eligibility criteria for severe PMS and the same outcome measures after 2–3 months treatment. *Results:* Progesterone shows no mood effects greater than placebo but produces fatigue and somnolence similar to alprazolam, i.e., evidence of sedating but not anxiolytic effects. Leuprolide reduces the entire constellation of premenstrual symptoms, including depression, but does not reduce major depression. Serotonergic and noradrenergic drugs reduce depression, but the serotonergic antidepressants are better tolerated in treating the cyclic symptoms of PMS. *Conclusions:* Exogenous progesterone appears to have no direct effects on mood, but the remission of symptoms that is obtained by supressing ovulation suggests indirect involvement of the gonadal hormones. The antidepressants effectively improve the mood and behavioral symptoms of PMS, but whether the effect is specific to the serotonergic system is not identified.

S-26-5 Psychopharmacology of Pregnant and Postpartum Women

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Pregnancy and childbirth represents a period of significant neuroendocrine and psychosocial alterations. There is sparse data to indicate that these periods are protective and studies suggest that there is increased vulnerability for both affective and anxiety disorder exacerbations. The use of psychotropic medications during pregnancy and lactation is a complex clinical issue laden with ethical concerns and handicapped by limited data. The wide-spread use of selective serotonin re-uptake inhibitors (SSRI) for a variety of disorders underscores the need to obtain meaningful data on these agents. A recent meta-analysis (Altshuler and Cohen) summarizes the teratogenetic data, but the issue of neurobehavioral sequelae from chronic exposure remains an enigma. The pharmacokinetics of psychotropic medications during pregnancy and lactation will be reviewed with an emphasis on developing treatment guidelines based on: 1) past treatment history; 2) the available literature; and 3) the physicochemical properties of drugs. To highlight the complexity of the pharmacokinetics of placental passage and excretion into breast milk, recent data on SSRIs (sertraline and fluoxetine) will be discussed. Maternal and umbilical cord serum pairs indicate incomplete placental passage (ratio 0.78) and complete passage (ratio 1.2) for sertraline and fluoxetine, respectively. There was no evidence that infant exposure to sertraline via breast milk had any adverse effects on growth, developmental milestone achievement, and number of sick visits at 12 month follow up.

S-26-6 The Psychobiology of Female Specific Mood Disorders — Discussion

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Of all the neurotransmitters studied to date there is increasing evidence that serotonin may be important in the pathogenesis of mood and anxiety disorders. The serotonergic system is in very close reciprocal relationship with gonadal hormones. A disturbance in the interaction between the hypothalamic-pituitary-gonadal axis and the serotonergic cascade may be of particular relevance to mood disorders in women. The higher incidence of mood disorders among women as compared to men is primarily seen from puberty on and is less marked in the years after menopause. Data presented in this symposium support the notion that the serotonergic system is more vulnerable to dysregulation in females than in males. Future research will have to establish whether the genetic expression and function of serotonergic receptor subtypes are influenced by gonadal and adrenal steroid hormones and whether an imbalance in the interaction of these two systems may contribute to the vulnerability of women to mood disorders.

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S-27 Imidazoline Receptors: CNS Pharmacology and Clinical Relevance

S-27-1 Platelet Immunoreactivity and Radioligand Binding to Imidazoline Receptors in Depression

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The binding of ^{3}H-clonidine, an imidazoline compound, to platelet α_2-adrenoceptors has been reported by numerous groups to be elevated in depressed patients. However, it has only recently been realized that ^{3}H-clonidine can also bind to a non-adrenergic imidazoline binding site (I_1) on platelets, which is pharmacologically identical to the brain imidazoline receptor (IR_1). Results are presented from three separate platelet binding studies with p[^{125}I]iodoclonidine, indicating that previous data with ^{3}H-clonidine may have been misinterpreted as indicative of an elevation of α_2-adrenoceptors. We now postulate these binding changes are mostly due to an elevation in platelet I_1 sites in depression. Furthermore, a selective anti-imidazoline receptor antibody was obtained (courtesy of Dr. D. Reis). Using this antiserum it has been possible to identify a platelet imidazoline-like receptor by Western immunoblotting, at 100-fold improved sensitivity compared to the radioligand binding assay. The intensity of a single platelet immunoreactive band (33 kDa) was cross-validated with the radioligand binding assay by showing it to be linearly correlated with the I_1 Bmax values obtained on the same samples from control subjects. Using this antiserum, we confirmed that depressed patients displayed a marked elevation in the density of a platelet I_1-like immunoreactive 33 kDa protein in plasma membranes. Thus, we have discovered a novel protein which is elevated in depression as assayed by two independent techniques and using two demographically different patient populations. Data will also be presented that this IR_1-like protein is regulated by chronic antidepressant treatments, and has specificity for depression since elevations in its density are not observed in generalized anxiety disorder or Alzheimer's patients. Supported by MH42859 and MH49248 grants.

S-27-2 Imidazoline Receptors: CNS Pharmacology and Clinical Relevance

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The understanding of the role of any receptors is critically dependent on the availability of selective ligands. To this end we have synthesized a number of imidazoline containing compounds such as 2BFI, BU-224 and BU-239 that show low nM affinity at I_2 sites and micromolar affinity at α_2 and other receptors. One of these compounds has been labelled and ^{3}H-2BFI is now in the public domain. Binding studies have revealed interesting differences in the distribution of I_2 sites between species and markedly reduced binding in basal ganglia of patients with Huntington's disease. Functional studies reveal it to increase extracellular levels of noradrenaline in frontal cortex and dopamine in striatum which may explain its antidepressant profile in the Porsolt test and its ability to induce eating (see Jackson et al, this meeting). The clinical potential of such compounds in neurologic and psychiatric disorders needs exploring and work is in progress to make PET and SPECT versions for human receptor labelling *in vivo*.

[1] Nutt DJ et al (1995) In: The imidazoline receptor: pharmacology, functions, ligands and relevance to biology and medicine. Eds. Reis DJ, Bousquet P, Parini A. New York Academy of Sciences, New York. pp. 125–139.

[2] Hudson, AL et al (1996) Identification and characterization of ligands selective for central I_2-imidazoline receptors. Neurochem Int (in press).