ST. MICHAEL'S HOSPITAL

Transplant Digest

Issue 5
Fall/Winter 2008

In this issue:

Renal Transplant Symposium 2008: A Huge Success!

The second Renal Transplant Symposium hosted by the St. Michael's Hospital Renal Transplant team held on May 9, 2008 at the Grand Hotel in downtown Toronto was a huge success. The event was entitled "Current Trends in Renal Transplantation: Advancing Care Together".

The objective of the Symposium was to inform front line staff from referring centres of the new initiatives recently implemented by the St. Michael's Hospital transplant team that have positively impacted our patients, their friends and families.

The event was attended by 175 Registered Nurses and Allied Health Professionals from a number of dialysis and pre-dialysis centres from Ontario and Quebec.

The day was appropriately started by a talk from Dr. Frank Markel, Chief Executive Officer of the Trillium Gift of Life Network. He set the stage for the day's events by speaking on the Recent Developments in Organ and Tissue Donation in Ontario.

Dr. Kathryn Tinckam, Co-Director of the Histocompatibility Laboratories, had a discussion on Practical Transplant Immunology. She was followed by Galo Meliton, Transplant Nurse, who spoke on several desensitization protocols.

Dr. Jeffery Zaltzman, Medical Director of the Diabetes Comprehensive Care Program, spoke on the other new initiatives recently implemented at St. Michael's Hospital: Extended Criteria Donation, Donation after Cardiac Death, Paired Exchange and List Exchange Programs, and Anonymous Donation.

Dr. Prasad gave an update on Out of Country Transplantation, focusing on St. Michael's Hospital's experience. His second talk was on kidney donor outcomes.

Several Allied Health Professionals facilitated afternoon breakout sessions, addressing different aspects of pre and post transplant care.

Dr. Kenneth Pace, Staff Surgeon, spoke about the Surgical Issues Affecting Suitability for Transplantation. He also gave an update on Laparoscopic Donor Nephrectomy.

The Planning Committee would like to thank the corporate sponsors, Ms. Trixie Williams, Clinical Leader/Manager of the Ambulatory Clinics, and Dr. Ramesh Prasad, for their help and support toward the success of this event.

The feedback from the attendees was excellent, making it very encouraging for the team planning another information filled event in 2010!

Galo Meliton, RN, C.Neph(C)

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ST. MICHAEL'S HOSPITAL
A teaching hospital affiliated with the University of Toronto

From the Editor's Desk...

Taking care of patients with kidney transplants is complex and multidisciplinary, requiring the expertise of nephrologists, surgeons, nurses, pharmacists, dieticians, social workers, and administrative staff. Together, the transplant team is at your service to help provide the ongoing care and monitoring needed to ensure that your kidney transplant achieves its full potential as a long-term success. What is sometimes overlooked, however, is that there are other health care professionals who provide their expertise both before and after the transplant, especially for the most challenging patients. Without their help, the transplant team would not be able to provide the optimum care that we constantly strive towards.

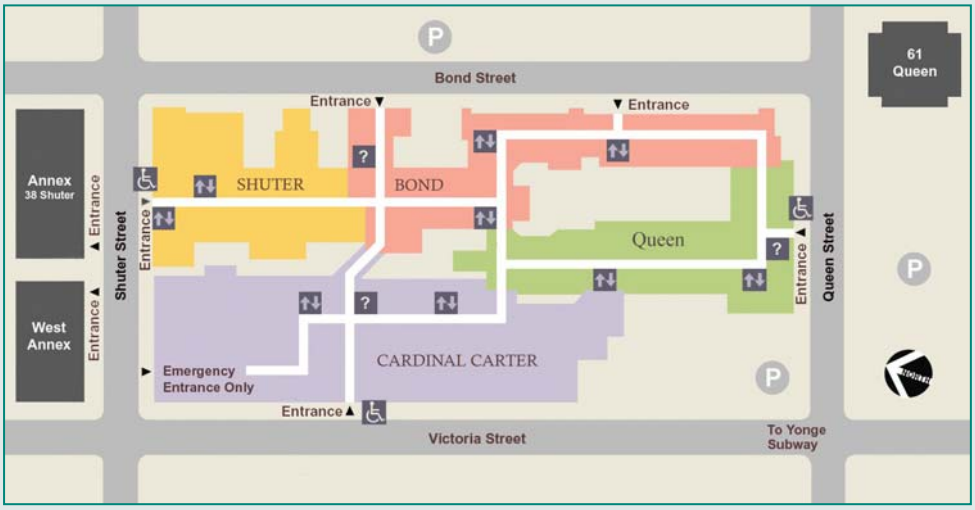
This issue of Transplant Digest contains articles from three specialist consultants who help the transplant team on a regular basis. Dr. Tinckam has provided an overview of the tissue typing and cross-match process, Dr. Leong-Poi discusses at length pre-transplant cardiac screening, and Dr. Dang reviews the subject of depression. In addition, Dr. Prasad explains disease recurrence after kidney transplantation. Galo Meliton reports on our successful Renal Transplant Symposium 2008. Post-transplant chat addresses some common questions asked by patients about infections after transplantation.

Transplant Digest always welcomes articles from transplant patients for inclusion. It is, after all, all about the patient. If you would like to contribute please contact Meriam Jayoma.

Dr. Ramesh Prasad,
Editor

Contact Information

Dr. Ramesh Prasad – Editor
Meriam Jayoma-Austria, RN, CNeph(C) – Newsletter Coordinator



St. Michael's Hospital
Renal Transplant Program
(across the hospital)

61 Queen Street 9th Floor
Toronto, Ontario
M5C 2T2
Canada

Phone: (416) 867-3665

Please send comments or suggestions of topics for future publication to:
Meriam Jayoma-Austria - jayomam@smh.toronto.on.ca

Disclaimer Note:

Views presented in this newsletter are those of the writers and do not necessarily reflect those of St. Michael's Hospital or the University of Toronto. Subject matter should not be construed as specific medical advice and may not be relevant to individual patient circumstances. For all questions related to your own health please contact your health care provider.

Cardiac Screening Prior to Kidney Transplantation

By Dr. Howard Leong Poi
Staff Cardiologist, St. Michael's Hospital

Cardiovascular disease remains one of the leading causes of morbidity and mortality in patients with end-stage renal disease, especially those on dialysis. In suitable candidates, renal transplantation is the treatment of choice, as mortality is significantly reduced in kidney transplant recipients compared to those patients who are listed for transplantation but remain on dialysis. Because atherosclerotic coronary artery disease (CAD) – narrowings and blockages in the arteries that feed the heart muscle – is associated with an increased morbidity (including graft failure, acute myocardial infarction (heart attack) and heart failure) and mortality after transplantation, cardiac screening of patients prior to listing for transplantation has been recommended. While there is general agreement that a cardiovascular assessment is required for many patients prior to proceeding with transplantation, there is no consensus regarding 1) which patients need to be assessed, 2) the optimal method of testing and 3) the frequency of screening. This is important as cardiac screening for all patients listed for transplantation is expensive and time-consuming, both to the health care system and to patients. Screening for the presence of cardiovascular disease will likely be of higher yield in patients who are at greater risk of adverse events than the general end-stage renal disease population. In particular, those patients with 1) symptomatic CAD, 2) a prior history of ischemic heart disease, stroke or peripheral arterial disease, 3) diabetes, 4) older patients (men >45 years, and women >55 years, 5) an abnormal baseline electrocardiogram (ECG), 6) history of smoking, 7) hypertension, 8) reduced left ventricular systolic function and 9) those on longer term dialysis (>2 years) are at higher risk, especially if there are multiple risk factors, should be screened. In contrast, younger, asymptomatic, non-diabetic transplant candidates without a prior history of CAD or left ventricular systolic dysfunction are at low risk for cardiovascular complications, and do not always require routine cardiac evaluation.

Cardiovascular Evaluation and Testing

The evaluation of the pre-renal transplant patient begins with a complete history and physical examination, along with routine tests, such as a resting electrocardiogram (ECG) and a chest X-ray. A resting 2-D echocardiogram (heart ultrasound) provides important information regarding left ventricular function and hypertrophy, cardiac valvular function, pulmonary arterial pressures and the presence of a pericardial effusion. Depending on the presence or absence of symptoms of cardiac disease, such as angina (chest pain from the heart) or exertional shortness of breath, and the presence of risk factors, further testing to rule out important underlying coronary artery disease may be warranted. There are several non-invasive screening tests used to identify patients at high risk for cardiac events. The most commonly used tests include treadmill exercise electrocardiogram (ECG) testing and exercise or pharmacologic imaging tests, namely 1) myocardial perfusion imaging (nuclear testing), such as thallium and sestamibi scintigraphy, looking for inducible perfusion defects, and 2) stress echocardiography with exercise or intravenous dobutamine infusion, looking for inducible regional wall motion abnormalities. In general, exercise ECG testing has not been shown to identify patients at increased risk in the pre-transplant population, due in part to the markedly reduced exercise capacity of patients with end-stage renal disease, and the higher incidence of resting ECG abnormalities, such as left ventricular hypertrophy. The additional information provided by concomitant cardiac imaging during stress improves the sensitivity and

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specificity of detecting CAD, and the prediction of adverse cardiovascular events. In addition, as exercise testing is not feasible in many patients with renal failure, many clinical studies have focused on pharmacologic (drug) stress imaging tests, such as persantine or dipyridamole thallium/sestamibi scintigraphy, and dobutamine stress echocardiography. While results of studies vary, the overall utility of both nuclear and echocardiographic testing for the detection of CAD are comparable, and the choice of one versus the other should be based on the experience and expertise of local imaging laboratories.

While non-invasive stress testing remains useful, coronary angiography remains the gold-standard for the detection of CAD. As this test is invasive, requiring placement of catheters in the heart and arteries, as well as injection of a contrast dye, only selected cases will undergo coronary angiography as the first screening test prior to renal transplantation. Potential indications for coronary angiography include 1) significant symptoms of ischemic heart disease, such as low-threshold chest pain, 2) a documented history of CAD and heart attack, and 3) a moderate to high-risk result on non-invasive stress testing.

Management

Once coronary stenoses or blockages are identified, the need for coronary revascularization (to restore blood flow to the heart muscle) becomes the next important decision. Importantly, the decision to undergo revascularization, either angioplasty (balloon dilatation/procedure) and stenting or coronary artery bypass grafting surgery, should be a clinical decision based upon the need to relieve cardiac symptoms and improve long-term outcomes, beyond the pending kidney transplant operation. One has to remember that, while the hope is that revascularization prior to transplantation will improve kidney allograft, reduce complications and improve patient survival in the post-operative period, there is no good, consistent data to support this. Once revascularization is planned, transplant surgery is generally delayed until at least 3-6 months after stenting, when potent anti-platelet medications can be safely stopped, or 3 months after bypass surgery. Certain medications remain important in the short-term (prior to and immediately after transplantation) and long-term management of patients with documented coronary artery disease. These include in selected patients, aspirin, lipid-lowering agents (statins), beta-blockers, and angiotensin converting enzyme (ACE) inhibitors and angiotensin-receptor blockers (ARBs). Finally, patients with extensive CAD who are deemed at high risk for cardiac complications and are not amenable to revascularization (balloon/stent or surgery), may not be suitable candidates for renal transplantation.

Conclusions

In summary, despite the improvement in cardiovascular mortality after renal transplantation, the risk of cardiac complications remains a significant concern. Thus many kidney transplant candidates will need to undergo further testing on their heart, to detect coronary artery disease and to determine whether medical, interventional or surgical treatment is warranted, prior to proceeding with kidney transplantation.

Mysteries of the Tissue Typing Lab..... Revealed

By Dr. Katherine Tinckam
Co-director, Histocompatibility Laboratory
Assistant Professor of Medicine, University of Toronto

What is the Tissue Typing Lab anyways?

Also called the HLA Lab or the Histocompatibility Lab, it is where pre-transplant immune system testing examines how good a "match" a donor is for a recipient and also where we look for antibodies (immune system proteins) in the recipient blood that may be harmful to a donor kidney after transplant.

All patients who are receiving a transplant and all potential donors (living or deceased) undergo testing at the HLA laboratory.

Why do we need to test the immune system?

Your immune system consists of cells in the bloodstream (white blood cells) and proteins (antibodies which are produced by certain types of white blood cells) that are always looking for foreign substances in your body. Most of the time, the foreign substances are related to infections and the immune system helps to rid your body of the infection. However, a transplanted kidney is also seen by the immune system as "foreign" and so the immune system will try to attack it also; immunosuppressive medications are used to prevent this.

We do testing to determine:

a) HOW foreign the kidney is to the recipient (what is the match between donor and recipient)
b) If antibodies that may be harmful to a transplanted kidney are present.

These tests are only some of the tools that your doctors use to guide your immunosuppressive medications, and to give you more information about risk of rejection.

How is "matching" determined?

Every cell in your body has a set of HLA molecules (proteins) on its surface. One job of HLA molecules is to allow your immune system to identify your own tissues as "myself". There are hundreds of different HLA molecules such that most people in the population have at least some different HLA molecules from each other. So most of the time when a kidney is transplanted, at least some, if not all the HLA in the kidney are different from the recipient's HLA. Thus the immune system targets the kidney as "foreign" and could initiate an attack.

We are able to test your DNA to determine which HLA molecules you have, and then we can compare this to the HLA molecules of a kidney donor. Typically we test 6 HLA molecules in each of the donor and the recipient; 2 each of A, B and DR molecules.

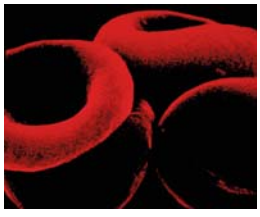
The other kind of "matching" is related to blood group, which will not be discussed here.

What happens if my donor is not a perfect HLA match?

In 2008, because of the good immunosuppressive medications available, HLA matching is not as important to ensure a good transplant outcome. In fact, most kidney transplants have at least some HLA that are mismatched. Even if you are completely mismatched you can still have an excellent transplant outcome. But determining the HLA types is still valuable information for your doctor to help determine your immune risk.

What are antibodies and why do we worry about them?

When the immune system is fighting off a "foreign invader" (like an infection) specific proteins that bind specifically to the foreign molecules may be formed by specialized white blood cells. These proteins, called ANTIBODIES, are a normal healthy part of the immune system and when bound to the foreign molecules, allow them to be more easily removed by the immune system. All of us have antibodies in our blood at all times. These help prevent repeat infections from things like chicken pox, mumps etc. and are very important and necessary.



If the immune system has previously been exposed to HLA molecules that are "not self" antibodies can form to these also. While these antibodies are not

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dangerous by themselves, if a kidney were transplanted into a recipient with antibodies that bind to the foreign HLA on that particular kidney, immediate and severe kidney damage could occur.

How would I get antibodies to HLA molecules?

You might form antibodies to HLA molecules if you have been exposed to foreign HLA molecules in the past. The most common way for your immune system to have this exposure is with pregnancy (during which the fetus's HLA molecules are in contact with the mother's immune system in the bloodstream), blood transfusions and with previous transplants. We also believe that certain healthy antibodies to infectious agents (such as bacteria and viruses), may cross react with HLA molecules.

NOT EVERYONE with HLA molecule exposure will form antibodies, but about a quarter of all transplant patients have at least some HLA antibodies. The HLA antibody test result is called the PRA and is expressed as a percent. For example if your PRA is 40%, it means you have antibodies to HLA molecules in APPROXIMATELY 40% of potential donors.

What happens if I have HLA Antibodies?

Having antibodies MAY limit the number of potential kidney donors that are suitable for you. It may also mean that you need different immunosuppression before and at the time of transplant. Your doctor will review what these test results mean to you specifically.

Why is my blood sent to the HLA lab every three months while I am waiting for a kidney?

1. Antibodies may appear and disappear over time. We test frequently so that we can identify all antibodies, as it helps your doctors assess your risk at the time of, and after transplant.
2. A portion of this blood sample is frozen on trays in the HLA lab in case a kidney becomes available – at which point a crossmatch can be done with this "current" sample. (see below)

REMEMBER: If your blood sample is not received in the HLA lab in time, you may miss out on an opportunity for a transplant. Your dialysis unit sends this blood, but it is important for you to be a partner in your own care, and be aware that this important sample has been sent!!

What is a crossmatch?

In a crossmatch we test a sample of recent recipient blood against cells from a potential kidney donor. This test tells us if you have antibodies in your current blood against the HLA molecules of that particular donor. Even if you have some HLA antibodies in your blood, there may be donors available to whom your antibodies will not bind and therefore will be low risk for you. The crossmatch is the definitive test between the donor and the recipient for "compatibility".

For patients with HLA Antibodies (PRA) who are called in for deceased donor transplant we must be even more careful to ensure that new HLA antibodies have not formed since the time of the last blood sample (even within 3 months!!!) so a crossmatch will be repeated on blood drawn when you arrive at the hospital and the transplant only proceeds if this test is negative also.

What role do I have in immune testing?

- Be aware of your blood sample being sent to the HLA lab every three months. Talk to your dialysis nurses so you know when it is being sent. If you will be away from town when this is normally sent, they can make arrangements to have it sent earlier or later!
- If you receive a blood transfusion, let your transplant centre/coordinator know – they may want to test your blood for antibodies sooner than the regular three month schedule.
- Ask your doctor if you have HLA antibodies, and if so, discuss your options with him or her.

Depression in Kidney Transplant Recipients

By Dr. Kien Dang
Staff Psychiatrist, St. Michael's Hospital

Receiving a kidney transplant is most often a joyful and positive experience. However, the kidney transplantation journey is full of stresses. The waiting time for a kidney is 5 to 8 years, or more, and the stress of dialysis during this time can take its toll. Although most kidney transplants go smoothly, after transplantation, there is always the possibility of unexpected complications with the surgery, the new kidney not working as planned, or the new kidney being rejected by the body. Having to adjust to a life with new medications, and a life without dialysis in itself can be stressful. The stress of the transplant process can lead to clinical depression, a potentially serious, but treatable illness.

What is depression?

Major depression is a medical illness that affects approximately 1 in 9 people over the course of their lifetime. Symptoms of depression include feeling sad or depressed, and/or a loss of interest in activities or motivation. Depressed people may also notice more difficulties concentrating, being unable to sleep or sleeping too much, loss of appetite, excessive feelings of guilt or hopelessness, fatigue, a general feeling of slowness, and increased thoughts of dying. In more severe depression, most concerning symptoms would be thoughts of suicide, or having hallucinations or paranoid thoughts.

How can depression affect the transplantation process?

While waiting for a kidney transplant, people who develop depression may lose motivation to care for their health, and comply with their treatment regimen which could include medications and/or dialysis. This can affect the status of being listed for transplantation until the depression is well controlled.

In post-transplant patients, depression can affect the ability to be compliant with anti-rejection medications which can result in shortening the lifespan of a new kidney. Depression also affects the quality of life during a time when patients should be enjoying a life free from dialysis.

How can depression be treated?

The most important step in treating depression is being able to identify it. This can only come about if both patients and health care workers feel comfortable doing so. The symptom that patients often have the most difficulty talking about is suicidal thinking. Patients should feel comfortable discussing these thoughts with physicians and other health care providers. Antidepressants are safe and effective in the treatment of depression, and are used commonly in patients on dialysis, as well as in combination with post-transplant anti-rejection medications. Although requiring more of a time commitment, and less readily available, appropriate psychotherapy is also helpful in treating depression.

Some Final Words

Depression is a potentially serious medical illness that can occur over the course of the stress of the transplantation process. A stigma still exists against psychiatric illness, and some people still feel that depression is a sign of weakness. In many ways, it takes more strength to be able to ask for help from loved ones and health care providers. Effective treatment is available, but only if depression is identified in the first place.

Recurrent Kidney Disease After Transplantation

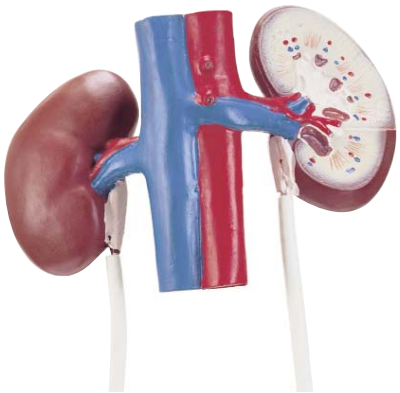
By Dr. Ramesh Prasad

Transplantation is the best way to treat end-stage kidney failure since it provides the maximum amount of replacement of kidney function, more than what dialysis can provide. One hopes that this would be a cure for kidney failure, but unfortunately kidney transplants are not meant to last forever. In the two previous issues of Transplant Digest we discussed two major problems that can happen with the transplant: acute rejection and chronic rejection. Today we will discuss a less common but important problem of the original kidney disease recurring (coming back) in the transplant.

Certain types of kidney diseases are more likely to recur in transplants than others. Glomerulonephritis (GN) is an example of a group of kidney disease that recurs. A disease called focal segmental glomerulosclerosis (FSGS) is one of the more common types of GN that recurs, sometimes on the operating room table itself. Patients who get a recurrence are typically younger and have more aggressive disease to begin with. Fortunately, treatment for recurrence is available, that can involve for example plasmapheresis (a procedure similar to hemodialysis). Other examples of diseases that recur include IgA nephropathy, membranous nephropathy (MGN) and membranoproliferative GN (MPGN). If a previous transplant was lost due to disease recurrence then the chances for recurrence in a subsequent transplant are higher. If the cause of your kidney failure was some form of GN, discuss with your doctor both before and after your transplant about the risks and possible therapies for recurrence. It is important to point out that many times the original, specific cause of kidney failure is unknown, often due to late diagnosis. In this case the risk for recurrence cannot be predicted. Some types of GN (for example, MGN) can also occur for the first time in the transplant. The cause for disease recurrence remains a mystery, but hopefully medical research will point towards the answer in the foreseeable future.

Diseases such as diabetes and hypertension can also eventually damage the kidney transplant if it survives long enough. Remember, these diseases take a long time to cause kidney failure in the first place. Provided the donor kidney was perfectly healthy it is very unlikely that kidney transplants will be lost due to these conditions alone. However, poor diabetes and blood pressure control will make any existing kidney condition worse. The good news is that there are some diseases that do not recur in the transplant, such as polycystic kidney disease and Alport's syndrome, because these are structural diseases of the kidney itself and not "transmitted" through the bloodstream.

Sometimes the diagnosis can be made by history alone but often a biopsy is required to establish disease recurrence. This can be important since the treatment for recurrence can be quite different from say, treatment for chronic rejection. Difficult BP control, protein in the urine and leg swelling (edema), and a rising creatinine may point towards this problem. If you are having any of these symptoms or signs, please discuss them with your doctor.



Post-Transplant Chat: Infections After Kidney Transplantation

By Jennie Huckle, RN, Thelma Carino, RN and Fernanda Shamy, RN

1 What are the common types of infection seen after kidney transplantation?

Patients with kidney transplants can get wound infections, pneumonia (lung infection), and urinary tract infections. Less commonly they can get infections in other parts of the body as well. Infections can be caused by viruses, bacteria, fungi, and parasites. Occasionally these infections can spread to other parts of the body through the bloodstream. Some patients also get more than one type of infection at the same time.

2 Why do transplant patients get infections?

The immune system, which consists mainly of white blood cells and lymphoid tissue, is extremely important in protecting your body from foreign germs. The immune system also protects you from foreign tissues such as a kidney transplant. Immunosuppressive drugs are needed to prevent rejection of the new kidney, so unfortunately the ability to fight infections is weakened as well. Besides, patients can also have reasons for infections (e.g. an abnormal urinary tract) that made them more susceptible to infections even before the transplant.

3 When do infections most commonly occur?

Although variable, the type of infection often depends on the time since transplant. Wound infection, pneumonia and urine infections occur early after the transplant. The period between one and six months after transplant is the high risk period for developing “opportunistic” infections like cytomegalovirus (CMV), tuberculosis (TB), fungal infections, and Pneumocystis carinii pneumonia (PCP). After six months, the pattern of infections gradually reverts to that seen in the general population, although transplant patients are always at higher risk for any infection.

4 Are there any special risk factors for getting infections?

Patients who get more immunosuppression than normal, for example because of rejection, seem to be more susceptible to getting infections, as well as older patients, those with urine tract structural anomalies, CMV mismatch patients (donor had CMV before but recipient never had it), and those who do not take their antibiotics (e.g. septra) properly. However, anybody can get an infection at any time.

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5 What can be done to prevent infections?

Many times, there is little that can or could have been done to prevent a particular infection. We do recommend preventative treatment for TB in those who have are known to have a positive TB skin test (PPD). Patients may get septra (or an alternative if there is a sulfa allergy) for a fixed period after the transplant (usually 1 year) to prevent PCP. For CMV mismatch the doctor will often prescribe an anti-CMV drug for a few months.

6 What should I do if I get an infection?

If you have a fever, feel very weak and tired or "dehydrated", or have localizing symptoms such as discharge from a wound, severe diarrhea, cough and/or sputum, flank pain, burning urine, or cloudy urine, then you probably have an infection. You should report to your doctor or an emergency room right away. Be sure to tell your health care provider that you have a kidney transplant and are receiving immunosuppressive drugs. Also do not forget to tell them of any allergies you may have.

7 Nurse, I seem to be getting urine infections all the time. What can I do?

Some women are especially prone to getting urine infections. If you have to self-catheterize, be very careful when doing so. Drink enough fluids. Some women find that drinking cranberry juice is helpful. Do not hold your bladder for too long, and void whenever the opportunity is available. When cleaning yourself, always wipe from front to back, never from back to front. Adequate lubrication during sex may be helpful. Go to the bathroom immediately after having sex. Although some sources recommend taking a preventative antibiotic after having sex, this is controversial. Use of spermicides and intrauterine contraceptive devices (IUD) may be a risk factor for infection. If your infections are frequent and problematic, ask for a referral to an Infectious Diseases specialist.

8 Can I keep a supply of antibiotics at home?

Infections in transplant patients can be complicated to treat, often requiring a longer duration of therapy, and sometimes requiring IV antibiotics, multiple antibiotics, or antiviral/antifungal agents. Delayed treatment, especially with using the wrong drug in the meantime, could lead to spread of the infection and threaten your life. Drug resistance can develop and become a serious problem when treating future infections. It is always important to know exactly what is causing the infection so that the appropriate antibiotic(s) may be prescribed. For these reasons, we strongly discourage transplant patients from treating infections on their own.

Congratulations!!!

The faces behind the success of the symposium....

L-R (Front): Jackie Chen, Francine Garraway, Sulagna Sarker, Fernanda Shamy, Jackie Pangilinan, Jenny Huckle, Galo Meliton, Meriam Jayoma-Austria, Weiqiu Yuan, Maria Salanga, Mona Udit, Susie Par, Lisa Liberatore, Thelma Carino, Tess Montada-Atin, Sharon Lee, Trixie Williams (Clinical Leader Manager)

L-R (Back): Maureen Connelly, Jane Mason, Karen Burleigh, Dr. Ramesh Prasad, Michelle Nash, Dr. Jeff Zaltzman

ANNOUNCEMENT!

For a limited time 24 hour ambulatory monitoring may be available to SMH kidney transplant recipients without charge. For more information please contact the Transplant Office.

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