**UNITED STATES DISTRICT COURT**
**MIDDLE DISTRICT OF FLORIDA**
**ORLANDO DIVISION**

**IN RE: Seroquel Products Liability Litigation**

**MDL DOCKET NO. 1769**

This document relates to:

| | |
|---|---|
| Linda Guinn | 6:07-cv-10291 |
| Janice Burns | 6:07-cv-15959 |
| Richard Unger | 6:07-cv-1581 2 |
| Connie Curley | 6:07-cv-15701 |
| Linda Whittington | 6:07-cv-10475 |
| Eileen McAlexander | 6:07-cv-10360 |
| ~~Sandra Carter~~ | ~~6:07-cv-13234~~ |
| ~~Clemmie Middleton~~ | ~~6:07-cv-10949~~ |
| ~~Hope Lorditch~~ | ~~6:07-cv-12657~~ |
| David Haller | 6:07-cv-15733 |
| ~~Charles Ray~~ | ~~6:07-cv-11102~~ |
| ~~William Sarmiento~~ | ~~6:07-cv-10425~~ |

**DECLARATION OF WILLIAM WIRSHING, M.D.**

My name is William C. Wirshing. I am over twenty-one years of age, am of sound mind, have never been convicted of a felony, and am otherwise competent to make this Declaration-Report. I have personal knowledge of all factual statements contained herein and all such factual statements are true and correct as outlined herein in this declaration-report.

**Qualifications and Expertise**

1. I graduated in 1978 from the College of Engineering at the University of California at Berkeley with highest honors and a Bachelors of Science degree in Electrical Engineering and Computer Science (minor in bioelectric systems). I received my M.D. from the University of California at Los Angeles in 1982, receiving the Sandoz Award for "Excellence in the Behavioral Sciences." I remained at UCLA for both my rotating

internship, during which I focused on internal medicine, neurology, and pediatrics and for my three-year residency training in psychiatry. My final year of residency was at the West Los Angeles Veterans Affairs Medical Center where I was Chief Resident in Geropsychiatry. Over the next two years, I was a Post Doctoral Research Scholar at UCLA, a fellowship position through the National Institute of Mental Health during which I learned and applied clinical research techniques for the study of persons with severe schizophrenia.

2. I am the Vice-President in charge of research and continuing medical education for Exodus Inc. in Culver City, California and also Clinical Director of Exodus Real Recovery in Agoura Hills, California. In my clinical psychiatric practice, I see approximately 325 new patients in a typical month; supervise nearly a dozen psychology doctoral candidates; and teach over a dozen nursing, social work, and nurse practitioner students.

3. Over the decades between 1986 and 2006, both my clinical work and research focus remained on the treatment of persons with schizophrenia. I was the Chief of the Schizophrenia Treatment Unit at the VA Medical Center during the vast bulk of this time frame, and was also the Co-Chief of the Schizophrenia Outpatient Research Clinic during the last ten years.

4. Given my expertise in the treatment of schizophrenia, I have had occasion to prescribe Seroquel and the other antipsychotic agents and have extensive first hand clinical and academic experience with the medication. I was invited to be one of nineteen experts who presented their findings and opinions at the consensus development conference in November 2003 before the American Diabetes Association; the American Psychiatric

Association; the American Association of Clinical Endocrinologists and the North American Association for the Study of Obesity. It was the findings of this conference that resulted in the February 2004 Consensus Statement in the journal *Diabetes Care*, cited by counsel.

5. I have also been involved in litigation regarding another anti-psychotic agent, olanzapine (Zyprexa). I was found qualified to testify before the MDL court in that litigation. Moreover, as a lead witness for the State of Alaska in litigation involving Zyprexa, Eli Lilly did not challenge my qualifications and I presented my opinions in that recent trial which settled before verdict.

6. I have attached my *curriculum vitae* and the report I submitted to counsel for Plaintiffs in this litigation, and I incorporate those documents by reference herein. I also incorporate my deposition testimony.

**Definitions**

7. I have been asked to provide some basic definition of some salient medical terms : OGTT, two hour and fasting glucose and HbA1c.

> OGTT is a standard test of glucose metabolism wherein a patient in a fasting state is administered a standard oral glucose load (usually 75gm) and has his/her blood glucose measured at standard intervals out to two hours.
>
> Two hour glucose: The plasma glucose measured two hours after the oral glucose load in the OGTT
>
> Fasting glucose: Plasma glucose measured in the fasting state (i.e., at least 8 consecutive hours of fasting--though sometime the definition is extended to 12 hours.
>
> HbA1C: This is glycosolated hemoglobin. It is a measure of the percentage of the hemoglobin (the oxygen carrying molecule of red blood cells) that has an attached glucose element. It is integrated

summary of the severity of glucose elevations a person has had over the preceding 60 days. It integrates both the severity of the elevated glucose and the amount of time such elevations occurred. It does not though distinguish between levels and time (i.e., low elevations over a protracted period and high levels over a briefer epoch will both result in an elevated HbA1c).

**Responses to Particular AstraZeneca Statements**

8. I have reviewed the brief of AstraZeneca that criticizes my opinions and methodology and I believe it is important to respond.

9. AZ lawyers state "Dr. Wirshing has no scientifically reliable basis for extrapolating from weight gain allegedly related to Seroquel to diabetes. Dr. Wirshing ignores the data that contradict his opinion and relies instead on the cherry-picked weight gain data." I respond as follows:

10. The fact that Seroquel induces significant and sometimes massive increases in adiposity is indisputable. The data supporting this have been available to the company since before launch. The data are so compelling in fact that the company recently (July 2008, Jeffries & Alam) proposed that weight gain be changed to a "very common" undesirable side effect in their labeling. There are literally hundreds of studies to support this observation. Among the more recent of these studies carried out and reported by AstraZeneca (July 2008, Jeffries & Alam Weight Gain in Adolescents) concerns the impact on weight gain in adolescent populations treated from three to 26 weeks. In the 3-week trial a jaw dropping 12% gained in excess of 7% of their body weight (FDA definition of clinically significant for pharmaceutical studies) versus 0% in the placebo group (on average 1.7kg vs. 0.4kg). During the 26-week study patients gained an average of 4.4kg with a startling 45% gaining

more than 7% of their body weight.

11. I have personally treated in excess of 3000 patients with quetiapine over the last decade. Of these, several hundred have developed diabetes and I have been responsible for delivering their endocrinologic care over the years. I have designed, implemented, and currently run programs to help my patients control and loose the weight gain associated with quetiapine and other related psychoactive compounds. For me, weight gain and diabetes are not abstract constructs to be sifted from the voluminous data of trials but stark daily clinical realities. The weight gain in my patients is at least as resistant to weight reduction techniques as the "normal" weight gain. It requires diligence, focus, and consistency over a protracted period of time which is difficult for any group of people, nevertheless those with mental illness.

12. The causal relationship between weight gain and diabetes is established, robust, and unarguable. The connection between Seroquel and diabetes has become generally accepted in the medical community. It is referenced not just in multiple peer reviewed journals, but also in numerous recognized text books, including Harrison's *Internal Medicine*; Goodman and Gillman's *The Pharmacological Basis of Therapeutics* and psychiatry texts including Schatzberg, MD, Alan F., Charles B. Nemeroff, MD, PhD, The American Psychiatric Publishing Textbook of Psychopharmacology. 3rd Ed. Arlington, VA: American Psychiatric Publishing, Inc.

13. Indeed the defense's own expert stated in his report that the causal connection between excessive weight (obesity) and diabetes is larger than the causal impact of smoking on lung cancer. Dr. Koplan however, seeks to draw an artificial line between the risk and

import of obesity, or pre-existing BMI and added weight gain, suggesting that because obesity is such an important risk factor, any other risk factors pale by comparison and are thus epidemiologically and clinically inconsequential.

14. As a clinical and academic physician practicing with this patient population, I was surprised by such an incorrect and flippant approach to the very real risk of the Seroquel induced weight gain in this already high risk population. Dr. Koplan disregarded an abundance of literature that establishes the risk. For example, the Fontaine study, *Estimating the Consequences of Anti-Psychotic Induced Weight Gain on Health and Mortality Rate,* used the Framingham Heart Study's public use data set and national statistics on population demography to estimate the expected effect of weigh gain on number of deaths and incident cases of IGT [Impaired Glucose Tolerance] and HTN [hypertension] for a 10 year period. Critically "results indicated that the estimated deleterious effects of weight gain were greater for people with higher BMI's at baseline, for greater degrees of weight gain." Indeed, the study found that the relationship of impaired glucose tolerance with BMI is "monotonically increasing." Pages 277-278. In the discussion, Fontaine et. al., noted that the impact of weight gain would be even more deleterious amongst the schizophrenic population, precisely because of their increased baseline risk:

> [i]t seems likely that additional weight gain from atypical agents will increase both the prevalence and severity of elevated BMI, as well as further increase the medical diseases that are associated with weight gain and higher BMIs (Henderson et.al., 2000). This will cause the BMI distribution from the Framingham sample, a sample of primarily non- schizophrenic individuals, to result in conservative estimates when extrapolated to the schizophrenic population. Fontaine, *ibid.*, at 283.

15. I was also surprised to see Dr. Koplan's Declaration minimizing the import of

weight gain superimposed on underlying elevated BMI in light of the fact that he was a co-author of a paper by Mokdad and others entitled *The Continuing Epidemics of Obesity and Diabetes in the United States*, JAMA 2001: 286910. In that study, Dr. Koplan and his co-authors note that "**Both** BMI and weight gain are **major** risk factors for diabetes....For every 1-kg increase in measured weight, the risk of diabetes increased by 4.5% in a national sample of adults." (bold added for emphasis) Mokdad at 1197.

16. Similarly, Resnick, HE et. al. suggest in the article *Relation of Weight Gain and Weight Loss on Subsequent Diabetes Adults,* Journal of Epidemiology and Community Health; (Aug 2000; 54,8) that many overweight people have not reached a threshold at which additional weight gain fails to increase diabetes risk reflecting that an increased weight for that population, which pushes them over that threshold, will have obvious deleterious clinical consequences including of course, diabetes. Finally, the literature on this issue is ever growing. Just this week the New England Journal of Medicine published a study from Sweden entitled *Clinical Risk Factors, DNA Variants and the Development of Type 2 Diabetes* by Lysenko N. Engl. J. Med 2008:359:2220-32. This study looked at risk factors beyond obesity and weight gain, and considered genetic risk factors as well. Lysenko notes "[w]e also evaluated whether genetic risk factors would further increase the risk imposed by an increase in the BMI...There was a stepwise increase in diabetes risk with an increasing number of risk alleles and increasing quartiles of BMI or a disposition index above or below the median..." Lysenko at 2229.

17. The above data reflect a fundamental premise of clinical medicine – that each incremental risk factor can worsen outcomes and can be contributory, or in legal parlance,

are substantial contributing factors. The Koplan analysis which disregards the import of incremental drug induced weight gain in an already obese person is incorrect and plainly contrary to good medicine and science. Obviously all these risks are important and hence they are all substantial contributing factors in assessing the etiology of the diabetes.

18. Indeed, the ADA Consensus Conference developed important clinical guidelines including baseline monitoring (including for personal and family history of obesity, etc.) and measurements of weight, blood pressure, fasting plasma glucose and fasting lipid profile prior to inception of antipsychotic medication and thereafter follow-up monitoring at specific intervals. Moreover, the consensus tells physicians that "if a patient gains greater than or equal to five percent of his or her initial weight at any time during therapy, one should consider switching the SGA." The data reflect that Seroquel causes such an appreciable weight gain or higher in a significant number of patients. These recommendations would be superfluous if the Koplan view of the evidence was correct since if the underlying obesity or other underlying or "confounding" risk factors already exist, the incremental weight gain independently related to Seroquel would be immaterial. Of course, it is highly material to real patients in the clinical setting and hence those guidelines are well founded. Even AZ has recognized their validity in the additional recommendations in the later package inserts.

19. It has been and continues to be my opinion that quetiapine induces its most deleterious impact on endocrinologic functioning (i.e., glucose regulation) largely through its impact on weight gain. Diabetes, though, is but one of the many possible downstream consequences of excessive adiposity. Additionally, though weight gain is a large and often

times dominant causal factor for Type II diabetes, it is by no means the only one. Other established risk factors include family history, smoking status, ethnicity, and hepatic functioning (Lyssenko et al, 2008), as well as emerging specific genetic factors (Meigs, et. al., *Genotype Score in Addition to Common Risk Factors for Prediction of Type 2 Diabetes*Meigs, et. al., N. Engl. J. Med 2008; 359:22008-19. 2008.

20. Thus, while the defense is correct in stating that "on average" it can take an extended time for the deleterious impact of excessive weight to exert its ultimate effect on diabetes, there is enormous variance in this figure. In patients, for example, who were obese at baseline, and had several of these additional clinical factors, quetiapine induced weight gain would be expected to have a much more rapid impact on glucose metabolism and ultimately the expression of frank diabetes.

21. In addition to the well-established and recurrently documented connection between quetiapine induced weight gain and diabetes, there is a growing body of evidence to suggest that quetiapine may have an additional deleterious impact on glucose metabolism. For example, Studies 126 and 127, which formed the basis for the recent changes in the adverse experiences section, suggested that quetiapine use resulted in a several fold increase in new onset diabetes over an extremely brief period of time. While there were only a small percentage of patients who developed diabetes, the brevity of exposure suggests that quetiapine was exerting this toxicity through "extra-adiposity" avenues. It is not known exactly what these mechanisms might be (hepatic, neurogenic, and pancreatic have all been suggested), however such an effect could easily account for the many rapid onset diabetes cases that have been reported. It would also account for the few cases I have personally seen

where discontinuing the quetiapine caused a remediation of the diabetes and reintroduction resulted in additional diabetic decompensation. In any event, even though I believe that the weight gain adiposity is the most obvious, if not predominant mechanism, it does not exclude other co-occurring mechanisms. In medicine, the development of disease is frequently multifactorial and there are often multiple mechanisms that explain how a drug causes an effect. In any event, one does not need to fully appreciate the mechanism of action to accept that a certain adverse or salutary response is related to a medication's ingestion. We still do not fully understand the mechanism of action as to how the SGA's, including Seroquel, have a beneficial effect on certain mental illnesses and the same is true for many medications, if not the majority of all medications. Nevertheless certain adverse drug reactions are widely appreciated.

22. Study 125 further highlights this latter point. This study is touted by AstraZeneca as the only study designed to examine the question of whether Seroquel may cause diabetes. On the contrary, Study 125 was actually designed NOT to detect certain important markers for Seroquel-induced glucose dysregulation. Significantly, despite the design limitations, proper interpretation of the results of Study 125 provides evidence that Seroquel does indeed cause diabetes by inducing insulin resistance.

23. Study 125 was a 24 week, open label study comparing effects of glucose metabolism and insulin sensitivity in patients taking Seroquel, and its closest market competitors, Zyprexa and Risperdal. It was not a blinded study, nor was it placebo-controlled, two very important features of well-designed trials. The design of the study did attempt to control for factors which might confound indicators of glucose dysregulation: it

was conducted in primarily white Eastern Europeans, with average baseline BMI of 24, and intended to exclude patients with history of diabetes or recent atypical antipsychotic use. In other words, the study population was (generally speaking) metabolically healthy. As explained below, it is for precisely this reason that the primary endpoint of the study fails to properly measure Seroquel's diabetic potential.

24. The primary endpoint of the study was the change at 24 weeks of the "area under curve" in a 2 hour oral glucose tolerance test (OGTT). The OGTT is a standard clinical measure to detect abnormalities in glucose metabolism. Indeed, a peak blood sugar exceeding 200mg/dl following a glucose load is part of the definition of DM. It is, though, a decidedly down stream effect in a person with Type II DM. Area under curve values such as those identified as the primary endpoint of this study would be very unlikely to shift in an endocrinologically healthy group in but 24 weeks time, even with the significant weight gain that occurred in Study 125. Given what we know about DM, one would not expect a population of increasingly obese patients to manifest an average shift in OGTT for years (though marked individual variation would be expected—see above). A much more sensitive measure of glucose regulation are so-called clamp studies (gold standard) or calculating a HOMA index (less rigorous and more variable). These tests are able to detect subtle changes is glucose regulation well before the insensitive OGTT.

25. The primary endpoint used in Study 125 measures how well a patient's body disposes of glucose immediately following a glucose load; essentially, whether these generally healthy patients were able to produce enough insulin to meet the load. Not surprisingly, the results indicated no statistically significant change from baseline to Week 24

in these metabolically healthy patients. The primary endpoint of this study does NOT measure the body's regulation of glucose in the fasting state, nor does it measure insulin resistance. In other words, the primary endpoint will NOT reveal whether Seroquel has increased insulin resistance in these patients, whether the pancreas must now produce more insulin in order to meet the glucose load, or whether Seroquel has produced a disturbance in fasting blood glucose levels.

26. What is truly important and informative about the results of Study 125 are the statistically significant positive findings in the secondary parameters, particularly taken in the context of the small sample size (110 patients completing the study in the Seroquel arm) and relatively short duration (24 weeks). There were statistically significant increases in both mean fasting blood glucose (3.19 mg/dl) and HbA1c (0.122%), indicating that Seroquel may have disrupted the body's ability to regulate glucose in a fasting state. Fasting C-peptide (a measure of endogenous insulin production) also increased, indicating that these patients were now producing more insulin in a fasting state: a marker for insulin resistance. Further, patients taking Seroquel experienced a mean weight gain of 3.65 kg (8 pounds) in just 24 weeks. All of these findings were statistically significant despite the fact that the study was powered to look at another (less useful) primary endpoint. The results of Study 125 provide additional evidence that Seroquel causes diabetes, and that it may do so by inducing insulin resistance, even over a comparatively brief epoch.

27. Overall it appears that there are some additional non-adiposity factors that may be contributing to the diabetes seen with quetiapine use. Though I continue to be of the opinion that the lion's share of the causal equation goes to increases in adiposity, in certain

patients these other factors may in fact predominate.

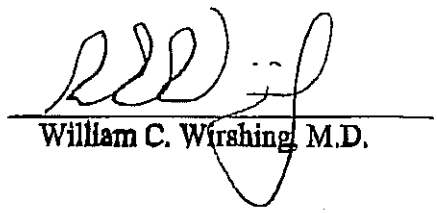
28. Defendant's make other incorrect comments about my opinions. Defendant claims that I improperly extrapolate from an accepted premise – that obesity can cause diabetes – to an unfounded claim –"that any amount of weight gain over any period of time will cause diabetes." The defendants misstate. I explain that quetiapine leads to weight gain and that weight gain leads to diabetes. I did not say "any weight gain." Rather, I explained, "[u]sing the FDA's definition of clinically pertinent weight gain (i.e., a 7% increase) quetiapine routinely impacted over 25 percent of the treated population."

29. Defendant states that I do not actually offer an opinion that Seroquel causes diabetes. Instead, they claim I opine that Seroquel causes weight gain and, as a result, "it is axiomatic" that Seroquel will lead to diabetes – eventually." The word "eventually" is tacked on by the defendants. I state that "it is axiomatic that increases in obesity will result in subsequent increases in hyperglycemia, frank diabetes, hyperosmolar coma, and even death due to endocrinologic complications." As I explained above, there is a wealth of literature showing that each incremental kg of weight increase correlates to development of diabetes in some.

30.. I hold additional relevant opinions as set forth in my expert report in this matter, which is attached and incorporated by reference. Additional opinions were elaborated in my deposition. The documents I reference in this Declaration-Report are annexed as exhibits to the Declaration of Paul Pennock, Esq.

I declare under penalty of perjury that the foregoing is true and correct.

Executed this 24th day of November 2008.



William C. Wirshing, M.D.

IN THE SUPERIOR COURT OF THE STATE OF DELAWARE

IN AND FOR NEW CASTLE COUNTY

IN RE: SEROQUEL LITIGATION C.A. No.: 07C-SER-1

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THIS DOCUMENT RELATES TO:

ALL CASES IN FIRST HALF OF
INITIAL TRIAL GROUP

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# EXPERT REPORT AND DECLARATION OF WILLIAM C. WIRSHING, M.D.

William C. Wirshing, M.D.

Educational and Professional Background

Education
I graduated in 1978 from the College of Engineering at the University of California at Berkeley with highest honors (cumulative G.P.A. 3.93) and a Bachelors of Science degree in Electrical Engineering and Computer Science (minor in bioelectronic systems). During my tenure there, I was elected to membership in the Phi Beta Kappa and Tau Beta Pi honor societies. The former is traditionally reserved only for those pursuing a "liberal" educational experience (e.g., College of Letters and Science) and the latter is the equivalent entity for students in the science-intensive curriculum of the School of Engineering. Although I then began medical school at UCLA almost immediately following my undergraduate studies, my education was interrupted when my youngest brother developed and then succumbed to brain cancer during my first and second years. During several lengthy arranged absences from school in southern California, I assisted my mother in caring for my brother and worked as an engineer in Mountain View (i.e., "Silicon Valley") California through the beginning of my third year at UCLA.

I completed my undergraduate medical schooling ("on time", despite my protracted absences from campus) with a 3.97 GPA and was given the Sandoz award for "Excellence in the Behavioral Sciences" at graduation in 1982. In addition, I was elected to the Alpha Omega Alpha Medical Honor Society at the end of my third year. I remained at UCLA for both my rotating internship during which I focused on internal medicine, neurology, and pediatrics and for my three-year residency training in psychiatry. My final year of residency training I was the Chief Resident in Geropsychiatry at the West Los Angeles Veterans Affairs Medical Center. Over the next two years, I was a Post Doctoral Research Scholar at UCLA, a fellowship position through the National Institute of Mental Health during which I learned and applied clinical research techniques for the study of persons with severe schizophrenia. My mentors were Professors Van Putten, Goldstein, and Marder.

Clinical, Research, and Teaching Background
I remained at both UCLA and the affiliated West Los Angeles Veterans Affairs Medical Center until late in 2006. Over the two decades between 1986 and 2006 though, both my clinical work and research focus remained on the treatment of persons with schizophrenia. I was the Chief of the Schizophrenia Treatment Unit at the VA Medical Center during the vast bulk of this epoch, and was also the Co-Chief of the Schizophrenia Outpatient Research Clinic during the last ten years. Though I rose through the traditional academic ranks at UCLA and even reached the level of full Professor over five years ahead of "schedule", I never lost my fascination with clinical care and never traded it for more administrative tasks as my career wandered through the decades. Since leaving the traditional ranks of academia, I have been able to continue and even expand my dual interests in clinical work and teaching. Over the last year I have been Vice President in charge of research and continuing medical education for Exodus Inc. in Culver City, CA and also Clinical Director of Exodus Real Recovery in Agoura Hills.

CA. In a typical month, I now see approximately 325 new patients; supervise nearly a dozen psychology doctoral candidates; and teach over a dozen nursing, social work, and nurse practitioner students. Over the course of my career, I have taken care of over twenty five thousand patients, the vast majority of which have suffered from one or another psychotic illness.

As is usual among clinical academicians, my patient care tasks and research interests dovetailed consistently and have always taken place in a setting with medical trainees at every level of experience. Teaching these persons over the years has been the third major leg of my vocational life. Unlike most of my academic colleagues, I never thought of these teaching duties as an obligation to be tolerated and where possible shunted to my younger colleagues. In fact, it generally occupied the top spot in my personal emotional ranking of our traditional tasks (i.e., teaching, research, and patient care). My teaching has been honored over the years with several awards from both my students and colleagues, including 2006 when I was again nominated for the Golden Apple Award by the graduating medical school class (the highest teaching accolade in the School of Medicine). I currently give over 125 routine lectures per year at my various work sites.

Within the context of these various positions and responsibilities, I have been able to experience, study, and then teach others about the care of seriously mentally ill patients. While I have been most consistently compelled by and fascinated with the prototypic psychotic illness schizophrenia, persons with bipolar illness (i.e., "manic depressive disorder") have taken up a close second place over the years. Like any academician in my area, I have sought and received grants to continue my studies and have published in the peer reviewed literature (with the substantial aide of my colleagues and assistants—see my attached CV for the details). I believe that I have been fortunate in the extreme to have had these professional opportunities. They have permitted me to live an enviable work life that I was never able to master and was therefore neither predictable nor routine.

Experience With Industry

These sundry positions also brought me into contact with the pharmaceutical industry that coincidentally became increasingly interested in the treatment of psychotic persons at the very onset of my career in the mid 1980's. This time marked the beginning of the second significant epoch of pharmacologic treatment of psychosis (The first one having begun in the early 1950's but which had plateaued by the late 1960's). This period saw the development, testing, and subsequent marketing of what came to be known as the "Second Generation" or "Atypical" antipsychotic compounds. Though not truly revolutionary or even novel per se (see below), they did constitute a significant advance in many, though not all, aspects over the older medications. This mutual interest in the treatment of psychosis allowed me to "test" potential medications in my patients under controlled protocol conditions from the beginning of their development by industry. Although not every medication that we tested over the years survived the gauntlet of clinical testing, we were able to test every medication that did receive the approval to market by the Food and Drug Administration.

The approval process for medications is a lengthy one that has become increasingly burdened by regulation and requirements over the years. As a consequence, it can take years for a given compound to move from first testing in patients to full marketing approval. Among the medications that we tested and studied that went on to receive approval have been risperidone (approval 1994), olanzapine (1996), ziprazadone (2000), aripiprazole (2002), and quetiapine (1997). The early and prolonged nature of this experience allowed us to develop a clinical knowledge of the real world effects of these drugs that was often at the very forefront of the entire field. As is usual with pharmacologic compounds, our novel discoveries and observations generally involved the toxic effects rather than the therapeutic impacts of the drugs.

In the early to mid 1990's we were among the very first to report on the curious metabolic effects. In particular, we noticed that many of our patients gained weight when first begun on these drugs and at a rate that was, on occasion, singular in our experience. We also noted that these patients soon began to suffer the usual downstream consequences of gaining weight (e.g., glucose intolerance, frank diabetes, and even severe hyperglycemia with resultant hyperosmolar coma). As is customary in the academic world, we described our experience in the peer reviewed literature and reported it at any number of scientific meetings. In addition, though, we worked with industry to extend, understand, and hopefully find ways to remediate these various toxicities. The increasingly high economic stakes of the field sometimes lead those in industry to confuse the message and the messenger (at least from my perspective). As a consequence, our relationships would, or at least could, sour and blossom suddenly, depending on the details of our latest report. As one might expect, our observations and conclusions were not infrequently challenged by one company only to be embraced and promoted by its competitor.

I did not have any direct dealings with Imperial Chemical Industries, as Zeneca was called prior to their name change, while they were developing their antipsychotic compound ICI 204636 (quetiapine's "name" prior to its receiving a formal designation by the nomenclature committee). I was, however, very familiar with the published preclinical and clinical literature on the drug in the 1980's and early 1990's. Immediately after launch in the United States in 1997, I began to lecture for the company and started negotiations with them to perform a high dose clinical trial in a subpopulation of persons with schizophrenia whose symptoms were unresponsive to other available antipsychotic compounds. While a variety of regulatory, legal, and logistical impediments conspired to ultimately thwart my hopes for such a trial, our interest in and experience with high dose treatment did result in a single publication (Pierre, et al, 2005). I continued to lecture and provide ad hoc consultation at the company's request (the last time was August of 2008), though the frequency of these interactions has diminished considerably over time. I have, however, kept them apprised of my concerns about and observation of their drug, including this last spring when I sent them a prepublication copy of a letter that was recently published in the American Journal of Psychiatry (Murphy, et al, 2008). Through out this lengthy association, I would characterize our relationship as mutually respectful and professionally cordial. In notable contrast to some of their corporate peers in the pharmaceutical industry, Astra Zeneca never treated

me dismissively or disrespectfully simply because I would describe an observed toxicity or express an unflattering opinion about quetiapine's clinical characteristics.

History of Antipsychotic Drugs

It can, I think, be persuasively argued that the origins of the "modern" biological theories of psychiatry can be traced directly to the serendipitous discovery of antipsychotic medications in the early 1950's. During that epoch, a trio of French physicians (psychiatrists Delay and Deniker and neurosurgeon Henri Laborit) determined that the experimental Rhône-Poulenc compound RP 4609 (i.e., chlorpromazine or "Thorazine") had a singular power to reduce psychotic symptoms in chronically and severely ill patients with schizophrenia. Schizophrenia is the prototypic psychotic illness that consistently afflicts 0.9 percent of the population, is life long and incurable, runs in families, and generally has its origins in late adolescence or early adulthood. It is further the exclusive province of the human animal—even our closest primate relatives do not develop schizophrenia. It would be difficult to overstate the magnitude of this pharmacologic discovery, coming as it did at a time when wet wraps, hydrotherapy, and frontal lobotomies were the only "effective" palliative treatments. The pharmacologic efficacy of chlorpromazine, though, came with an apparently obligatory neurotoxicity that developed after about two weeks of treatment. This neurotoxicity, which came to be called extrapyramidal symptoms or EPS, included parkinsonism (i.e., slowed movements and mentation, a specific tremor, and muscular rigidity), akathisia (i.e., an intensely dysphoric sense of restlessness), and dystonia (i.e., sustained, uncontrollable, and functionally disruptive muscular contractions). While these acute EPS could be dramatic and overwhelming, they were transitory and would eventually disappear once the offending agent was discontinued. Unfortunately, there also developed a later, sometimes grotesque disorder of excessive motor movement that was termed tardive dyskinesia (literally "late bad movement"). It was eventually observed that this tardive dyskinesia (TD) would accrue with each passing year of cumulative exposure to the medication at a rate of three to five percent of the treated population per annum. More ominous still was the observation that unlike acute EPS, TD proved to be lifelong and irreversible in a large number of those afflicted (circa 50%), even if the causal agent were permanently discontinued. These neurotoxicities were so consistent, predictable, and uniform that they eventually came to be seen as the hallmark of this class of medications which were termed "neuroleptics" (i.e., "to seize the neuron"). In other words, these antipsychotic medications were defined quite literally by the toxicities they produced.

Though these EPS were the clinical bane of antipsychotic compounds, they were a crucially exploitable characteristic for drug developers. Because there is no animal model for schizophrenia per se, it is not possible to screen potential molecular candidates for this property. There are, however, many excellent animal models for EPS and related behavioral toxicities. It was thus possible to search for potential antipsychotic compounds by simply screening for extrapyramidal liability in one or another of these models. It should come as no surprise then that all antipsychotic medications shared the neurotoxic characteristic—it was this toxicity that allowed them to be discovered in the first place. Arvid Carlsson and colleagues detailed the mechanisms that are believed to underlie this duality (i.e., antipsychotic potential and neurotoxic liability) in the early

1960's. In a series of clever animal experiments and brilliant deductions he proposed that antipsychotics exerted both effects by binding to and blocking dopamine receptors (more specifically the D2 receptor subtype) in the brain. It is of historical note that he shared psychiatry's first Nobel Prize for Medicine in 2000 for these discoveries.

As an ultimate consequence of this process, there came to clinical market an array of often times chemically dissimilar compounds that had equipotent antipsychotic efficacy and were uniformly neurotoxic. They did, of course, vary in a number of secondary characteristics (e.g., anticholinergic potency, sedative potential, tendency to induce orthostatic hypotension, etc.), but their primary efficacies and core toxicities were effectively equivalent. It is important to note that these dopamine receptors are important not only in motor control and psychotic symptoms, but they are also crucial in mediating reward learning. Thus, any antipsychotic molecule that blocks these dopamine receptors will attenuate and possibly destroy an animal's (or a person's) ability to normally experience pleasure. In clinical practice these drugs are notoriously dysphorogenic and exceedingly difficult to subjectively tolerate.

The singular exception to these generalizations about antipsychotics is the compound clozapine. This molecule is a modified structural analog of the tricyclic antidepressant imipramine (a revolutionarily useful and powerful antidepressant medication that has no antipsychotic power whatsoever) and was synthesized by Sandoz Pharmaceuticals in 1959. Though its road to market was torturously long and marred by a number of tragically toxic detours, it ultimately proved itself to be a truly different antipsychotic. It was eventually shown that clozapine had greater antipsychotic power than conventional neuroleptics (as the rest of the antipsychotic market came to be named) and at ordinary antipsychotic doses it failed to cause the EPS that characterized its conventional counterparts. Clozapine then became the prototypic "atypical" antipsychotic in that it alone was a non-neuroleptic antipsychotic: a drug capable of separating antipsychotic efficacy from neurotoxic liability. While a number of often clever and sometimes even compelling explanations of how clozapine is able to exert these clinical behaviors have been elaborated, none have to date been proven. In addition, though the group of more recently developed and marketed antipsychotics (i.e., risperidone, olanzapine, quetiapine, aripiprazole, and ziprazidone) have claimed kinship to clozapine by usurping its "atypical" label, none has matched clozapine's antipsychotic power and all are variably more neurotoxic. This is not to say that as a "class" they have failed to improve upon the conventional compounds, but only that they have not succeeded in truly inheriting clozapine's legacy.

Quetiapine's Development

Imperial Chemical Industries first elaborated what they designated ICI 204636 in the early 1980's. It is a structural analog of clozapine and technically considered a dibenzothiazepine. Its receptor (i.e., the proteinaceous components on the lipid neural membranes of the central nervous system [CNS]) binding profile indicates that it has weak and easily reversible affinity for the classic D2 receptor that Carlsson identified in 1963. It also binds with weak to moderate intensity to a wide spectrum of other receptors in the CNS, but in a pattern that is really unlike any other antipsychotic compound.

including clozapine, upon which its structure is based. These other binding characteristics are conceptualized to account for quetiapine's observed clinical effects. In brief, they confer on quetiapine: sedation, low EPS liability, minimal impact on prolactin, orthostatic hypotension (i.e., a fall in blood pressure when standing), anticholinergic toxicity (i.e., constipation, dry mouth, blurred vision, memory disturbances, and tachycardia), and weight gain liability. All of these ultimately observed characteristics would be expected based only on the neuromolecular characteristics of quetiapine.

Though the knowledge of quetiapine's unique receptor binding profile allowed for the easy prediction of its pattern of toxicity in humans, its low and weak affinity at the critical D2 receptor posed a challenge for protocol designers during its early years of clinical testing. For all conventional compounds the appropriate dose to achieve optimal antipsychotic activity is exactly the dose that also begins to produce EPS. With an "atypical" drug though, the appropriate dose would be an unknown amount lower. Thus, an early hurdle for quetiapine was determining just where the optimal antipsychotic dose range was located. Ultimately quetiapine's FDA registration trials involved multiple doses (five) of quetiapine over a ten fold dosing range compared to single dose of the reference conventional neuroleptic haloperidol. Despite the methodologic asymmetry of this design that markedly favored quetiapine, it failed to beat its conventional comparator at any dose. In fact, the haloperidol arm was generally slightly better (though not statistically so) than any of the five doses of quetiapine. This pattern of being marginally equal to or slightly inferior to comparator drugs has been repeated numerous times over the years of testing. When AZ attempted to perform a meta-analysis (i.e., combining multiple trials to achieve greater statistical power in an effort to show a small effect that is not apparent in any single study) on its accrued dataset, they discovered this very pattern. This disappointing result prompted the marketing personnel within AZ to "spin" these conclusions by touting that quetiapine had "unsurpassed efficacy". While technically correct from a statistical point of view because no single study had shown that any conventional comparator was statistically superior to quetiapine, such hype is clearly disingenuous sophistry.

When considered across many trials involving schizophrenic subjects, quetiapine has been demonstrated to be about 10-20 percent less effective than standard doses of conventional medications. This was shown most clearly in the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study that was reported in late 2005. This NIMH funded trial compared four atypical medications (quetiapine, ziprazidone, risperidone, and olanzapine) to a single typical medication (perphenazine) and involved 1460 subjects treated over an 18-month epoch. The primary outcome variable was "time to discontinuation" of the assigned drug. The results revealed that quetiapine was about 20 percent less effective than the conventional agent perphenazine (4.6 vs. 5.6 months) and about 50 percent less effective than olanzapine (9.2 months).

While these efficacy facts were disappointing and clearly contributed to quetiapine's dismal market share when it was first approved for use in 1997, it also suggested to me a tantalizing possibility. Because conventional antipsychotic medications were all

essentially equi-efficacious and seemed to share a single underlying mechanism of action, any drug that had demonstrably less efficacy might possibly work through a dissimilar mechanism. This possibility was a major motivating factor in my wanting to pursue a higher than standard dose experimental trial with the company after the drug was launched. I continue to believe that quetiapine does, in fact work through largely distinct mechanisms. Unfortunately this distinction translates into slightly less pharmacologic power on average than conventional medications. AZ has "oversold" quetiapine's efficacy in their marketing endeavors for years.

Quetiapine's Toxic Metabolic Profile

The dataset that Zeneca had compiled on quetiapine prior to its launch in 1997 clearly indicated that clinically significant weight gain was a common side effect of quetiapine. The data from Zeneca's Phase II/III trials demonstrated a clear dose related impact on weight that compellingly worsened over time. Using the FDA's definition of clinically pertinent weight gain (i.e., a 7% increase), quetiapine routinely impacted over 25 percent of the treated population (somewhat lower for lower doses of quetiapine and somewhat higher with higher quetiapine doses). The average shift in weight was 6.2 lbs over the first six months of treatment and 11 lbs after six months of treatment. This is approximately halfway between the weight gain induced by risperidone and olanzapine—quetiapine's major competitors at launch. Weight gains of this magnitude are impressively large and impact an amazingly large and consistent percentage of patients. Despite these data, which have been available to the company since before launch, the label for quetiapine has never, even to the present day, "warned" of this predictable and serious toxicity. Instead, the label has merely listed in the adverse experiences section that quetiapine is "sometimes associated with increases in body weight". Further, their marketing materials over the years have consistently touted that quetiapine is "weight neutral". This is palpably inappropriate and inadequate at best and deceptively misleading at worst. It is my opinion that this labeling deficiency rises to the legal definition of gross negligence (i.e., "willful disregard for the safety of others"). It is unconscionable that after more than a decade's time that the warnings section is still silent about the single most prominent serious toxic characteristic of the compound.

There are a number of well-known health consequences to increases in adiposity. Among these are increased risks for glucose intolerance and even frank diabetes, increases in total cholesterol and triglycerides in the blood, secondary risks for cardiovascular disease, increased rates of degenerative osteoarthritis, and even increased risks for certain malignancies (e.g., colon cancer). The fact that quetiapine use results in weight gain and therefore causes diabetes in susceptible patients cannot be rationally disputed. This was confirmed by the APA/ADA consensus conference on the metabolic toxicities of the atypical antipsychotics held in 2004. That conference of independent (i.e., non-industry) experts (at which I provided the presentation on the monitoring protocol) concluded that quetiapine use could result in significant weight gain, increased rates of diabetes, and pathologic changes in lipid profiles. Although the current label change implemented in 2007 does direct one to a new section in the adverse events section that documents, to a degree, some of the measured increases in new onset diabetes, it remains inadequate and misleading. Firstly, the "class labeling" warning section on endocrinologic toxicities is

laced with generalities, disclaimers, and distracting verbiage. It fails completely to state the measured increases in new onset diabetes that are specific to quetiapine and that are detailed in the adverse experiences section. Secondly, it fails to make the known connection between increases in adiposity and subsequent changes in glucose regulation. It gives the mistaken impression that the risks of diabetes only apply to a decidedly minor (circa 2-4%) portion of treated patients when, in fact, nearly one third of patients treated with standard doses for as little as a year are at decidedly increased risk of glucose disregulation. The company personnel have opined in depositions that the details of quetiapine's measured risk of diabetes and related endocrinologic disturbances were unknown until the results of these later done studies were completed. Such rhetoric is intellectually and clinically dishonest as it requires one to deny the clinical fact that increases in adiposity that are caused by quetiapine (and were known to the company before launch in 1997) will result in predictable increase in endocrinologic dysfunction. It is axiomatic that increases in obesity will result in subsequent increases in hyperglycemia, frank diabetes, hyperosmolar coma, and even death due to endocrinologic complications. To deny otherwise, as AZ officials continue to do to the present day, is negligently irresponsible.

Additionally, the label is virtually silent (or at least it is decidedly unclear) about quetiapine's ability to induce massive changes in circulating triglycerides and thereby lead to secondary and potentially lethal pancreatitis (i.e., marked inflammation of the pancreatitis). When a person gains significant adiposity, there is a predictable increase in the levels of circulating lipid pools (i.e., triglycerides, VLDL, LDL, etc.) because to body must manage a larger flow of fats from the gut and to and from the tissues. These changes, while potentially of long-term clinical pertinence, are usually of ordinary magnitude. Quetiapine, though, also results in massive acute elevations in triglycerides that can, on occasion, overwhelm the body's fat management system and cause secondary pancreatitis. The precise mechanisms whereby this toxicity is mediated have yet to be elucidated, however, it is likely that interference with one of the early lipid management enzymes in the liver (e.g., lipoprotein lipase A) causes a "backup" of the triglyceride transport vehicle (i.e., chylomicrons) from the gut that leads to the hypertriglyceridemia. This additional metabolic-like toxicity is unrelated to changes in weight, tends to occur during the first several months of treatment, and is markedly more acutely serious than the more pedestrian increases in the sundry lipid pools that predictably follow increases in adiposity. This toxicity has clearly emerged during the post marketing surveillance period, has been reported frequently in the case report literature, and was discussed at length at the consensus conference in 2004.

Addictive Potential

The single most consistent toxic effect of quetiapine is sedation. This property when coupled with quetiapine's low EPS profile has prompted clinicians to use the drug excessively off-label for such conditions as anxiety and insomnia. These characteristics also raise a reasonable concern that quetiapine may have some addictive potential. In fact clinical experience and a number of case reports have suggested that certain patients will abuse, divert for sale, and become physically dependent on quetiapine (Pierre, et al,

2004; Murphy et al. 2008). Despite these facts the label has been virtually silent about this reality.

Off Label Use

Quetiapine has come to dominate the atypical antipsychotic market primarily because it is used excessively off label (current estimates are about two thirds of the prescriptions are off-label). I am of the opinion that primary among the reasons for this disproportionate off label use are the facts that quetiapine is sedating and highly subjectively tolerable and the inaccurate clinical impression that it is also comparatively free of concerning toxicities and devoid of abuse potential. A secondary reason is that quetiapine's share of the on label market is reduced because it is simply not as potent an antipsychotic as other available products. While prescribing a drug for off label use is a common and often clinically reasonable practice, promoting a drug for off label use is illegal. AZ was clearly aware of the excessive off label use of quetiapine over the years. Their officials have stated repeatedly in depositions that AZ endeavored to provide label support of these "passively observed" prescriptive habits by investing heavily in confirmatory studies. Though many such studies were performed, I consider the claim largely dishonest. If true, then it would have been imperative for AZ to study the largest and most excessive off label use, to wit, insomnia. Such a study would have been logistically and economically trivial to perform, at least in comparison to the studies done in mood and psychosis based disorders. There is to date no evidence of any quality that demonstrates that quetiapine decreases sleep latency, increases total sleep time, normalizes sleep architecture, or improves daytime wakefulness. There is, in fact, ample evidence that quetiapine impairs significantly daytime wakefulness. I believe that AZ knew that any real detailed sleep study would ultimately be an indictment of clinical practice and would potentially cut the total use of their product by more than half. It is further my opinion that AZ mischaracterized the true toxic potential of their product and that this behavior has in part prompted clinicians to use their product inappropriately and excessively off label. If clinicians had been aware of the true metabolic toxicities and addictive liabilities of quetiapine then I do not believe that we would have the amount of off label usage we see today. It is my opinion therefore that AZ has been engaged in "indirect" off label marketing. While their behavior may have in fact been technically within the "letter of the law", it was and continues to be irresponsible, improper, and ethically indefensible.

Conclusions/Summary

AZ's marketing of quetiapine has consistently exaggerated the true efficacy of the compound.

AZ has been aware of the true metabolic toxicities of quetiapine since before launch in 1997. Despite this they have engaged in a marketing campaign that has minimized, obfuscated, or frankly denied these metabolic realities. Their product label has been consistently and continuously inadequate in its warnings about the impact on lipid and glucose metabolism, hyperglycemia, and diabetes. Their label continues to be wholly inadequate to the point of being decidedly misleading in its warnings about weight gain.

Additionally, the current label is inadequate regarding quetiapine's ability to markedly disrupt normal lipid metabolism and cause massive hypertriglyceridemia and secondary pancreatitis.

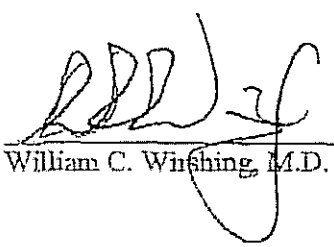
The current label is inadequate in its description about the abuse potential of quetiapine. AZ should have identified and warned of this abuse liability based on the clinical characteristics of quetiapine and the curious and excessive off label use patterns. Further, their tacit acceptance of the excessive use of their product for routine insomnia for the past decade without ever having investigated the effects of their product on sleep, is tantamount to passive marketing for an off label indication. This failure to investigate has been compounded by their insistence that they have behaved responsibly by investing heavily in research to establish on label support for the prescriptive patterns they knew to exist.

AZ's behavior has given prescribing clinicians an inaccurate impression of quetiapine's toxic profile and addictive potential which has robbed physicians of the ability to make informed risk/benefit analysis prior to prescribing quetiapine to a patient. This has led in part to the excessive and inappropriate off label use of the product and to injury and damage to patients who would not have otherwise ever received the medication.

My opinions as stated in this report are based on my education, training, and experience and my review of the relevant literature, internal Astra Zeneca documents, corporate depositions, and public documents and are stated to a reasonable degree of medical probability. It is my understanding that discovery is ongoing and I thus reserve my right to supplement or expound upon my opinions pending review of additional information.

My fees for work in this litigation are $500 per hour.

A list of my testimony for the past 4 years is attached.



William C. Wirshing, M.D.

**TESIMONY LIST – DR. WILLIAM C. WIRSHING**

I have been asked to supply a list of my deposition and trial testimony for the prior 4 years. The following is a list to the best of my ability to recall:

Alaska V. Lilly 2008

Insurance Carries v. Lilly 2008

Olenic v. Lilly 2008

Class Action case filed in FL against Janssen 2005

In addition, I have given testimony in several small lawsuits involving malpractice question for both the defense and plaintiff whose names and details I no longer have access to.

# CURRICULUM VITAE

## WILLIAM C. WIRSHING, M.D.

**Address**


Work: Exodus Recovery Acute Treatment Center
3828 Delmas Terrace
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Tel (310) 253-9494

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Woodland Hills, CA 91303

Tel (310) 413-4200
Home Fax (818) 595-1367

E-mail: WIRSHING@UCLA.EDU


**Birthdate** 11 June, 1956

**Birthplace** Palo Alto, CA

**Education**

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|---|---|
| 1982 | M.D. - UCLA |
| 1978 | B.S. Electrical Engineering & Computer Science, University of CA, Berkeley |

**Internship, Residency, & Fellowship**

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|---|---|
| 1986-88 | Postdoctoral Research Fellowship in Schizophrenia Research, UCLA, Department of Psychology, Los Angeles, CA |
| 1983-86 | Resident in Psychiatry, UCLA Neuropsychiatric Institute, Los Angeles, CA |
| 1982-83 | Intern in Medicine, UCLA Center for the Health Sciences & Wadsworth VA Medical Center, Los Angeles, CA |

**Licensure**

1983 California License No. G 50986, DEA No. FW0654447

**Certification**

1991 Added Qualification in Geriatric Psychiatry, American Board of Psychiatry and Neurology (#000479)

1988 Diplomat, American Board of Psychiatry and Neurology (#30125)

**Academic Appointments/Positions**

2008- Medical Director Real Recovery. Agoura Hills, CA

2007- Vice President in charge of continuing medical education and research Exodus Corp. Los Angeles, CA

1996-06 Professor of Clinical Psychiatry, Department of Psychiatry and Biobehavioral Sciences, UCLA School of Medicine

1993-06 Chief, Schizophrenia Treatment Unit, West Los Angeles VA Medical Center, Brentwood Division

1993-96 Associate Professor of Clinical Psychiatry, Department of Psychiatry and Biobehavioral Sciences, UCLA School of Medicine

1987-06 Director, Brentwood Movement Disorders Laboratory, West Los Angeles VA Medical Center

1988-93 Co-Chief, Schizophrenia Treatment Unit, West Los Angeles VA Medical Center, Brentwood Division

1986-93 Adjunct Assistant Professor of Psychiatry, Department of Psychiatry & Biobehavioral Sciences, UCLA School of Medicine

1986-88 Postgraduate Research Scholar, Department of Psychology, UCLA

1986-88 Co-Chief, Geropsychiatry Treatment Unit, West Los Angeles Veterans Administration Medical Center

1985-86 Chief Resident, Geropsychiatry Treatment Unit, West Los Angeles Veterans Administration Medical Center, Brentwood Division

**Awards & Honors**

2006 Nominated for Golden Apple Award for Clinical years by graduating class of 2006

2003 Award in Recognition of Dedication in Teaching Excellence from the Graduating Class of 2003, David Geffen School of Medicine at UCLA

1999 Departmental Teaching Award, UCLA School of Medicine, Department of Psychiatry & Biobehavioral Sciences

1999 Lucien B. Guze Golden Apple Award for Outstanding Teaching Class of 2001, UCLA School of Medicine

1998 Certificate of Excellence, West Los Angeles Success 98 Award Program, West Los Angeles Veterans Administration Medical Center

1996 Distinguished Educator Award, UCLA School of Medicine, Department of Psychiatry & Biobehavioral Sciences

1994 Departmental Teaching Award, UCLA School of Medicine, Department of Psychiatry & Biobehavioral Sciences

1993 UCLA Medical School. Class of 1995 - Outstanding Teacher Award

1991 Departmental Teaching Award, UCLA School of Medicine, Department of Psychiatry & Biobehavioral Sciences

1988 Travel scholarship to attend the 4th Biannual Workshop on Schizophrenia in Badgastein, Austria.

1982 Sandoz Award for Excellence in the Behavioral Sciences

1982 Alpha Omega Alpha

1978 Tau Beta Pi (Engineering National Honor Society)

1978 Phi Beta Kappa

1978 B.S. Summa Cum Laude

**Major Teaching Experience**

2007- Weekly Continuing Medical Education Lecture Exodus Urgent Care Center, Culver City, CA.

2000-06 Case Conference: Diagnostic Dilemmas - Psychiatry (#425 Sec. 5) This weekly case conference focuses on differential diagnosis, with an emphasis on the various etiologies of psychotic symptoms including schizophrenia, substance-induced psychosis, malingering,and other disorders.

1995-06 Movement Disorders Seminar - Psychiatry (#446) a weekly, clinical based, interactive seminar focusing on the examination and treatment of patients with a broad range of movement disorders for psychiatry residents,

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| | neurobehavior fellows, medical students, and research staff (with DA Wirshing, M.D., CS Saunders, M.D., and JM Pierre, M.D.). (1.5 hrs/week) |
| 1992-2004 | Course director - Psychopathology (#201) for 2nd-year medical students. (6 hrs/week) |
| 1991-2002 | Faculty sponsor - Student Research Program. (1-8 hrs/week) |
| 1990-1992 | Faculty advisor for biweekly seminar for psychiatry residents on critical reading of the literature (with Joel Yager, MD, and Alison Doupe, MD, PhD). (1 1/2 hrs/2 weeks) |
| 1989-92 | Movement Disorders Seminar (Psychiatry Course #453), a weekly forum for psychiatry residents, neurobehavior fellows, and medical students (with JL Cummings, MD). (1 hr/week) |
| 1988-1991 | Class Organizer/Lecturer of "Topics in Geropsychiatry", a weekly seminar for psychiatry residents, medical students, and psychology interns. (1 1/2 hrs/week) |
| 1988-06 | Ward teaching supervisor (Psychiatry Course #403) for 1st- and 3rd-year psychiatric residents and for 3rd- and 4th-year medical students on the Schizophrenia Treatment Unit, BVAMC. (9 hrs/week) |
| 1986-06 | Off-ward teaching supervisor (Psychiatry Course #403) for 1st-, 2nd-, and 3rd-year psychiatric residents in the UCLA Residency Training Program. (2-4 hrs/week) |
| 1986 | Lecturer: "The Psychiatric Hospital in Historical Perspective" (with Dora B Weiner, PhD), a class for undergraduates, College of Letters and Sciences, UCLA. |
| 1985-88 | Ward teaching supervisor for first- and second-year psychiatric residents and for first-year geriatric medicine fellows on the Geropsychiatry Ward, WLA/VAMC. |
| 1985 | Lecturer: "The Historical Roots of Modern Medicine" (with Dora Weiner, PhD), a class for undergraduates, College of Letters and Sciences, UCLA. |

**Hospital/University Committees**

| | |
|---|---|
| 2005-06 | Academic Advancement Committee Department of Psychiatry and Biobehavioral Sciences, UCLA School of Medicine |
| 2000-02 | Academic Advancement Committee Department of Psychiatry and Biobehavioral Sciences, UCLA School of Medicine |
| 1999-03 | Medical Student Education Strategic Planning Committee |
| 1999-02 | Human Subjects Protection Committee, Veterans Affairs |
| 1998 | Neuroscience Sub Committee, UCLA School of Medicine |
| 1997- 00 | Faculty Executive Committee |
| 1997- 01 | Voluntary Clinical Faculty Academic Appointments and Adjustments Committee |

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|---|---|
| 1996-99 | Second Year Curricular Block Planning Committee, UCLA School of Medicine |
| 1995-98 | Academic Advancement Committee Department of Psychiatry and Biobehavioral Sciences, UCLA School of Medicine |
| 1992-94 | Ad Hoc Committee for Dementia, UCLA School of Medicine |
| 1992-96 | Student Affairs Committee, UCLA School of Medicine |
| 1992-94 | Human Subjects Protection Committee, Veterans Affairs |
| 1991-93 | Residency Fellowship Nominating Committee, UCLA |
| 1991 | Chief of Psychiatry Search Committee, Veterans Affairs |
| 1990-93 | Residency Education Curriculum Committee, UCLA |
| 1988-90 | Human Subjects Protection Committee, Veterans Affairs |
| 1988-03 | Pharmacy and Therapeutics Committee, Veterans Affairs |

**Grants Awarded**

2005-06 "Management of Antipsychotic Medication Associated Obesity"
Co-Principal Investigator Donna A. Wirshing, M.D. PI
VA Merit Review

2005-06 "Relapse Prevention: Long Acting Atypical Antipsychotics"
Co-Investigator , Donna A. Wirshing, M.D. PI
NIMH RO1 (Multicenter Collaborative)

2002-05 Veterans Affairs Merit Review
"Cigarette Smoking by Schizophrenic Patients (Phase II)"
Collaborator. Jarvik Murray, M.D., Ph.D. - P.I.

2000-02 National Institute of Mental Health, MH41573-11A1
"Management for Risk of Relapse in Schizophrenia"
Co-Investigator. Stephen R. Marder, M.D. - P.I.

2000-03 National Institute of Mental Health, MH59750-01A1
"Treatment of Negative Symptoms and Cognitive Impairments"
Co-Investigator. Stephen R. Marder, M.D. - P.I.

1998-00 Veterans Affairs Merit Review
"Brief Hospitalization for Schizophrenia: Strategies to Improve Treatment Outcome"
Co-Investigator. Donna A. Wirshing, M.D. - P.I.

1997-02 Veterans Affairs Merit Review
"Quetiapine vs. Haloperidol Decanoate for the Long-Term Treatment of Schizophrenia and Schizo-Affective Disorder"
Co-Investigator. Stephen R. Marder, M.D. - P.I.

1995-98 National Institute of Health, 1R01-DA09570-01A1
"Dopaminergic Modulation of Nicotine Reinforcement"
Co-Investigator. Murray E. Jarvik, MD, PhD - P.I.

1995-99 National Institute of Health, 1R01-MH46484-01
"New Antipsychotics: Clinical Trials and Naturalistic Follow-up."
Co-Investigator. Stephen R Marder, MD - P.I.

1993-95 Veterans Affairs Merit Review to examine cigarette smoking by schizophrenic patients.
Co-Investigator. Murray E. Jarvik, MD, PhD - P.I.

1993-96 Veterans Affairs Merit Review to examine the risks and benefits of typical and atypical antipsychotic drugs in the treatment of acute psychotic episodes.
P.I.

1992-95 National Institute of Health: MH46484-03
"Clozapine - Treatment Response and Disability."
Co-Investigator.

1990-92 NARSAD (National Alliance for Research on Schizophrenia and Depression) Young Investigators Grant to develop a method of quantifying drug-induced akathisia and to apply this method of determining the relative akathisic liability of the atypical neuroleptic clozapine.

1986-05 National Institute of Health: MH41573
"Management of Risk of Relapse in Schizophrenia."
Co-Investigator. Stephen R Marder, MD and Robert P. Liberman, MD Co-P.I.s

1988-90 Veterans Affairs Merit Review to examine the feasibility of using a battery of electromechanical instruments to prospectively follow patients with tardive dyskinesia.
Co-Investigator. JL Cummings, MD, P.I.

1988-89 NARSAD Young Investigators Grant to continue research on the instrumentation of drug-induced movement disorders.

1987-88 Biomedical Research Support Grant from the Department of Psychiatry, UCLA School of Medicine, to develop a system to measure and analyze the movements of the human larynx.

**Industry Sponsored**

**Investigator Designed and Initiated**

1999-03 Janssen Pharmaceutica: Investigator designed protocol.
"Brief Hospitalization for Schizophrenia: Strategies to Improve Treatment Outcome"
Co-Investigator. Donna A. Wirshing, M.D. - P.I.

2000-05 Eli Lilly, Inc.: Investigator designed protocol.
"Olanzapine vs. Risperidone in Treatment Refractory Schizophrenia"
Co-Investigator. Donna A. Wirshing, M.D. - P.I.

**Industry Designed and Initiated**

1998-99 Merck & Company, Inc.
"A Double-Blind, Active and Placebo-Controlled, Safety Tolerability, and Preliminary Antipsychotic Activity Study of MK-0869 in Hospitalized Schizophrenia Patients"
P.I. William C. Wirshing, M.D.

1998-99 Hoechst Marion Roussel, Inc.
"A Multicenter, Placebo and Active Control, Double-Blind Randomized Study of the Efficacy, Safety and Pharmacokinetics of M100907 (10 and 20 mg/d in Schizophrenic and Schizoaffective Patients."
Co-Investigator. Donna A Wirshing, M.D. - P.I

1997-00 Organon 041002
"A Double Blind, Five-Armed, Fixed Dose, Active and Placebo Controlled Dose-Finding Study With Sublingual ORG 5222 in Subjects With Acute Phase Schizophrenia"
P.I. William C. Wirshing, M.D.

1997-99 Otsuka America: 42,776
"An Open Label Follow-on Study on the Long-Term Safety of Aripiprazole in Patients with Psychosis"
P.I. William C. Wirshing, M.D.

1997-99 Otsuka America: 31-97-202
"A Phase III Double-Blind Study of Aripiprazole and Risperidone in the Treatment of Psychosis"
P.I. William C. Wirshing, M.D.

1997-98 Janssen Pharmaceutica: RIS-USA-112
"A Multicenter, Randomized, Double Blind, Parallel Group Trial Comparing the Safety and Efficacy of Risperidone and Olanzapine in the Treatment of Psychosis in Patients with Schizophrenia and Schizoaffective Disorder."
Co-Investigator. Donna A. Wirshing, M.D. - P.I.

1997-99 Janssen Pharmaceutica: RIS-USA-113
"A Multicenter, Randomized, Double Blind, Parallel Group Trial Comparing the Safety and Efficacy of Risperidone and Olanzapine in the Treatment of Psychosis in Patients with Schizophrenia and Schizoaffective Disorder."
Co-Investigator. Donna A. Wirshing, M.D. - P.I.

1995-98 Hoechst Marion Roussel
"An Open-Label, Follow-Up, Multicenter, Long-Term Maintenance Study of MDL 100, 907 in Patients with Schizophrenia."
Co-Investigator. Donna Ames, M.D. - P.I.

1995-98 Otsuka: 31-95-201
"OPC-14597: An Open-Label Tolerability Study in Schizophrenic Patients."
P.I. William C. Wirshing, M.D.

1995-96 Hoechst Marion Roussel: IND# 47,372
"A Randomized, Double-Blind, Placebo-Controlled, Parallel, Multiple Dose, Multicenter Study to Determine the Safety, Tolerability, Pharmacokinetics, and Biochemical Activity of MDL 100,907 in Patients with Schizophrenia."
Co-Investigator. Donna Ames, M.D. - P.I.

1995-96 Merck & Company, Inc.
"A Double-Blind, Placebo-Controlled, Safety, Tolerability and Preliminary Antipsychotic Activity Study of L-745,870 in Hospitalized Schizophrenic Patients"
P.I. William C. Wirshing, M.D.

1995-96 Otsuka: 31-94-202
"A Dose Ranging Study of the Efficacy and Tolerability of OPC-14597 in Acutely Relapsing Hospitalized Schizophrenic Patients."
P.I. William C. Wirshing, M.D.

1993-97 Eli Lilly Incorporated: F1D-MC-HGAP
"Fixed Dose Olanzapine versus Placebo in the Treatment of Schizophrenia."
Co-Investigator. Donna Ames, M.D. - P.I.

1994-99 Pfizer, Inc.: 128-116B
"A 52-Week, Open Extension Study Evaluating the Safety and Outcome of 40-80 mg BID of Oral Ziprasidone (CP-88,059-1) Daily in the Treatment of Subjects Who Have Participated in Previous Ziprasidone Clinical Trials."
Co-Investigator. Donna Ames, M.D. - P.I.

1993-94 R.W. Johnson: M92-083
"Multi-Center, Randomized, Double-Blind, and Controlled, 4 Week, Multiple Oral Rising Dose Study to Determine Safety Tolerability, Pharmokinetics and Behavioral Activity of RWJ-37796 in Male Schizophrenic Subjects Phase II."
P.I. William C. Wirshing, M.D.

1992-98 Abbott Laboratories - Neuroscience Venture: M92-795
"An Open Label Assessment of the Long Term Safety of Sertindole in the Treatment of Schizophrenic Patients."
Co-Investigator. Donna Ames, M.D. - P.I.

1994-96 Pfizer, Inc.: 128-115
"Phase III, Six Week, Double Blind, Multi-Center, Placebo Controlled Study Evaluating the Efficacy and Safety of Three Fixed Doses of Oral Ziprasidone (CP-88,051-1) and Haloperidol in the Acute Exacerbation of Schizophrenia and Schizo-Affective Disorder."
Co-Investigator. Donna Ames, M.D. - P.I.

1992-94 Glaxo, Inc.: S3B-201
"A Randomized, Double-Blind, Placebo-Controlled, Crossover Evaluation of the Effects of GR68755C on Serum Levels of Haloperidol in Patients with a Diagnosis of Schizophrenia."
Co-Investigator. Stephen R. Marder, M.D. - P.I.

1992-93 Abbott Laboratories - Neuroscience Venture: M92-762
"A Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of Sertindole in Schizophrenic Patients."
Co-Investigator. Stephen R Marder, M.D. - P.I.

1992-93 Schering Plough Research Corporation: SCH39166
"Safety, Tolerance and Pilot Efficacy of Rising Multiple Doses of SCH39166: An Open Label Trial."
Co-Investigator. Stephen R Marder, M.D. - P.I.

1988-89 Astra Pharmaceuticals
"Raclopride in Schizophrenia: a Haloperidol-Controlled, Double-Blind, Dose-Finding Clinical Trial."
Co-Investigator. Theodore Van Putten, M.D. - P.I.

1990-91 Sandoz Pharmaceuticals
"A Randomized, Double-Blind, Placebo-Controlled, Multi-Center, Multi-Stage, Dose-Finding Study of SDZ HDC 912 in DSM-III-R Defined Hospitalized Schizophrenic Patients."
Co-Investigator. Theodore Van Putten, M.D. - P.I.

**Reviewer / Editor**

Reviewer:

American Journal of Psychiatry
Archives of General Psychiatry
Biological Psychiatry
Brain Dysfunction
CNS Spectrums
Comprehensive Psychiatry

International Journal of Psychiatry in Medicine
Journal of Clinical Psychiatry
Journal of Psychiatric Research
Journal of Clinical Psychopharmacology
Neuropsychiatry, Neuropsychology, and Behavioral Neurology
Psychiatry Research
Psychopharmacology
Psychopharmacology Bulletin
Psychosomatics
Schizophrenia Bulletin

**Invited Presentations**

04/07 "Schizophrenia and Related Psychoses" Grand Rounds Northridge Hospital, Northridge CA 15 Apr 2007

08/06 "Tailored Management of Schizophrenia in the Real World: A Naturalistic Approach" Presented at Evansville State Hospital, Evansville, IN, 17 Aug 06

08/06 "The Metabolic Mayhem of Atypicals: The TD of the New Millennium" Grond Rounds Antelope Valley Hospital 11 Aug 06.

08/06 "Use of Atypical Antipsychotics in Bipolar Illness"1 Aug 06 Honolulu, HI.

03/06 "Treatment of Agitation with Behavioral Interventions and Atypical Antipsychotics in Schizophrenia" Presented at American Association for Geriatric Psychiatry, San Juan, Puerto Rico, 11 Mar 06.

02/06 "Addressing Metabolic Disturbances with Antipsychotic Treatments" Presented at San Francisco General Hospital, Dept of Psychiatry, San Francisco, CA, 24 Feb 06

12/05 "Metabolic Impact of Atypical Antipsychotics: The View from Two Decades of Experience" Presented at Eden Medical Center, Castro Valley, CA 7 Dec 2005

11/05 "Clinical Management of Behavioral and Psychological Symptoms in Dementia" Presented at Salem Hospital, Salem, OR, 16 Nov 05

10/05 "Marketing Atypical Antipsychotics and the Opacity of Adiposity" Presented at Grand Rounds, Sepulveda VA, Los Angeles, CA, 26 Oct 05

07/05 "Treatment of Agitation in Elderly Demented Patients" Presented at Grand Rounds, Hawaii State Hospital, Kaneohe, HI, 12 Jul 05

07/05 "Metabolic Disturbances During Antipsychotic Treatment" Presented at Grand Rounds, Castle Medical Center, Kailua, HI, 12 Jul 05

04/05 "Metabolic Disturbances During Antipsychotic Treatment" Presented at Grand Rounds, Battle Creek VA Med Center, Battle Creek, MI, 7 Apr 05

12/04 "Considerations in Long-Term Management of Schizophrenia" Presented at Grand Rounds, Corcoran State Prison, Corcoran, CA 1 Dec 04

12/04 "Management of Associated Comorbidities of Schizophrenia" Presented at Grand Rounds, Atascadero State Hospital, Atascadero, CA 1 Dec 04

09/04 "Pharamacological Treatment of Psychosis and Agitation in Dementia of the Elderly" Presented at Grand Rounds, Scripps Mercy Hospital, San Diego, CA, 7 Sep 04

08/04 "Metabolic Disorder" Presented at Grand Rounds, Kedren Hospital, Los Angeles, CA 16 Aug 04

06/04 "Atypical Antipsychotics in Special Populations" Presented at Grand Rounds Terrell State Hospital, Terrell, TX, 21 Jun 04

06/04 "The Many Faces of 'Wartime' PTSD" Presented at Grand Rounds, Mountain Crest Hospital, Fort Collins, CO, 15 Jun 04

05/04 "Pharmacology Treatment of Psychosis and Agitation in Dementia of the Elderly" Presented at Grand Rounds, Utah State Hospital, Provost, UT, 20 Mau 04

05/04 "Psychiatric Research Ethics" Presented at NIH Neuroscience Center, Bethesda, MD, 17 May 04

05/04 "Lab Science to Clinical Practice: Neurochemical Model of Antipsychotic Effects" Presented at Grand Rounds, Metropolitan State Hospital, Norwalk, CA, 12 May 04

04/04 "New Indications for Antipsychotics for Bi-Polar Disorders" Presented at Grand Rounds, Cedars Sinai, Los Angeles, CA, 29 Apr 04

03/04 "A Century after Bleuler, What Do We Really Know About Schizophrenia, Its Origin, Cause, and Treatment?" Presented at WASP (World Association of Social Psychiatry), 1st Regional Congress of Social Psychiatry in Africa; Johannesburg, Gauteng, 24 Mar 04

03/04 "The Antipsychotics: Their Developmental History, Clinical Limitations, Major Toxicities, and Anticipated Future." Presented at WASP (World Association of Social Psychiatry), 1st Regional Congress of Social Psychiatry in Africa; Johannesburg, Gauteng, 24 Mar 04

02/04 "Consideration in the Long-term Management of Schizophrenia" Presented at Grand Rounds, Stanford University Hospital, Stanford, CA, 19 Feb 04

02/04 "The Marketing of Atypical Antipsychotic Drugs: A War for Our "Loyalties" Moves Into its Guerilla Phase" Presented at Grand Rounds, Sepulveda VA Mental Health Center, Los Angeles, CA, 11 Feb 04

02/04 "Drug Induced Metabolic Symptoms with Antipsychotic Paradigm Shift in an Approach to Patient Care" Presented at Grand Rounds, Atascadero State Hospital, Atascadero, CA, 4 Feb 04

01/04 "Risperdal Consta" Presented at Grand Rounds, Indianapolis VA, Indianapolis, IN, 15 Jan 04

12/03 "Strategies for Controlling Psychotic Symptoms" Presented at Grand Rounds, Riverside County Department of Mental Health, Hemet CA, 9 Dec 03

12/03 "The Side Effects of the Atypical Antipsychotics: Marketing Mischief, Metabolic Mayhem, or Mechanistic Magic?" Presented at Grand Rounds, Castle Medical Center, Kailua, HI, 2 Dec 03

11/03 "Monitoring Patients on Antipsychotic Drugs for Glucose Intolerance and Other Features of the Metabolic Syndrome" Presented at Alexandria, VA, 19-20 Nov 03

11/03 "Antipsychotics: Overcoming Side Effect Treatment Barriers" Presented at Grand Rounds, Long Beach VA Medical Center, Long Beach, CA, 12 Nov 03

11/03 "The Side Effects of the Atypical Antipsychotics: Marketing Mischief, Metabolic Mayhem, or Mechanistic Magic?" Presented at Grand Rounds, Fresno, CA, 11 Nov 03

11/03 "A Broad Spectrum in Psychotropics" Presented at Grand Rounds, Golden Valley Health Center-Corner of Hope, Modesto, CA, 6 Nov 03

10/03 "The Mechanistic Similarities and Distinctions Among Antipsychotics: A Treatment Refractory Model" Presented at Grand Rounds, Hawaii State Hospital Auditorium, Oahu, HI, 24 Oct 03

10/03 "The Side Effects of the Atypical Antipsychotics: Marketing Mischief, Metabolic Mayhem, or Mechanistic Magic?" Presented at Grand Rounds, San Francisco Clinic, San Francisco, CA, 4 Oct 03

10/03 "Kaiser/Group Health Cooperative AP Advisory Board" Presented at San Francisco, CA, 4 Oct 03

10/03 "Improvement in Cognitive Function, Dosing and Titration" Presented at Grand Rounds, Olive View Hospital, Sylmar, CA, 2 Oct 03

09/03 "Strategies for Controlling Psychotic Symptoms" Presented at Grand Rounds, Seattle Hospital, Seattle, WA, 11 Sep 03

08/03 "Neurocognition and Schizophrenia Including Issues on Nicotine Receptors" Presented at Grand Rounds, Ventura County Behavioral Health Inpatient Unit, Ventura, CA, 13 Aug 03

05/03 "Switchover from Clozapine to Quetiapine: Mixed Results" Presented at Biological Psychiatry, San Francisco, CA, 15 May 03

05/03 "Effects of Novel Antipsychotics on Glucose and Lipid Levels" Presented at Grand Rounds, Eugene VA Clinic, Eugene, OR, 13 May 03

05/03 "Effects of Novel Antipsychotics on Glucose and Lipid Levels" Presented at Grand Rounds, VA Medical Center, Portland, OR, 12 May 03

05/03 "Atypical Antipsychotics: Marketing Mischief or Metabolic Mayhem" Presented at Grand Rounds, Harbor-UCLA Medical Center, Torrance, CA, 6 May 03

04/03 "Metabolic Consequences of Antipsychotic Therapy" Presented at Grand Rounds, Atascadero State Hospital, Atascadero, CA, 30 Apr 03

03/03 "Metabolic Toxicities of Atypical Antipsychotic Agents: Speculations, Etiology, and Treatment" Presented at Grand Rounds, RJ Donovan Correctional Facility, San Diego, CA, 12 Mar 03

03/03 "Aripiprazole" Presented at Grand Rounds, Patton State Hospital, Patton, CA, 5 Mar 03

02/03 "Applied Neuropsychopharmacology: The Spectrum of Clinical Outcomes with Atypical Antipsychotics" Presented at the CNS Advisory Summit, Scottsdale AZ, 22 Feb 03

02/03 "The Use of Atypical Antipsychotics in Mood Disorders" Presented at Grand Rounds, Region IV Parole Headquarters, Diamond Bar, CA, 21 Feb 03

01/03 "Metabolic Side Effects of Atypical Antipsychotics" Presented at Grand Rounds, King Drew Medical Center, Los Angeles, CA, 28 Jan 03

01/03 "TD - What if Anything is New?" Presented at Grand Rounds, VA Hospital, Neurology Department, Los Angeles, CA, 24 Jan 03

01/03 "Metabolic Toxicities of Atypical Antipsychotic Agents: Speculations, Etiology, and Treatment" Presented at Grand Rounds, Sepulveda VA, Los Angeles, CA, 22 Jan 03

12-02 "Aripiprazole" Presented at Grand Rounds, Loma Linda University, Redlands, CA 20 Dec 02

12-02 "Aripiprazole" Presented at Grand Rounds, Arrowhead Regional Medical Center, Colton, CA, 17 Dec 02

12-02 "Treatment Emergent Movement Disorders in Current Clinical Practice" Presented at Grand Rounds, Queens Hospital, Honolulu, HI, 13 Dec 02

12-02 "Advancement in Treatment of Schizophrenia" Presented at Grand Rounds, Tripler VA Army Hospital, Honolulu, HI, 11 Dec 02

11-02 "Evolution of Antipsychotic Therapies: A Pathophysiologic Approach" Presented at National Network if Psychiatric Educators, Laguna Niguel, CA, 15 Nov 02.

10-02 "Side Effects Involving Newer Antipsychotic Medications Including Risk of Cardiovascular Disease and Diabetes" Presented at Grand Rounds, Bakersfield Memorial Hospital, Bakersfield CA, 24 Oct 02.

03-02 "The Atypical Antipsychotic Compounds: What is the Crucial Difference Among Them?" Presented at Psychopharmacology Course, Stanford University, Stanford CA, 9 Mar 02.

03-02 "The Relative Metabolic Toxicities Among the Newer Antipsychotic Compounds." Presented at Grand Rounds, Waco, TX, 7 Mar 02

03-02 "The Relative Metabolic Toxicities Among the Newer Antipsychotic Compounds." Presented at Grand Rounds, Dallas VA Medical Center, Dallas, TX, 7 Mar 02

11-01 "Aripiprazole: Is anything Really New in the Wold of Antipsychotic Medications?" Presented at Abilitat Investigators Meeting, Scottsdale, AZ, 29 Nov 01.

09-01 "The Past, Present, and (Near) Future of Antipsychotic Medications: The Under-appreciated Role of Luck!" Presented at The Annual Meeting of the Northern California Psychiatric Society, Saratoga, CA, 19 Sep 01.

07-01 "The Metabolic Side Effects of the Newer Antipsychotic Compounds: The TD of the New Millennium." Presented at Grand Rounds, UC Irvine, Irvine, CA, 17 Jul 01.

05-01 "The Toxicities of the So-Called 'Atypical Antipsychotics'--Focus on Dyslipidemia." Presented at Grand Rounds, Utah Neuropsychiatric Institute, Salt Lake City, Utah, 22 May 01.

04-01 "Prodromal Phase of Schizophrenia: Diagnosis and Treatment." Presented at W. Covina Mental Health Office, W. Covina, CA, 19 April 01.

03-01 "Risperidone: A Clinical Research Update." Presented at Le Royal Meridien, Toronto, Ontario, Canada, 31 Mar 01.

03-01 "Ziprasidone: A New Treatment Option for Schizophrenia." Presented at University Of Tennessee, Memphis, TN, 9 Feb 01

03-01 "Ziprasidone: A New Treatment Option for Schizophrenia." Presented at University Of Arkansas for Medical Science, Little Rock, AR, 8 Feb 01

02-01 "Use of Antipsychotic Drugs on Treatment Approach for Drug Induced Psychosis." Presented at San Quentin State Prison, San Quentin, CA, 21 Feb 01.

01-01 "EPA and TD with Novel Antipsychotics." Presented at Lanterman State Hospital, Pomona, CA, 25 Jan 01.

12-00 "Optimal Management of Psychosis and Agitation in the Elderly." Presented at VA Hospital, Seattle, WA, 15 Dec 00.

12-00 "Efficacy and Safety Data of the Atypical Antipsychotics." Presented at Atascadero State Hospital, Atascadero, CA, 14 Dec 00.

12-00 "Optimal Management of Psychosis and Agitation in the Elderly." Presented at Grand Rounds, VA Hospital Outpatient Clinic, Roseburg, OR, 12 Dec 00.

12-00 "Optimal Management of Psychosis and Agitation in the Elderly" Presented at Grand Rounds, USC Ingleside Hospital, Rosemead, CA, 8 Dec 00.

12-00 "Optimal Management of Psychosis and Agitation in the Elderly." Presented at Grand Rounds, University of Southern California, Los Angeles, CA, 6 Dec 00.

11-00 "Safety and Efficacy Among Atypicals; Treatment Refractory Schizophrenia." Presented at Los Angeles County Jail, Los Angeles, CA, 30 Nov 00.

11-00 "Optimal Management of Psychosis and Agitation in the Elderly." Presented at Olive View Hospital, Sylmar, CA, 16 Nov 00.

11-00 "Long-Term Outcomes with Antipsychotic Medications: The limitations of Our Current Technology." Presented at Ziprasidone National Consultants Forum, Scottsdale, AZ, 14 Nov 00.

11-00 "Optimal Management of Psychosis and Agitation in the Elderly." Presented at USC Ingleside Hospital, Rosemead, CA, 9 Nov 00.

10-00 "Newer Antipsychotics: Approaches to Treatment Refractory Patients." Presented at 2000 MIRECC Retreat, Los Angeles, CA, 25 Oct 00.

10-00 "Weight Gain and Atypical Antipsychotic Medications: The TD of the New Millennium?" Presented at MHC of Greater Manchester, Manchester, NH, 12 Oct 00.

09-00 "Side Effects of Typical and Atypical Antipsychotic Agents." Presented at the UCLA Medical Plaza, Los Angeles, CA, 11 Sep 00.

09-00 "Safety and Efficacy Among Atypicals." Presented at Sacred Heart Hospital, Spokane, WA, 12 Sep 00

09-00 "Safety and Efficacy Among Atypicals." Presented at Skagit Valley Mental Health, Mt. Vernon, WA, 13 Sep 00.

09-00 "Update on Atypical Antipsychotics." Presented at Porterville Developmental Center, Porterville, CA, 14 Sep 00.

07-00 "Schizophrenia: Treatment with Risperdal." Presented at the Office of Mental Health, New Orleans, LA, 25 Jul 00.

07-00 "Atypicals and Treatment Resistant Schizophrenia." Presented at Loma Linda Behavior Medicine Center, Redlands, CA, 21 Jul 00.

06-00 "Movement Disorders." Presented at Palacio de Exposiciones y Congresos, Seville, Spain, 16 Jun 00.

06-00 "Tools for Assessing Symptoms: Side Effect Scales." Presented at Palacio de Exposiciones y Congresos, Seville, Spain, 17 Jun 00.

05-00 "Optimal Management of Psychosis and Agitation in the Elderly." Presented at UC Irvine Medical Neuropsychology Center, Orange, CA, 30 May 00.

05-00 "Optimal Management of Psychosis and Agitation in the Elderly." Presented at Dave & Buster's, Orange, CA, 24 May 00.

05-00 "The Side Effects of Antipsychotic Compounds." Presented at Kaiser Permanente, Fontana, CA, 17 May 00.

04-00 "Atypical Antipsychotics" Presented at Riverside County Inpatient, Riverside, CA, 27 Apr 00.

03-00 "The Novel Antipsychotics." Presented at Loma Linda University, Loma Linda, CA, 29 Mar 00.

03-00 "The Cardiovascular Liabilities of the Atypical Antipsychotics: The Next 'Big' Thing." Presented at Grand Rounds, University of Hawaii, 24 Mar 00.

03-00 "The New Antipsychotic Compounds Really 'New'?" Presented at Grand Rounds, Contra Costa County Regional Medical Center, Martinez, CA, 14 Mar 00.

03-00 "Treatment Refractory Schizophrenia: Is there a rational approach?" Presented at American Psychiatric Association & Nevada Association of Psychiatric Physicians, Las Vegas, NV, Sat, 4 Mar 00.

02-00 "The Use of Risperidone in Acutely Psychotic Patients." Presented at Italian Society of Psychopathology (V SOPSI Congress), Rome, Italy, 23 Feb 00.

02-00 "The Differential Toxicities Among the Atypical Antipsychotics." Presented at Grand Rounds, Cedars Sinai Medical Center, Los Angeles, CA, 17 Feb 00.

12-99 Visiting Scholar-numerous presentations, Presented at University of Arkansas, Little Rock, AR, 5-8 Dec 99

11-99 "The Novel Antipsychotic Medications." Presented at Anaheim, CA, 12 Nov 99.

11-99 "The Side Effects of Antipsychotic Compounds." Presented at University of Kansas Medical Center, Kansas City, MO, 5 Nov 99.

11-99 "Atypicals Antipsychotics: Efficacy and Side Effects." Presented at The American Restaurant, Kansas City, MO, 4 Nov 99.

11-99 "Side Effects of Antipsychiatric Compounds." Presented at Colmery O'Neil V A M C, Topeka, KS, 4 Nov 99.

11-99 "The Side Effects of Antipsychotic Compounds." Presented at Western Missouri Mental Health South Auditorium, Kansas City, MO, 4 Nov 99.

10-99 "Is Clozaril still relevant?" Presented at Atascadero State Hospital, San Luis Obispo, CA, 14 Oct 99.

10-99 "Interested in Geriatric population & Economics of the drugs." Presented at Grand Rounds, Loma Linda University, Loma Linda, CA, 8 Oct 99.

09-99 "Side Effects of Atypical Antipsychotics: What can we expect in the short and long term?" Presented at Riverside, CA, 30 Sep 99.

09-99 "New Treatment Options in the Acute Management of Psychosis." Presented at New York, NY, 26 Sep 99.

08-99 "How to Choose the Correct Medication Regimen for the Treatment of Psychotic Manifestations." Presented at Lanterman Developmental Center, Pomona, CA, 26 Aug 99.

07-99 "Schizophrenia and Overview Movement Disorders." Presented at UCLA School of Nursing, Westwood, CA, 26 Jul 99.

07-99 "New and Novel Antipsychotics." Presented at Fairview Developmental Center, Costa Mesa, CA, 15 July 99.

06-99 "Schizophrenia-Current and New Treatment Trends." Presented at San Joaquin County Mental Health Services, Sacramento, CA, 24 Jun 99.

05-99 "Research Experience with the Newer Neuroleptics-Grand Rounds." Presented at Kaiser, San Francisco, CA, 25 May 99.

05-99 "New Treatment Options in the Acute Management of Psychosis." Presented at Boston Marriott Long Wharf, Boston, MA, 22 May 99.

05-99 "The Neurophysiology of Schizophrenia: Focus on the action of the Novel Antipsychotics." Presented at Kaiser, Woodland Hills, CA, 12 May 99.

04-99 "The New Generation of Antipsychotic Medications." Presented at Kaiser Sunset Family Practice, Los Angeles, CA, 26 Apr 99.

04-99 "Relative Efficacies and Toxicities of Risperidone and Olanzapine." Presented at Leeds, England, United Kingdom, 9 Apr 99.

04-99 "Relative Efficacies and Toxicities of Risperidone and Olanzapine." Presented at Southampton, England, United Kingdom, 8 Apr 99.

04-99 "The Neurophysiology of Schizophrenia: Focus on the Action of the Novel Antipsychotics." Presented at The Schizophrenic Patient: Profiles, Diagnosis and Treatment Conference, Loma Linda University, Loma Linda, CA, 7 Apr 99.

03-99 "Pharmacological Bases for the Putative Neurocognitive Enhancing Impact of Atypical Antipsychotic Agents." Presented at Neurocognitive Impairment in Schizophrenic and Alzheimer's Disorders: Therapeutic Approaches Workshop, International Academy for Biomedical and Drug Research, Paris, FR, 12-13 Mar 99.

02-99 "Antipsychotic Toxicity in the Elderly." Presented at 9th Annual Geriatric Psychiatry Conference, Dallas, TX, 13 Feb 99.

02-99 "Typical and Atypical Neuroleptics: A Geropsychiatric Perspective." Presented at 9th Annual Geriatric Psychiatry Conference, Dallas, TX, 13 Feb 99.

02-99 "Somatic Treatments of Psychotic Disorders" Given with course entitled "Recovery from Madness", Alex Kopelowicz, MD and Robert Liberman, MD--Course Chairs.

02-99 "The Comparative Toxicities of the New Antipsychotic Medications." Presented at Harbor UCLA, Torrance, CA, 2 Feb 99.

01-99 "The Treatment of Schizophrenia at the Turn of the Millennium: What Have We Learned?" Presented to local lay chapter of the California Alliance for the Mentally Ill, UCLA Medical Plaza, Los Angeles, CA, 14 Jan 99.

01-99 "Treatment Refractory Schizophrenia: The Role of the "New" Antipsychotic Compounds" Presented at Grand Rounds, UCI Medical Center, Irvine, CA, 5 Jan 99.

11-98 "Treatment of Schizophrenia." Presented at Grand Rounds, UC Davis Medical Center, Sacramento, CA, 11 Nov 98.

11-98 "Atypicals and Side Effects." Presented at Sutter Family Practice Residency Program, Sacramento, CA, 11 Nov 98.

11-98 "Treatment of Refractory Patients and Partial Response." Presented at Janssen-Cilag SpA Laboratories, Beerse, Belgium, 6 Nov 98.

10-98 "The Role of Novel Antipsychotics in the Control of the Acute Psychotic Symptoms." Presented at the WPA Symposium, Guadalajara, MX, 30 Oct 98.

10-98 "Efficacy of Risperdal and the Atypical Antipsychotics." Presented at Grand Rounds, Porterville State Hospital, Porterville, CA, 21 Oct 98.

10-98 "Treatment of the Refractory Patient." Presented at the Grand Geneva Resort Symposium, Lake Geneva, IL, 3 Oct 98.

10-98 "Treatment Resistant Schizophrenia" Presented at the APA-IPS Symposium, Los Angeles, CA, 2 Oct 98.

09-98 "Treatment Refractory Schizophrenia." Presented at Grand Rounds, Oregon Health Sciences University Department of Psychiatry, 29 Sep 98.

09-98 "The Second Generation of 'Anti-schizophrenic' Drugs." Presented at the 1998 William Rondeau Memorial Lecture, Oregon Health Sciences University Department of Psychiatry, 28 Sep 98.

09-98 "Movement Disorders in Psychiatry." Presented at VA Hines, IL, 23 Sep 98.

09-98 "The Role of Atypical Antipsychotics." Presented at Napa State Hospital, CA, 19 Sep 98.

09-98 "Atypical Antipsychotics and Schizophrenia." Presented at Grand Rounds, Menlo Park VAMC, Menlo Park, CA, 11 Sep 98.

08-98 "New Treatment Options in Schizophrenia." Presented at ComCare, Phoenix, AZ, 18 Aug 98.

07-98 "Schizophrenia Overview and Movement Disorders." Presented at the Neuropsychiatric Nurse Practitioner Program, UCLA School of Nursing, Los Angeles, CA, 27 Jul 98.

07-98 "New Treatment Interventions for Psychotic Disorders." Presented at San Joaquin County Mental Health Services, Stockton, CA, 16 Jul 98.

07-98 "Strategies for Rapidly Controlling Acute Psychotic Symptoms." Presented at Napa State Hospital, Napa, CA, 3 Jul 98.

06-98 "New Directions in Psychosis." Presented at Grand Rounds, San Francisco General Hospital, San Francisco, CA, 26 Jun 98.

06-98 "The Clinical Choice: Is an Algorithm Possible?" Presented at Riverview Hospital, Vancouver, BC, 12 Jun 98.

06-98 "Treatment of Refractory Psychosis: Is There a Rational Approach?" Presented at Riverview Hospital, Vancouver, BC, 12 Jun 98.

06-98 "Drug Treatment of Schizophrenia" Presented as course number 63 with faculty S Marder, J Davis, P Janicak, at the 151st APA Annual Meeting in Toronto, Canada, 2 Jun 98.

05-98 "New Atypical Antipsychotics: Similarities and Differences" Presented via satellite program for Indio and Riverside County Mental Health Inpatient Treatment Facility, Riverside, CA, 28 May 98.

05-98 "New Advances in the Treatment of Schizophrenia" Presented by CME, Inc. at Sheraton Gateway, Los Angeles, CA, 17 May 98.

05-98 "Psychopharmacology Update: A Comparison of Current Antipsychotic Drugs" Presented at Merritheu Memorial Hospital, Martinez, CA, 12 May 98.

05-98 "Management of Cognitive Disruption in Schizophrenia" Presented at University of Illinois at Chicago Symposium in Bloomingdale, IL, 5 May 98.

05-98 "Neurocognition, Schizophrenia, and the Role of the Novel Antipsychotic Medications" Presented at the Panhellenic Psychiatric Congress, Limnos, Greece, 2 May 98.

04-98 "Neurocognitive and Functional Assessment - Rationale for M100907 Superiority" Presented at second Neuropsychiatry Forum of Hoechst Marion Roussel in Bridgewater, NJ, 24 Apr 98.

04-98 "Treatment Resistant Schizophrenia: Is there a Rational Approach?" Presented at Bergen Pines County Hospital, Paramus, NJ, 23 Apr 98.

04-98 "Treatment Resistant Schizophrenia: Is there a Rational Approach?" Presented at Rockland Psychiatric Center, Orangeburg, NY, 22 Apr 98.

04-98 "Update on Anti-psychotic Medications." Presented at Alaska Psychiatric Association's 5th Annual Spring Education Meeting, Anchorage, AK, 18 Apr 98.

03-98 "Psychopharmacology Update: A Comparison of Current Antipsychotic Drugs." Presented at Washington State Psychiatric Association Spring Meeting in Vancouver, BC, 28 Mar 98.

03-98 "Schizophrenia and Cognitive Function - Approaching the New Millennium" Presented at National Schizophrenia Symposium, Scottsdale, AZ, 27 Mar 98.

03-98 "Challenge: Making the most of Therapy with Atypical Antipsychotics" Presented at Eastern State Mental Hospital, Williamsburg, VA, 20 Mar 98.

03-98 "Past, Present and Future of Antipsychotic Drugs" Presented for the Virginia State Psychiatric Society, Richmond, VA, 21 Mar 98.

03-98 "Pharmacologic Impact on Neurocognitive Deficits in Schizophrenia:" Presented at Grand Round, Long Beach VA Medical Center, 4 Mar 98.

02-98 "Neurocognition in Schizophrenia: Magnitude, Functional Correlates and Pharmacologic Responsivity" Presented at USC School of Medicine Grand Rounds, 10 Feb 98.

02-98 "Biological bases for Schizophrenia" Presented at the seminar course for undergraduates Psychiatry 98P Professional Schools Seminar Program, UCLA, CA, 4 Feb 98.

11-97 "The New Generation of Antipsychotic Medications: Similarities and Differences" - Presented at V.A.Psychiatry Service Grand Rounds, Minneapolis, MI, 21 Nov 97.

11-97 "The New Generation of Antipsychotic Medications: Similarities and Differences" - Presented at HCMC Psychiatry Grand Rounds, MI. 21 Nov 97.

11-97 "Neurocognition in Schizophrenia: Magnitude, Functional Correlates, and Pharmacologic Responsivity" Presented at the Atascadero State Hospital, Atascadero, CA, 19 Nov 97.

11-97 "Pharmacologic Approach to Chronic and Treatment Refractory Schizophrenia" Presented at the Vancouver BCPA Conference, in Vancouver, Canada, 15 Nov 97.

11-97 "New Serotonin/Dopamine Antagonist" - Presented for the Loma Linda Psychiatric Residency Program, Loma Linda, CA, 14 Nov 97

11-97 "The Role of New Generation Antipsychotics in Treatment-Resistant Schizophrenia" - Presented in Grand Rounds at The Chicago Medical School Department of Psychiatry and Behavioral Sciences, Chicago, IL, 6 Nov 97.

10-97 "Beyond Conventional Symptoms" - Presented in Riyadh, Saudi Arabia, 20 Oct 97.

10-97 "Neurocognitive Changes in Schizophrenia" Clinical Pertinence and Impact of Pharmacotherapy" - Presented in Grand Rounds at the University of Nebraska Medical Center, Omaha, NE, 15 Oct 97.

09-97 "Treatment Resistance in Psychosis"- Presented at the Annual Meeting of the Huron Valley Medical Center in in Ypsilanti, MI, 24 Sep 97.

09-97 "Toxic Side Effects of Antipsychotic Medications - Focus on Neuromotor Syndromes" Presented at The Fall 1997 Symposium of Charter Behavioral Health Systems of New England, Nashua, New Hampshire, 20 Sep 97.

09-97 "Risperidone: Efficacy Beyond Conventional Symptoms" Presented at the 10th Annual Meeting of European College of Neuropsychopharmacology, Vienna, Austria, 15 Sep 97.

09-97 "Schizophrenia, Neurocognition, and Antipsychotic Meds" Presented in Grand Rounds at Oregon Health Science University, 9 Sep 97.

09-97 "Past, Present and Future of Antipsychotics" Presented at the Mendota Mental Health Institute Conference Center, Madison, WI, 29 Aug 97.

06-97 "Efficacy: A Clinician's Evidence from Experience" Presented at the Risperdal: Evidence from Experience Interactive Seminars in East Midlands, England, 19 Jun 97.

06-97 "Efficacy: A Clinician's Evidence from Experience" Presented at the Risperdal: Evidence from Experience Interactive Seminars in East Kilbride, England, 18 Jun 97.

06-97 "Efficacy: A Clinician's Evidence from Experience" Presented at the Risperdal: Evidence from Experience Interactive Seminars in Aberdeen, Scotland, 17 Jun 97.

06-97 "Antipsychotics: The Evidence from Experience" Presented at the Janssen Research Foundation in Beerse, Belgium, 16 Jun 97.

06-97 "Atypical Neuroleptics: Newer Antipsychotics" Presented at the Northampton VA Medical Center, Northampton, MA, 4 Jun 97.

05-97 "Beyond Conventional Symptoms: Focus on Risperidone" Presented in Grand Rounds at Vanderbilt University Medical Center, Nashville, TN, 27 May 97.

05-97 "Psychopharmacology in the Geriatric Patient: Utility and Limitations" Presented at the California Society of Internal Medicine annual meeting, San Diego, CA, 24 May 97.

05-97 "The Recognition and Management of Side Effects of Typical and Atypical Neuroleptics" Presented as course number 54 with faculty SR Marder, J Davis, G Simpson, P Janicak at the 150th APA Annual Meeting, San Diego, CA, 17-22 May 97.

05-97 "Overview of Treatment of Psychosis with New Atypical Antipsychotic Medications" Presented at the Psychiatric Institute, Washington, DC, 16 May 97.

05-97 "Overview of Treatment of Psychosis with New Atypical Antipsychotic Medications" Presented at the Commission on Mental Health, Washington, DC, 15 May 97.

05-97 "Practical Applications in Atypical Antipsychotics: Clients with Movement Disorders" Presented at Cambridge Hospital, Boston, MA, 14 May 97.

05-97 "The Newer Antipsychotics: Differences and Applications" Presented at Butler Hospital, Providence, RI, 13 May 97.

04-97 "Risperidone and Neurocognition". Presented at the Annual Meeting of the Dutch Psychiatric Society, Amsterdam, Netherlands, 18 Apr 97.

04-97 "Clozapine vs. Haloperidol: Drug Intolerance in a Controlled Six Month Trial" Presented at the International Congress on Schizophrenia Research, Colorado Springs, CO, 14 Apr 97.

04-97 "Antipsychotic Drug Side-Effects: Objective and Subjective". Presented at the International Congress on Schizophrenia Research, Colorado Springs, CO, 14 Apr 97.

03-97 "An Update on Atypcial Antipsychotics". Presented in Hyannis, MA, 28 Mar 97.

03-97 "An Update on Atypical Antipsychotics". Presented in New Bedford, MA, 27 Mar 97.

03-97 "The Management of Acute Exacerbations in Chronic Schizophrenia". Presented at Evidence From Experience, Lisbon, Portugal, 21 Mar 97.

03-97 "Beyond the Conventional Symptoms". Presented at Evidence From Experience, Lisbon, Portugal, 21 Mar 97.

03-97 "The Efficacy of Risperidone: The Evidence from the Controlled Clinical Experience". Presented in Beijing, China, 17 Mar 97.

03-97 "The Efficacy of Risperidone: The Evidence from the Controlled Clinical Experience". Presented in Nanjing, China, 15 Mar 97.

03-97 "The Efficacy of Risperidone: The Evidence from the Controlled Clinical Experience". Presented in Shanghai, China, 14 Mar 97.

03-97 "The Efficacy of Risperidone: The Evidence from the Controlled Clinical Experience". Presented in Wuhan, China, 12 Mar 97.

03-97 "The Efficacy of Risperidone: The Evidence from the Controlled Clinical Experience". Presented in Guangzhou, China, 11 Mar 97.

01-97 "Rational Approach to Antipsychotic Medications and Patient Selection". Presented at the Midwinter Program for Psychiatrists, Lake Tahoe, NV, 28 Jan 97.

01-97 "Current Therapy Options: Efficacy and Side Effects". Presented at the Reintegration: Therapeutic Horizons for Psychotic Disorders Symposium in Salt Lake City, UT, 25 Jan 97.

01-97 "Issues in Diagnosis of Schizophrenia". Presented at the Reintegration: Therapeutic Horizons for Psychotic Disorders Symposium in Salt Lake City, UT, 25 Jan 97.

12-96 "The New Generation of Antipsychotic Medications: Similarities & Differences". Presented to the Hawaii Psychiatric Medical Association, Waikiki, HI, 3 Dec 96.

12-96 "The New Generation of Antipsychotic Medications: Similarities & Differences". Presented at Hawaii State Hospital, Kaneohe, HI, 2 Dec 96.

11-96 "Risperidone: The Controlled Clinical Experience". Presented in Newcastle, England.

11-96 "Risperidone: The Controlled Clinical Experience". Presented in Glasgow, Scotland.

11-96 "Risperidone: The Controlled Clinical Experience". Presented in Birmingham, England.

11-96 "Risperidone: The Controlled Clinical Experience". Presented in Manchester, England.

11-96 "Risperidone: The Controlled Clinical Experience". Presented at Kyoto Prefectural University, Kyoto, Japan.

11-96 "Risperidone: The Controlled Clinical Experience". Presented at Hiroshima University, Hiroshima, Japan.

11-96 "Treatment Resistant Schizophrenia: Is There a Rational Approach?" Presented in Kurashiki (Okayama City), Japan.

08-96 "New Solutions to Treatment Resistant Schizophrenia". Presented at the 10th World Congress of Psychiatry, Madrid, Spain, 23 Aug 96.

07-96 "Critical Issues in Psychoses: Dementia, First-Break Patients, Refractory Cases, and Pharmacoeconomics of Schizophrenia". A CME presentation, Costa Mesa, CA.

06-96 "Critical Issues in Psychoses: Dementia, First-Break Patients, Refractory Cases, and Pharmacoeconomics of Schizophrenia". A CME presentation, San Francisco, CA.

06-96 "The New Generation of Antipsychotic Medications: How Are They Different?". A CME presentation, Staunton, VA.

05-96 "Treatment Resistant Schizophrenia" an industry-sponsored symposium presented at the 149th APA Annual Meeting, New York, NY, May 4-9, 1996.

05-96 "The Recognition and Management of Side Effects of Typical and Atypical Neuroleptics" Presented as course number 61 with faculty SR Marder, J Davis, G Simpson, P Janicak at the 149th APA Annual Meeting, New York, NY, May 4-9, 1996.

03-96 "Treatment Resistant Schizophrenia: Is There a Rational Approach?" Presented at Evolving Attitudes Across the Spectrum of Schizophrenia, Amsterdam, Netherlands.

03-96 "The Natural History of the 'Schizophrenias'". Presented at Evolving Attitudes Across the Spectrum of Schizophrenia, Amsterdam, Netherlands.

03-96 "Update on New Antipsychotic Medications". Presented at University of California, Davis, Davis, CA.

03-96 "Special Populations with Psychoses: First Break Patients, Adolescents and Geriatric Patients". A CME presentation, Long Beach, CA.

02-96 "Psychopharmacology in the Elderly: Cognition and Psychosis". Presented at the Area 7 Symposium, Las Vegas, NV.

02-96 "Side Effects of Antipsychotics: Recognition and Treatment". Presented at Grand Rounds, Stanford University Medical Center, Palo Alto, CA.

01-96 "The History and Current Status of Antipsychotic Drug Development". Presented at Grand Rounds, The Palos Verdes Regional Psychiatric Hospital, Tucson, AZ.

01-96 "The Risk Benefit Profiles of the Serotonin-Dopamine Antagonists". Presented at the University of Arizona, Tucson, AZ.

12-95 "Rational Approaches to Antipsychotic Pharmacotherapy". Presented at the Quarterly Meeting of the County of San Diego Mental Health Services, San Diego, CA.

11-95 "Special Populations with Psychosis: Adolescents, Geriatrics, and First Break Patients". A CME presentation, Seattle, WA.

11-95 "Special Populations with Psychosis: Adolescents, Geriatrics, and First Break Patients". A CME presentation, San Francisco, CA.

10-95 "The New Serotonin/Dopamine Antagonists: Are They Really Different?" presented to the Hirosaki University Department of Neuropsychiatry, Hirosaki University, Hirosaki, Japan.

10-95 "The New Serotonin/Dopamine Antagonists: Are They Really Different?" presented to the Akita University School of Medicine Department of Psychiatry, Akita University, Akita, Japan.

10-95 "The New Serotonin/Dopamine Antagonists: Are They Really Different?" presented to the Hokkaido University Department of Psychiatry, Hokkaido University, Hokkaido, Japan.

10-95 "Polypharmacy in the Treatment of Psychosis: Is There a Rational Approach?" presented at the SinYang Park Hotel, KwangJu, Korea.

10-95 "Polypharmacy in the Treatment of Psychosis: Is There a Rational Approach?" presented at the KwangJu Severance Mental Hospital, KwangJu, Korea.

10-95 "Update on Serotonin/Dopamine Antagonists: Are They Really Different?" presented to the Meeting of the Korean Neuropsychiatric Association at the Seoul Education Culture Center, Seoul, Korea.

09-95 "Pharmacologic Treatment of Depression" presented to the Quarterly Meeting of the Hawaii Psychiatric Association, Honolulu, Hawaii.

09-95 "Anti-psychotic Medications & Patient Selection: Is There a Rational Approach?" presented to the Hawaii Medical Association at the University of Hawaii, Honolulu, Hawaii.

08-95 "Side Effects of Antipsychotic Medications" presented at the Quarterly Meeting of the Memphis Psychiatric Association, Memphis, TN.

07-95 "Polypharmacy: When is it Reasonable?" Grand Rounds, Alameda County Psychiatric Hospital, Alameda, CA.

07-95 "Behavioral Skill Training in Schizophrenia: Utility and Limitation" Grand Rounds, Atascadero State Hospital, Atascadero, CA.

06-95 "Side Effects of Antipsychotic Medications" Grand Rounds, Loma Linda VA Hospital, Loma Linda, CA.

06-95 "The Treatment of Psychosis in the Elderly" Los Encinas Hospital Annual Symposium, Pasadena, CA.

06-95 "Update on the New Antipsychotic Medications" presented to the Annual Meeting of the California Department of Corrections Psychiatrists, Diamond Bar, CA.

05-95 "How to do research without an NIMH grant" presented at the 148th Annual Meeting of the American Psychiatric Association, Miami, FL, 20-25 May 95.

05-95 "The recognition and management of the side effects of typical and atypical neuroleptics" presented as Course 69 with Director SR Marder, and Faculty J Davis, G Simpson, Philip Janicek, and myself, at the 148th APA Annual Meeting, Miami, FL, 20-25 May 95.

05-95 "Behavioral Skills Training in Chronic Schizophrenia" presented at the Annual Conference of Western Reserve Psychiatric Hospital, Northfield, OH, 5 May 95.

03-95 "Dopaminergic Modulation of Cigarette Smoking" presented at the Society for Research on Nicotine and Tobacco with Murray E Jarvik, MD, PhD and Nicholas H Caskey, PhD, San Diego, CA.

03-95 "The Safety and Efficacy of Serotonin-Dopamine Antagonists" a Continuing Medical Education presentation, St. Louis, MO.

03-95 "The Safety and Efficacy of Serotonin-Dopamine Antagonists" a Continuing Medical Education presentation, Philadelphia, PA.

02-95 "The Next Generation of Antipsychotic Medications" presented at Grand Rounds, Veterans Affairs Hospital, Tuskegee, AL.

11-94 "Dosing Strategies with Antipsychotic Compounds: Conventional, SDAs, and Atypicals" presented at the Fall Symposium of New Approaches to Treating Schizophrenia, Chicago, IL, 12 Nov 94.

10-94 "Risperidone: Is It Really Different?" presented at the Fall Conference of the California Alliance For the Mentally Ill, San Francisco, CA, 29 Oct 94.

05-94 "The recognition and management of the side effects of typical and atypical neuroleptics" presented as Course 71 with Director SR Marder, and Faculty J Davis, G Simpson, Philip Janicek, and myself, at the 147th APA Annual Meeting, Philadelphia, PA, 24 May 94.

05-94 "Dementia and Movement Disorders in the Elderly," presented as Course 6 with Director JL Cummings, and Faculty WE Reichman, D Sultzer, and myself, at the 147th APA Annual Meeting, Philadelphia, PA, 20 May 94.

04-94 "Risperidone, is it really different?" presented at a Stanford University sponsored symposium on the treatment of schizophrenia Palo Alto, CA.

03-94 "The New Atypical Antipsychotics--Focus on Risperidone" presented to the Utah State Alliance for the Mentally Ill, Salt Lake City, Utah.

02-94 "The New Atypical Antipsychotics--Focus on Risperidone" presented to the Washington State mental health workers (psychiatrists and pharmacists), Seattle, WA.

01-94 "The Real Cost of Neuroleptic Treatments" presented to the California State Legislature, Sacramento, CA.

01-94 "The Rational Use of Neuroleptics" presented at the annual educational meeting of the Los Angeles Chapter of Family Practioners, Santa Monica, CA.

10-93 "The Therapeutic Window--The Role of Subjective Experiences" presented at the Quarterly Meeting of the Royal College of Psychiatrists in London, England.

05-93 "Optimum Dosing in Maintenance Treatment." Marder SR, Van Putten T, Wirshing WC, Lebell MB, McKenzie J, Johnston-Cronk K, presented at the 146th APA Annual

Meeting, San Francisco, CA, 26 May 93. In: 1993 CME Syllabus & Proceedings Summary, p. 238. (No. 87B)

05-93 "Combined Skills Training and Early Intervention." Marder SR, Wirshing WC, Van Putten T, Eckman TA, Liberman RP, presented at the 146th APA Annual Meeting, San Francisco, CA, 24 May 93. In: 1993 CME Syllabus & Proceedings Summary, p. 156. (No. 28D)

05-93 "Clinical Use of Neuroleptic Plasma Levels." presented at the 146th APA Annual Meeting, San Francisco, CA, 25 May 93.

05-93 "Dementia and Movement Disorders in the Elderly," presented as Course 2 with Director JL Cummings, and Faculty WE Reichman and myself, at the 146th APA Annual Meeting, San Francisco, CA, 22 May 93.

01-93 "Hyperkinetic Syndromes in the Elderly" presented at the Geriatric Supercourse in Marina del Rey, CA, 20 Jan 93.

11-92 "Clinical Consequences of Akinesia and Akathisia", presented as first author with T Van Putten and SR Marder at the Association of European Psychiatrists Congress, Barcelona, Spain, 5 Nov 92.

10-92 "The New Atypical Antipsychotics", presented to the South Coast Chapter of the Alliance for the Mentally Ill, Torrance, CA.

06-92 "Impact of Public Opinion and News Media on Psychopharmacology in the 1990's", with Louis Jolyon West, MD, at the College of International Neuropsycho-pharmacology Annual Meeting (CINP), 30 Jun 92, Nice, France.

05-92 "Drug-Induced Movement Disorders in the Elderly," presented at the 145th Annual American Psychiatric Association Meeting, Washington, DC.

03-92 "Fluoxetine-Induced Suicidality: Science, Spurious, or Scientology?" presented at the Daniel X. Freedman Journal Club, UCLA.

01-92 "The Placebo-Controlled Treatment of the Schizophrenic Prodrome," Biannual Winter Workshop on Schizophrenia, Badgastein, Austria.

01-92 "Management of the Neuroleptic-Intolerant Patient," presented with D Ames and T Van Putten at UCLA Grand Rounds, Los Angeles, CA.

01-92 "Akathisia with the New Atypical Neuroleptics," presented at Psychiatry Grand Rounds, UCLA-Harbor Medical Center, Torrance, CA.

12-91 "Management of Risk of Rèlapse in Schizophrenia," presented at the Annual Meeting of the American College of Neuropsychopharmacology, San Juan, Puerto Rico.

10-91 "Extrapyramidal Symptoms and the Atypical Antipsychotics," presented to the Southern . California Chapter of the California Alliance for the Mentally Ill, Los Angeles.

06-91 "Neuroleptic-Induced Extrapyramidal Symptoms," presented at the Southern California Psychiatric Society, West Hollywood, CA.

05-91 "Pharmacokinetics of Long-Acting Neuroleptics," presented with SR Marder, T Van Putten, J Hubbard, M Aravagiri, and KK Midha, at the American Psychiatric Association 144th Annual Meeting, New Orleans, LA.

05-91 "Fluphenazine Dose in Chronic Schizophrenia," presented with SR Marder, T Van Putten, M Lebell, J McKenzie, and K Johnston-Cronk, at the American Psychiatric Association Annual Meeting, New Orleans, LA.

05-91 "Early Prediction of Schizophrenic Relapse," presented with SR Marder, T Van Putten, M Lebell, K Johnston-Cronk, and J Mintz, at the American Psychiatric Association Annual Meeting, New Orleans, LA.

04-91 "Instrumental Quantification of Akathisia," presented with T Van Putten, SR Marder, JL Cummings, G Bartzokis, and MA Lee at the International Congress on Schizophrenia Research, Tucson, AZ.

04-91 "Antipsychotic Drugs of the Future: The Legacy of Clozapine," presented at the Annual Meeting of the Southcoast Alliance for the Mentally Ill, Fountain Valley, CA.

02-91 "Free Radicals, Movements Disorders, and their Possible Interrelationship," presented to the College of Pharmacy, University of Saskatchewan, Saskatoon, Canada.

11-90 "Primary and Secondary Effects of the Neuroleptics: An Historical Perspective." California Alliance for the Mentally Ill, Fall Conference, Ventura, CA.

11-90 "Antipsychotic Drugs of the Future: The Legacy of Clozapine." California Alliance for the Mentally Ill, Fall Conference, Ventura, CA.

10-90 "Instrumental Quantification of the Akathisic Liability of Clozapine." 2nd Annual NARSAD Scientific Symposium, Washington, DC.

06-90 "Instrumental Quantification of the Akathisic Liability of Clozapine." Regional Meeting of NARSAD Supporters, Pasadena, CA.

02-90 "Instrumentation of Drug-Induced Movement Disorders." Neurology Grand Rounds, West LA VAMC, Los Angeles, CA.

02-90 "Functional Versus Organic Psychoses." Psychiatry Grand Rounds, UCLA Harbor Medical Center, Torrance.

10-89 "Use of Quantitative Instruments in the Assessment of Neuroleptic-Induced Movement Disorders." Presented to regional representatives of NARSAD.

04-89 "Management of Risk of Relapse in Schizophrenia. "The Annual Spring Scientific Meeting of the Southern California Psychiatric Society, Hollywood, CA.

03-89 "Quantitative Approaches to Drug-Induced Movement Syndromes." Medical Staff of Camarillo State Medical Facility, Camarillo, CA.

01-89 "Social Skills Training in the Chronic Schizophrenic: A Workshop." 2nd Annual Winter Conference of the American Assn. of Community Psychiatrists, Charleston, SC.

11-88 "Instrumentation of Drug-Induced Movement Disorders." Presented to California state legislators, their aides, and advocates of national mental health groups (NAMI and NARSAD).

08-88 "Classical Cases in Schizophrenia", with JA Talbot, MD, Professor and Chair, Department of Psychiatry, University of Maryland. Program produced with an educational grant from Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT.

08-88 "Drug-Induced Extrapyramidal Syndromes in Psychiatric Patients." Texas State Hospital medical staff, Big Springs, TX.

06-88 "Role of Psychopharmacology in the Treatment of the Chronic Mental Patient." Department of Corrections at the California Medical Facility in Vacaville, CA.

04-88 "Psychosocial Rehabilitative Treatment of the Chronic Schizophrenic Patient." Presented to the staff of the Roseburg VA Medical Center, Roseburg, OR.

03-88 "Behavioral Rehabilitation of the Chronic Mental Patient." Workshop presented at the First Annual Winter Conference of the American Society of Community Psychiatrists, Colorado Springs, CO.

01-88 "Electromechanical Characteristics of Tardive Dyskinesia." The Biannual Winter Workshop on Schizophrenia, Badgastein, Austria.

10-87 "Medication/Consent." Symposium with Drs. R Liberman, J Vaccaro, and J Kane, presented at the 1987 Institute on Hospital and Community Psychiatry, Boston, MA.

09-87 "Medication Management and Patient Education." Annual Department of Mental Health Conference at Michigan State University, East Lansing, MI.

05-87 "Quantitative Assessment of Extrapyramidal Symptoms and Involuntary Movement," presented at a symposium on Acute and Chronic Extrapyramidal Symptoms and Tardive Dyskinesia, at the Annual Meeting of the APA, Chicago, IL.

10-86 "The Affective Disorders Spectrum," presented to the Graduate School of Psychology of the California Lutheran College in Thousand Oaks, CA.

04-86 "Unique Issues of Older Adults with Chronic Mental Health Problems, Focus on Schizophrenia." Mental Health and Aging Conference in Los Angeles, CA.

02-86 "The Geriatric Patient with Cardiac and Psychiatric Problems: Pharmacologic Concerns." VA Nursing Service for their Continuing Education Series in Los Angeles, CA.

10-85 "Psychopharmacologic Treatment of the Geriatric Population," presented to the Psychology interns at the VA as part of their Continuing Education Series in Los Angeles, CA.

**Publications**

**Articles**

98. Murphy D, Bailey K, Stone M, Wirshing WC. Addictive potential of quetiapine. *Am J Psychiatry*. 2008 Jul;165(7):918.
97. Tabibian JH, Wirshing DA, Pierre JM, Guzik LH, Kisicki MD, Danovich I, Mena SJ, Wirshing WC. Hepatitis B and C among veterans on a psychiatric ward. *Dig Dis Sci*. 2008 Jun;53(6):1693-8.
96. Pierre JM, Peloian JH, Wirshing DA, Wirshing WC, Marder SR. A randomized, double-blind, placebo-controlled trial of modafinil for negative symptoms in schizophrenia. *J Clin Psychiatry*. 2007 May;68(5):705-10.
95. Buckley PF, Wirshing DA, Buchan P, Pierre JM, Resinck SA, Wirshing WC. Lack of insight in schizophrenia: impact on treatment adherence. CNS Drugs. 2007;21(2):129-41.
94. Wirshing DA, Pierre JM, Wirshing WC, Guzik LH, Resinck SA, Goldstein D, Zorick TS: Community re-entry program training module for schizophrenic inpatients improves treatment outcomes. *Schizophr Res*. 2006 Oct;87(1-3):338-9.
93. Meyer J, Loh C, Leckband SG, Boyd JA, Wirshing WC, Pierre JM, Wirshing DA: Prevalence of the metabolic syndrome in patients with schizophrenia. *Journal of Psychiatric Practice* 2006; 12(1): 6-10
92. Wirshing DA, Smith RA, Erickson ZD, Mena SJ, Wirshing WC: A wellness class for inpatients with psychotic disorders. *Journal of Psychiatric Practice* 2006; 12(1): 24-29
91. Pierre JM, Peloian J, Wirshing DA, Wirshing WC, Marder SM. A placebo controlled trial of modafinil for negative symptoms in schizophrenia. *Schizophrenia Bulletin* 2005; 31:501
90. Pierre JM, Wirshing DA, Wirshing WC, Rivard JM, Marks R, Mendenhall J, Sheppard K, Saunders DG: High-dose quetiapine in treatment refractory schizophrenia. *Schizophrenia Research* 2005, 73(2-3): 373-375
89. Pierre JM, Wirshing DA, Wirshing WC: High-dose antipsychotics: desperation or data-driven? *Current Psych* 2004, 3(8): 31-37.
88. Pierre JM, Shnayder I, Wirshing DA, Wirshing WC: Intranasal quetiapine abuse. *Am J of Psychiatry* 2004, 161(9):1718
87. McGurk SR, Green MF, Wirshing WC, Wirshing DA, Marder SR, Mintz J, Kern R. Antipsychotic and anticholinergic effects on two types of spatial memory in schizophrenia. *Schizophr Res* 2004, Jun 1;68(2-3):225-33.

86. Marder SR, Glyn SM, Wirshing WC, Wirshing DA, Ross D, Widmark C, Mintz J, Liberman RP, Blair KE. Maintenance Treatment of Schizophrenia with Risperidone or Haloperidol: Two-Year Outcomes. *American Journal of Psychiatry*, 2003, 160:1405-1412

85. Wirshing DA, Danovitch I, Erhart SM, Pierre JM, Wirshing WC. Practical tips to manage common side effects. *Current Psychiatry*, 2003 2(3): 49-57

84. Pierre JM, Wirshing DA, Wirshing WC: "Iatrogenic malingering" in VA substance abuse treatment. *Psychiatric Services*, 2003, 54(2): 253-4

83. Wirshing DA, Wirshing WC: Aripiprazole: a viewpoint. *CNS Drugs*, 2002,16(11): 779-786

82. Wirshing DA, Boyd JA, Meng LR, Ballon JS, Marder SR, Wirshing WC: The effects of novel antipsychotics on glucose, and lipid levels. *J Clin Psychiatry 2002*; 63: 856-865

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77. Glynn SM, Marder SR, Liberman RP, Blair K, Wirshing WC, Wirshing DA , Ross D, Mintz J: Supplementing clinic-based skills training with manual-based community support sessions: Effects on social adjustment of patients with schizophrenia. *Am J Psychiatry* 2002; 159(5): 829-37.

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