FOURTH INTERNATIONAL CONFERENCE ON GERIATRIC NEPHROLOGY AND UROLOGY

The Fourth International Conference on Geriatric Nephrology and Urology will be held at the Chelsea Inn, Toronto, on April 19–21, 1996. Those interested please contact: Dr. D.G. Oreopoulos, The Toronto Hospital–Western Division, 399 Bathurst Street, Toronto, Ontario, Canada M5T 2S8; Telephone: 416-603-7974; fax: 416-603-8127.

ACUTE RENAL FAILURE IN THE 21ST CENTURY

An N.I.H.-sponsored conference concerning Acute Renal Failure in the 21st Century will be held May 6–8, 1996, on the NIH campus in Bethesda, Maryland. The purpose of the conference is to present the current state-of-the-art research, to identify and develop future research strategies, and to generate management care guidelines for acute renal failure patients. Competitive travel awards will be offered for trainees/fellows and junior investigators (instructors and assistant professors [not beyond five years]) will be offered. Attendance is limited by size of the hall (160). For further information, call or write: Mr. Fred Hill, Computer Craft/NIDDK, 6707 Democracy Blvd., Bethesda, MD 20817. Telephone: 301-493-9674; fax: 301-530-0634.

STATUS OF PERITONEAL DIALYSIS TREATMENT

An N.I.H.-sponsored conference on the Status of Peritoneal Dialysis Treatment in the United States will be held on May 6th and 7th at the Bethesda Marriott Inn. Statements on current status, recommendations, and research needs will be discussed in the areas of dialysis mortality and morbidity, modality choice and complications, dialysis dose, and nutrition. A workbook will be available for registrants. Potential attendees include academic/community physicians, government agencies, provider companies, and others. Attendance is limited by the size of the hall (160). For further information, call or write: Sharon Gist, DKUHD, NIDDK, NIH, Bldg. 31, Rm. 9A-17, Bethesda, MD 20892. Telephone: 301-496-6325.

RENALE DIALYSIS ACCESS SYMPOSIUM

"Vascular Access for Hemodialysis V: A Symposium on Dialysis Access," sponsored by the Department of Surgery, Division of Transplantation, Ohio State University Medical Center, will be held May 9–10, 1996, at the Westin La Paloma, Tucson, Arizona. The chairmen are Ronald M. Ferguson, MD, and Mitchell L. Henry, MD. CME Credits: 12.5 hours. Fees: Physicians, $375; allied health professionals, $150. Contact: ACCESS Medical Group, Ltd., 3880 RFD Salem Lake Drive, Suite A, Long Grove, IL 60047-7676; Tel: 708-550-0090; fax: 708-550-0095.

12TH COMPREHENSIVE NEPHROLOGY REVIEW COURSE

The UCLA School of Medicine Office of Continuing Medical Education is sponsoring the 12th Comprehensive Nephrology Review Course at the Miramar Sheraton Hotel in Santa Monica, CA on August 2, 1996–August 8, 1996. For more information, contact Deborah Carr, 10920 Wilshire Blvd. #1060, Los Angeles, CA 90024-6512. Phone: 310-794-2620.

ISPD 98, SEOUL

The Eighth Congress of the International Society for Peritoneal Dialysis (ISPD) will be held in Seoul, Korea, on August 23–26, 1998. For further information, contact Dr. Hi Bahl Lee, Hyonam Kidney Laboratory, Soon Chun Hyang University, 657 Hannam Dong, Yongsan Koo, Seoul 140–743, Korea. Telephone: 82-2-709-9171; FAX: 82-2-792-5812; E-mail: hblee@korea.com; Internet:http://korea.com.
THE AMERICAN SOCIETY OF NEPHROLOGY
Advances in Basic Science Conference:

Renal Developmental Biology

November 6-9, 1996
Hyatt Regency
New Orleans, Louisiana

ASN’s 1996 Advances in Basic Science Conference, “Renal Developmental Biology”, will be held November 6-9, 1996, immediately following the 29th Annual Meeting, in New Orleans, Louisiana. The meeting will bring together scientists from developmental biology and investigators in renal developmental biology to discuss areas of common interest from which the transfer of information may benefit both groups. The target audience is young trainees and physician-scientists interested in the basic mechanisms of renal development and its relationship to renal diseases.

Conference Co-Chairs:
Ellis D. Avner, M.D., Cleveland, Ohio
Richard P. Woychik, Ph.D., Oak Ridge, Tennessee

For further information contact:
American Society of Nephrology
1200 19th Street, N.W., Suite 300
Washington, DC, 20036-2422
Phone: 202/857-1190
Fax: 202/223-4579
American Society of Nephrology
Board Review Course

August 24-30, 1996

COURSE DIRECTOR: Robert G. Narins, M.D.

LOCATION: San Francisco
Sheraton Palace Hotel
2 New Montgomery Street
San Francisco, CA 94105

OBJECTIVE: This week-long, in-depth review of nephrology and hypertension
can be used to prepare for the Nephrology Board examination (Nov.
1996) or as a timely and extensive update. CME credits will be pro-
vided.

FACULTY: Nationally renowned speakers will be selected for their teaching
skills and past performance in similar courses.

SYLLABUS: Outlines of all lectures and copies of key slides will be provided.

FORMAT: Lectures, interactive workshops, computer-assisted programs, and
special, small group question and answer sessions will be integrated
into the program. Relevant physiology and pathophysiology will be
blended with clinical discussions aimed at reviewing, updating and
preparing for the 1996 Nephrology Boards.

This Will Be Your ASN Minifellowship!

For information on early bird registration, call or write the ASN National office.

American Society of Nephrology
1200 19th Street, N.W., Suite 300, Washington, DC 20036-2401
(202) 857-1190
Scott & White Clinic is seeking a fellowship trained Transplant Nephrologist to join our staff and assist in developing our kidney transplant program which is scheduled to begin in mid 1996. Initial responsibilities will include approximately 50% transplant, 50% general nephrology. Experience in all aspects of clinical nephrology is needed as well as a desire to teach residents and students. Faculty appointment at Texas A&M University Health Science Center College of Medicine is commensurate with credentials and experience. Female and minority candidates are encouraged to apply. Please forward a current CV along with names/addresses of 3 references to: Mike Nichols, Director of Physician Recruitment, Scott & White Clinic, 2401 South 31st Street, Temple, TX 76508 or call (800) 725-3627.

Join the ASN in New Orleans in 1996.

The American Society of Nephrology’s 29th Annual Scientific Meeting and Exposition will be held November 3-6, 1996, at the Convention Center in New Orleans, Louisiana.

ASN members will automatically receive the Call for Abstracts and Preliminary Program. Nonmembers can receive meeting information by contacting the ASN Office at 1200 19th Street, N.W., Suite 300, Washington, D.C. 20036, Phone: 202/857-1190; Fax: 202/223-4579.

We look forward to seeing you there!
Patients should be advised to take Neoral® on a consistent schedule with regard to time of day and relation to meals.

Laboratory Tests: Renal and liver functions should be assessed repeatedly by measurement of BUN, serum creatinine, serum bilirubin, and liver enzymes.

Drug Interactions: All of the individual drugs cited below are well substantiated to interact with Cyclosporine.

**Neoral® Soft Gelatin Capsules (cyclosporine capsules for microemulsion) Review**

**INDICATIONS AND USAGE**
Neoral® is indicated for the prophylaxis of organ rejection in liver, kidney, and allogeneic autologous transplants. Neoral® has been used in combination with azathioprine and corticosteroids.

**CONTRAINDICATIONS**
Neoral® is contraindicated in patients with a hypersensitivity to cyclosporine or to any ingredient.

**WARNINGS**
Cyclosporine, the active ingredient of Neoral®, can cause nephrotoxicity and hypertension when used in high doses. It is not useful for serum creatinine and BUN levels to be elevated during cyclosporine therapy. These elevations in renal transplant patients do not necessarily indicate rejection, and each patient must be fully evaluated more closely is done.

Based on the historical Sandimmune experience with oral solution, nephrotoxicity associated with cyclosporine had been reported in 28% of cases of first-time transplants, 37% of cases of second-time transplants, and 37% of cases of liver transplantation. Mild nephrotoxicity was generally noted 2-3 months after the start of therapy, with elevations in renal endpoint of more than 1.5 times the upper limit of normal (ULN) of creatinine at a range of 35-45 mg/dl to 20-25 mg/dl of respectively. These elevations were often reversible to cyclosporine therapy.

More overt nephrotoxicity was seen early after transplantation and was characterized by a rapidly rising BUN and creatinine. Since these studies are similar to renal rejection episodes, care must be taken to differentiate between the two conditions. Nephrotoxicity is usually responsive to cyclosporine dosage reduction.

Although specific diagnostic criteria which reliably differentiate renal graft rejection from toxicity have not been found, a number of parameters have been significantly associated with one or the other. It should be noted that a 35% of patients may experience transient nephropathy.

A form of cyclosporine-associated nephropathy is characterized by a decrease in renal function and morphologic changes in the kidneys. From 5% to 10% of transplant recipients who have received cyclosporine therapy will develop renal failure in the absence of rejection. The renal biopsy from these patients will demonstrate one or the following: a decrease in glomerular filtration rate and glomerulosclerosis, vacuolar degeneration of the tubular epithelium, and a striped form of interstitial fibrosis with tubular atrophy. Though none of these morphologic changes are specific to cyclosporine therapy, a diagnosis of cyclosporine-associated structural nephropathy requires evidence of these findings.

When considering the development of cyclosporine-associated nephropathy, it is noteworthy that several authors have suggested a relationship between the appearance of interstitial fibrosis and the use of high doses or persistently high circulating trough levels of cyclosporine. This is particularly true during the first six months post-transplantation when doses of 200-300 mg/day in adults, or 2-4 mg/kg/day in children, are administered. It appears that the organ appears to be most vulnerable to the toxic effects of cyclosporine. Among other contributing factors to the development of interstitial fibrosis in these patients are prolonged perfusion time, warming ischemia time, as well as episodes of acute toxicity, and acute and chronic rejection. The reversibility of interstitial fibrosis and its correlation to renal function have not yet been determined.

Reversibility of interlobar atrophy has been reported after stopping cyclosporine or lowering the dosage.

Impaired renal function at any time requires close monitoring, and frequent dosage adjustment may be indicated.

In the event of severe and unresolving rejection, when rescue therapy with pulse steroids and monocloual antibody may be used. If the patient fails to respond, a switch to alternative immunosuppressive therapy rather than increasing the Neoral® dose to excessive levels.

Occasionally, patients with a history of syndrome of the inappropriate of antidiuretic hormone and micrornagrophic hemolytic anemia which may result in graft failure. The vasculopathy can occur in the absence of rejection and is accompanied by fluid retention within the graft as demonstrated by Indium (111) labeled platelet agglutination and other evidence of intravascular hemolysis. The syndrome is characterized by a reduction in cardiac output which has occurred after reduction or discontinuation of cyclosporine and 1) administration of streptokinase and heparin, and 2) by the detection with Indium (111) labeled platelet scans. (See ADVERSE REACTIONS).

Signs of hyperkalemia (sometimes associated with hyperchloremic metabolic acidosis) and hyperuricemia have been seen occasionally in patients.

Hepatoxicity associated with cyclosporine use has been noted in 4% of cases of renal transplantation, 7% of cases of cardiac transplantation, and 4% of cases of liver transplantation. This was usually noted during the first month of therapy when high doses of cyclosporine were used and consisted of elevations of hepatic enzymes. The increase in enzymes may be related closely to skin. The increased risk appears related to the intensity and duration of immunosuppression rather than to the use of specific agents. In addition, the occurrence of hyperkalemia in patients resulting in increased risk of infection or malignancy, a treatment regimen containing multiple immunosuppressants should be used with caution.

There have been reports of convulsions in adult and pediatric patients receiving cyclosporine, particularly in combination with high dose methyldiprenalone.

Care should be taken when using cyclosporine with nephrotoxic drugs. (See PRECAUTIONS)

Because Neoral® is not bioequivalent to Sandimmune, conversion from Neoral® to Sandimmune using a 1:1 ratio (mg/kg/day) may result in lower cyclosporine blood concentrations. Conversion from Neoral® to Sandimmune should be done with increased monitoring to avoid the potential of undertreatment.

**PRECAUTIONS:** General: Cyclosporine is the active ingredient of Neoral®. Hypertension is a common side effect of cyclosporine therapy. (See ADVERSE REACTIONS) Mild or moderate hypertension is the increased frequency more severe than hypertension and the incidence decreases over time. Anti- hypertensive therapy should be given if the patient cannot tolerate the blood pressure. However, since cyclosporine may cause hyperkalemia, potassium-sparing diuretics are contraindicated. The patient should be monitored for history of hypertension. However, care should be taken since intercurrent with cyclosporine metabolism may require a dosage adjustment. (See Drug Interactions)

During treatment with cyclosporine, blood pressure may be less effective, and the use of antihypertensive medications should be avoided.

Information for Patients: Patients should be advised that any change of cyclosporine formulation should be made carefully and only under physician supervision because it may result in the need for a change in dosage.

Patients should be informed of the necessity of repeated laboratory tests while they are receiving the drug. Patients should be advised of the potential risks during pregnancy and informed of the increased risk of nephropathy.

Patients should be given careful dosage instructions. Neoral® Oral Solution (cyclosporine oral solution for microemulsion) should be diluted, preferably with orange or grapefruit juice that is at room temperature. Grapefruit and grapefruit juice affect metabolism of cyclosporine and should be avoided. The combination of Neoral® Oral Solution (cyclosporine oral solution for microemulsion) with milk can be unpalatable.

**Drug Interactions**
Careful monitoring of renal function should be practiced when Neoral® is used with nephrotoxic drugs.

**Neoral® Soft Gelatin Capsules (cyclosporine capsules for microemulsion) and Neoral® Oral Solution (cyclosporine oral solution for microemulsion) are bioequivalent in comparison to Sandimmune® Soft Gelatin Capsules (cyclosporine capsules, USP) and Sandimmune® Oral Solution (cyclosporine oral solution) in clinical trials. Neoral® capsules and solution can be used interchangeably without physician supervision. It is recommended that cyclosporine blood concentrations be monitored in patients taking Neoral® and that dose adjustments be made in order to avoid toxicity and to achieve desired immunosuppressant levels due to low drug elimination. For a given trough concentration, cyclosporine exposure will be greater with Neoral® than with Sandimmune®. A high dose of Sandimmune® is considered to be Neoral®, particular caution should be exercised. Comparison of blood concentrations in the published literature with concentrations obtained using current assays must be done with the knowledge of the assay methods employed.
Introducing

Neoral®
cyclosporine capsules and oral solution for microemulsion