat bipolar disorder. Both lithium and valproate (commonly used mood stabilizers) inhibit PKC (Hahn GG et al. *J Psychiatr Res* 2005;39(4):355-63). In preclinical models, stimulants have been shown to activate PKC (Einat H et al. *BiolPsychiatry* 2006;59(12):1160-71) and when compared to normal controls, platelets from patients with bipolar disorder have higher levels of PKC (Friedman E et al. *Biol Psychiatry* 1993;33(7):520-5). Tamoxifen, an antiestrogen used in breast cancer treatment, is currently the only PKC inhibitor capable of penetrating the central nervous system. In a pilot study of 7 patients with bipolar disorder, tamoxifen