

Original Articles

REPORT OF 200 RENAL TRANSPLANTATIONS FROM LIVING DONORS

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ABSTRACT

Two hundred cases of renal transplantation from living donors are reported from Shahid Hashemi Nejad Medical Center in Iran. There were 127 male and 73 female patients with 67% in the third and fourth decade of life. All patients received grafts from living donors with 114 cases of HLA haploidentical, 55 cases of HLA identical matches and 24 unrelated donors. One year patient and graft survival were 94.3% and 88.6% respectively. Despite the wartime conditions and lack of many modern facilities, the results are quite satisfactory and comparable to many other centers in the world. It seems more logical to replace costly chronic hemodialysis by renal transplantation programs in the Middle East and North African countries through planned and cooperative programs.

MJIRI, Vol.2, No.3, 165-170, 1988

Despite sporadic efforts in the field of renal transplantation, it was following the first successful graft between monozygotic twins that established the beginning of a new era in the field of organ transplantation which has continued to grow and flourish since then.¹² It is of interest that the results of this same operation remains the ultimate unreached goal in this field until today, since the recipient, without worries and hazards of rejection, achieved immediate renal function along with control of arterial hypertension and congestive heart failure. This remarkable step also served as a powerful stimulus for a sustained and indepth research in the field of immunology.¹⁶

According to Groth³ human renal transplantation began in Paris and Boston. The development of the artificial kidney adopted from Kolff by Merrill, Walter, and Thorn was a necessary prerequisite for attempts at transplantation in patients with terminal renal disease.¹¹ Some human unmodified renal allografts,

vascularized in the thigh with a cutaneous ureteros-tomy, survived longer⁴ than did laboratory models,¹⁹ an observation later confirmed using skin allografts in a clinical study.²

Investigation in dogs with renal autotransplants vascularized in the pelvis with a vesico-ureterostomy demonstrated that a solitary kidney could, contrary to then current observations, sustain normal function indefinitely.¹³ This laboratory preparation served as the model for monozygotic¹⁴ twin transplants.¹⁵ During the last 3 decades, development in surgical technique and increased expertise in immune modulation have had a major impact on both safety and efficacy of this procedure, such that kidney transplantation has now emerged as the treatment of choice for end stage renal failure.⁵⁻¹⁰

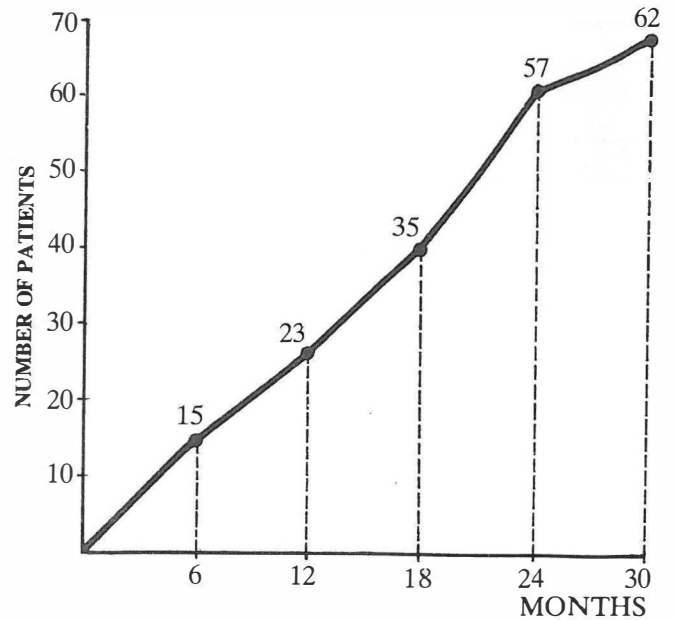
The present manuscript is a report of Shahid Hashemi Nejad Renal Transplantation Center from April 7, 1986 to October 22, 1988. The center was established in

April 7, 1986 primarily as a 24 bed unit in a hospital for treatment of renal diseases and an expansion ward was added two years later. The initiation of the program was during difficult wartime conditions and despite the back-breaking pressures of all kinds, it has continued to grow. Vast extent of shortages, even as simple as suture materials, drains, catheters or various medications were constantly present.

Program would suffer from numerous air and heavy missile attacks, with profound social effects, creating endless other priorities. Many pauses were imposed on the program due to the need for the surgical team to serve in front line hospitals during major attacks. Many hospitals were heavily damaged during air attacks, and daily programs had to be modified to fit the situation. Two of the transplants reported in this series were done on a day in which Tehran was under attack by five successive long range heavy missiles. One of these, landing close to S.H.N.M.C. shook the entire operating room during the procedure.

But despite the untoward above mentioned conditions, the program continued to grow.

A multispeciality transplant team, including nephrologists, transplant surgeons, immunologist, pathologist, nuclear medicine specialist, and radiologist was organized. In its regular meetings (twice a week) the team responsibility has been (1) final approval of new cases, and (2) discussion and review of the problem



Growth of renal transplantation program at H.N. April 1986-Oct 1988 6 Month Intervals

Figure 1

cases. The team also undertakes out-patient follow up of all transplanted patients on regular post-operative visits indefinitely.¹⁴ This team approach has proved to be extremely effective and helpful.

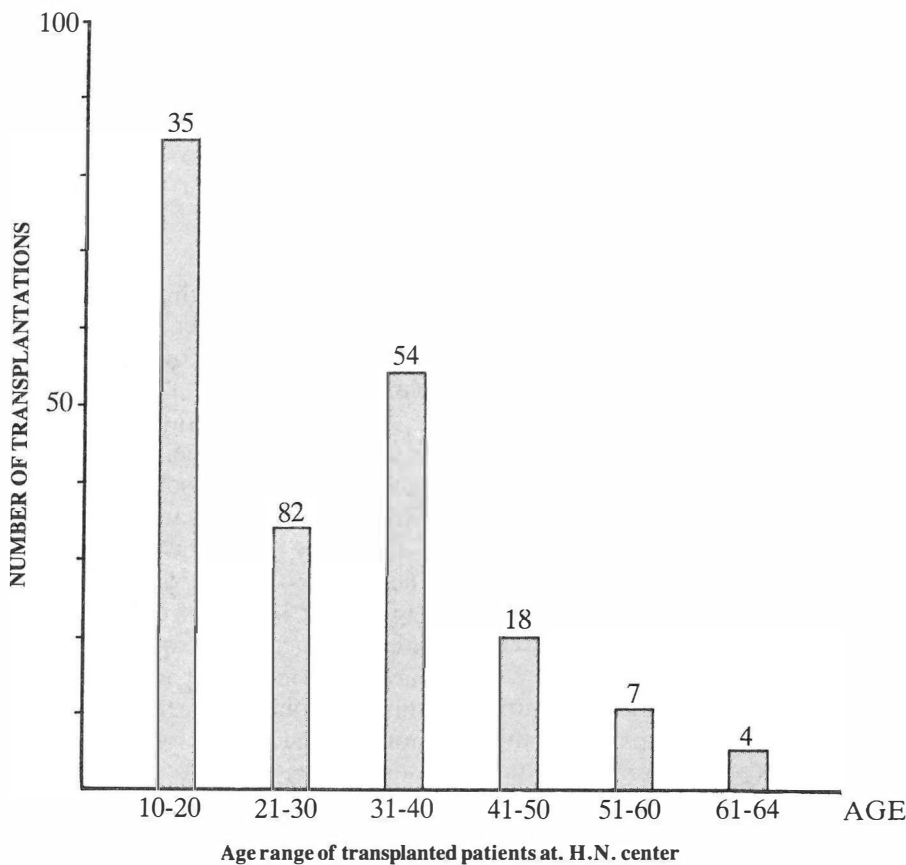


Figure 2

Besides having an active role in transplantation, the center is also responsible for training of new teams, both nephrologists and transplant surgeons for new centers in order to develop a complete network of renal transplantation centers in the country.

In the first six months, only 15 renal transplants were carried out. From then on, despite a multitude of difficulties, mostly secondary to wartime conditions of the country, the program continued to grow steadily and presently four transplants are being performed weekly. In the last six months 62 renal transplantations have been performed. (Figure1).

Pre-transplant dialysis period ranged from 3 months to 15 years. There were 127 male and 73 female patients. Ages ranged between 11 and 64 years with 40% of the patients in the third and another 27% in their fourth decade of life. A total of 35 cases were under 20 years of age (Figure2).

All patients received grafts from living donors. Donor and recipients were all from ABO compatible groups. HLA histocompatibility tests were carried out routinely in related donors with 114 haploidentical and 55 identical matches. There were 24 unrelated donors in whom DR matching was carried out for retrospective studies.⁸

The donor recipient relationship is shown in Figure3.

Cytotoxic antibodies in the recipient serum are measured using a panel of T- and B- lymphocytes to determine the degree of sensitization,¹ and the prospective donors.

Due to the beneficial effect of non-donor-specific blood transfusion on graft survival in patients receiving conventional immunosuppression¹⁷⁻²¹ and mounting evidence to indicate a similar effect in patients receiving cyclosporine (Cs)A,⁶⁻¹⁷ a requirement for between 3 and 5 units of blood transfusion prior to entry onto the transplant list had been adopted. As it was mentioned, all kidneys transplanted in this report were from living donors. Social and emotional preparation for kidney donation seems to be much higher in our countries in comparison to western world and people are more willing in kidney donation for their relatives who are in need of it.

In the meantime, cadaver donor brings forth a variety of difficulties which must be resolved in time by social preparation and training of new teams for more transplant centers.

On the other hand, survival studies indicated negligible donor morbidity and mortality. Unilateral nephrectomy in the healthy adult carries a mortality risk of less than 0.1 per cent,⁹ with a 5-year life expectancy comparable to that in the normal population. Follow-up studies over 10 to 15 years in large numbers of kidney donors shows no evidence of functional deterioration in the remaining kidney.

Selection of the living donors is based on clinical, immunological, and emotional criteria.

The donor age ranged between 18 and 65, with majority of donors being in the third and fourth decade of life.

A preliminary assessment of donor suitability was

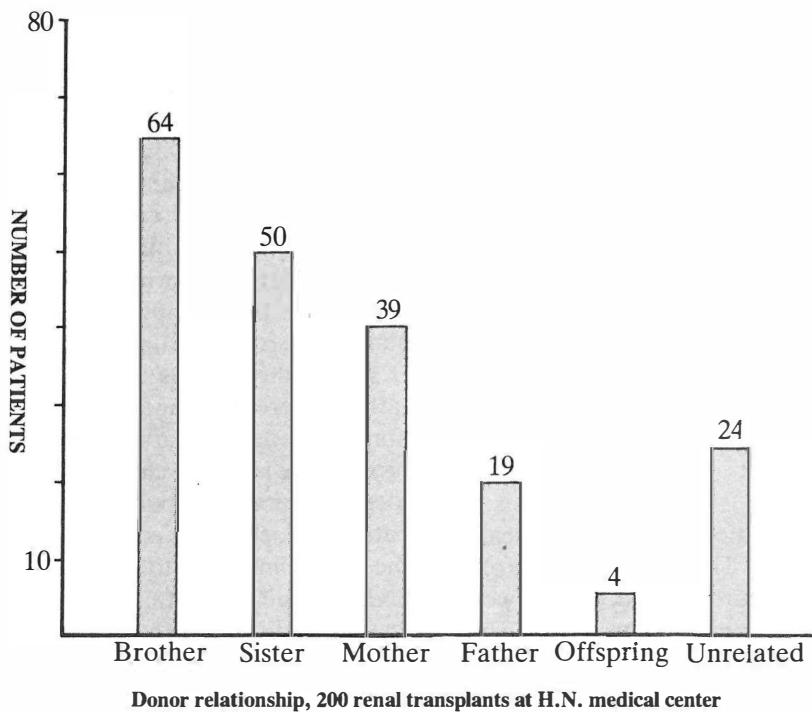
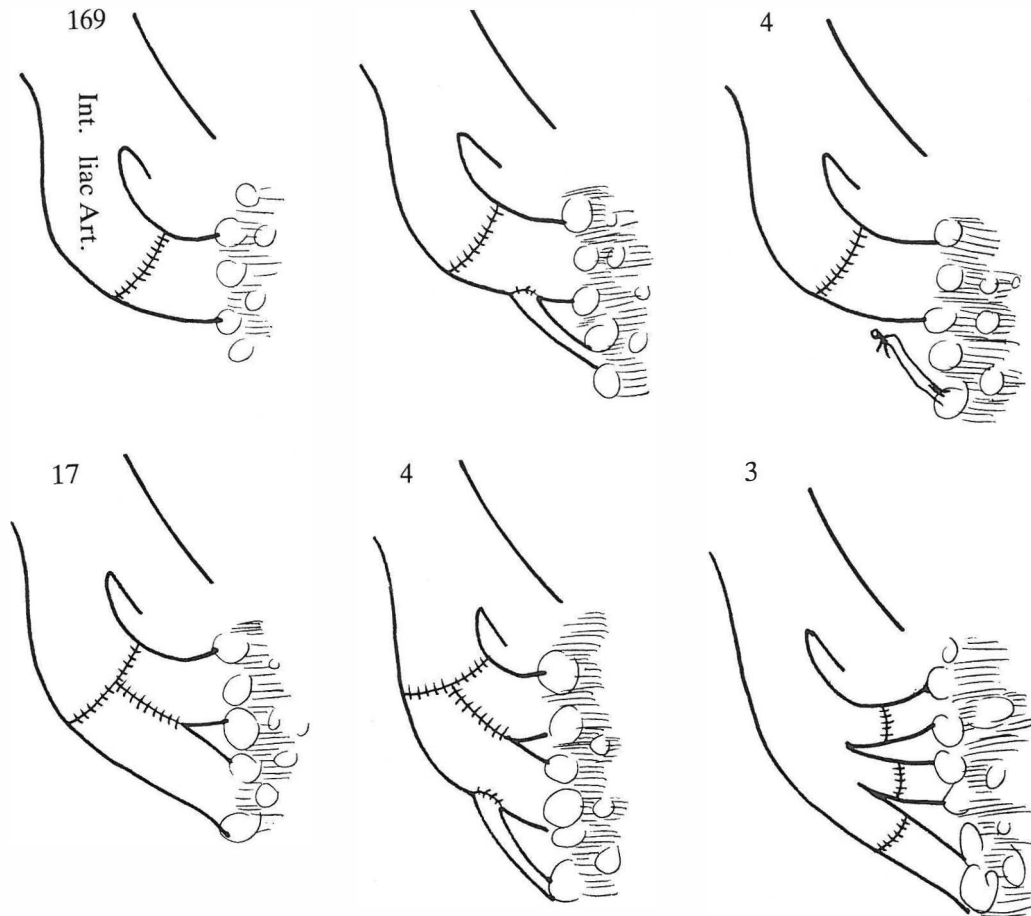


Figure 3



Renal artery anatomical variations in 200 live donors technique of anastomosis

Figure 4

performed on an out patient basis, in which a physical, immunological, and psychological analysis was carried out. A more intensive evaluation was performed on an inpatient basis in suitable cases to establish general health, to eliminate unsuspected hypertension or sub-clinical diabetes, and confirm normal renal function. An intravenous pyelogram and renal angiography were performed to demonstrate renal collecting system and vasculature.

The renal artery anatomical variations and techniques used for vascular anastomosis is shown in Figure 4.

Major surgical complications

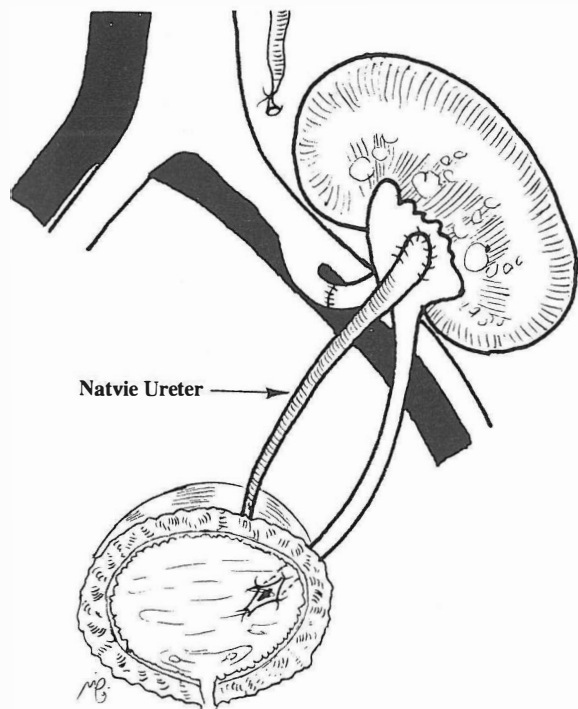
The major surgical complications requiring surgical intervention are discussed here. There were six cases of urinary leakage secondary to ureteral necrosis. Two patients had focal necrosis of urinary pelvis for which the patient's native ureter was used as a patch graft to cover the defect. Two cases were repaired by ureteral reimplantation and two by end to end anastomosis to

the patient's native ureter. All six patients are alive to date with functioning grafts (Figure 5).

One case of late distal ureteral stricture was also treated by using patient's native ureter.

Three patients suffered from bladder wound dehiscence. This was a trouble-some complication, requiring multiple corrective procedures. Two of the three patients with this complication had a long history of hemodialysis and shrunken urinary bladder.

One of the patients, a 19 year old female, developed rather severe signs and symptoms of Raynaud's phenomenon a few days after transplant procedure. Severe progressive ischemic changes developed in fingers and toes. All peripheral pulses were normal. Several sympathetic blocks were completely ineffective to relieve the symptoms. Due to development of early dry gangrene in one of the fingers, a $3\frac{1}{2}$ parathyroidectomy was carried out which resulted in complete and sustained relief of symptoms. She is now 28 months post-transplant with no further symptoms and excellent graft function.



Technique of repair of focal necrosis of renal pelvis.
The native ureter is used as a patch to cover the defect.
Figure 5

One case of transplant rupture occurred on 4th post-operative day. Interestingly, this was the only kidney with a complete double ureter in the entire series. Patient was immediately explored and a long longitudinal rupture, actively bleeding, was repaired by interrupted chromic sutures.

This was patient number 4 in the series and the kidney continues to have excellent function 29 months postoperatively.

A case of renal vein thrombosis due to technical error (twisting of the vein) was explored and thrombectomy carried out. Despite having about one liter of daily urine output, she had returned to chronic hemodialysis.

One of the patients with post-op ureteral necrosis treated by native ureter replacement, developed renal calculi 1½ years later. This was removed without further problems.

A case of arterial-calyceal fistula with massive hematuria developed following percutaneous renal biopsy in one of the patients, requiring emergency exploration. Within short period of time, large quantities of pure bright red blood was passed by the patient, requiring rapid replacement.

At the time of exploration, the upper pole (site of biopsy) was opened and an active jet of blood from a branch artery, injured by the biopsy needle, was noticed. This area was carefully repaired by fine chromic sutures and bleeding controlled. The kidney itself

Table 1

Shahid Hashemi-Nejad renal Transplantation center

Major complications	
Ureteral Necrosis	5
Bladder Wound Dehiscence	3
Wound Infection	7
Hematoma	3
Negative Exploration	5
Transplant Rupture	1
Severe Raynaud's Phenomenon	1
Lymphocele	1
Arterial Complications	0
Vascular	
Venous Thrombosis	1
Renal Calculi	1
Hematuria	1
Ureteral Stricture	1

was closed by interrupted chromic sutures. Although we were able to save this kidney, it continued to undergo a course of chronic rejection with the patient returning to dialysis program.

Seven cases of wound infection are reported, six of which occurred in patients requiring second or third exploration for treatment of other complications. The seventh one developed in a diabetic recipient. This young man recovered from this complication and lived with functioning graft only to die eight months later with a fulminating cavernous sinus thrombosis originating from a tooth abscess.

Table I shows list of complications.

Patient Survival

From 200 transplanted patients, 190 are alive, a total patient survival rate of 95%.

10 patients have been lost during a 30 month period. Causes of death are shown in Table II.

Except for 4 patients who never left the hospital after transplant procedure, others died from 5 to 18 months post-transplant. Six of these died while having good graft function, from extra-renal causes, mainly sepsis.

In this series, 88 patients have completed one year and 20 patients two year follow up period. One year patient survival is 94.3% and one year graft survival is 88.6%. The two year patient and graft survival figures

Table 2

Shahid Hashemi-Nejad renal transplantation center
patient mortality
Cause of death

SEPSIS	5(2.5%)
CEREBRAL HEMORRHAGE	1(0.5%)
PULMONARY EMBOLI	1(0.5%)
G.I. BLEEDING	1(0.5%)
GRADUAL DETERIORATION AND DEATH	2(1%)
TOTAL	10(5%)

Table 3
Patient and graft survival following renal transplantation from living donors

	Published Figures*	Hashemi Nejad
PATIENT SURVIVAL	95.6% (92-98)	94.3%
GRAFT SURVIVAL	90.0% (84-94)	88.6%

* Reported as mean (and range) of 1-year actuarial survival derived from published survival figures. (7)

are 90% and 85% respectively. The results and a comparison with published figures are shown in Table III.

DISCUSSION

Renal transplantation should be looked at and analysed in the Middle East and North African countries with close and serious attention to the social, political, and economical problems existing in this part of the world. Programs must be developed and carefully evaluated in order to come up with meaningful and realistic standards that would match the other unique problems involving the area.

It is certain that chronic hemodialysis, a very costly and import-dependent program, is not the best solution for the therapeutic needs of the growing number of patients with end stage renal disease.

Fluctuations in foreign policies, changes in foreign trade, outside political pressures and endless other problems all have a direct impact on the quality and even the quantity of treatment of these patients, endangering the life of many.

Due to the above mentioned factors, the presence of a growing and well controlled renal transplantation program is perhaps much more vital in the developing countries than in the developed ones. Besides offering the patient a considerably better quality of life, it would reduce foreign dependency as well as national foreign expenditure. Although it is heartwarming and reassuring to have units equipped with advanced and sophisticated medical technology, the real question for countries like our own is: "Is it absolutely necessary to be so?"

We are not competing with other large centers of the world for better results because we have numerous problems which are unheard of and nonexistent in those areas. Instead, we are performing renal transplantation in order to offer our patients a more secure and comfortable life. As far as we work hard and sincerely and continue to have remarkable improvement in the survival and quality of life of our patients, we have achieved our goals.

We must continue to grow in this field with close cooperation of our neighboring countries in order to

develop scientific guidelines for our future programs. In other words, it is time to have our own facts and figures and survival rates rather than accepting what comes from the west blindly. We should initiate a rather independent thinking and judgement based on realistic facts and figures drawn from our own experiences.

REFERENCES

- 1- Braun, W.E.: Histocompatibility testing in clinical renal transplantation. *Urol. Clin. North Am.*, 10:231-242, 1983.
- 2- Dammin, G.J., Couch, N., and Murray, J.E.: Prolonged survival of skin homografts in uremic patients. *Ann. N.Y. Acad. Sci.* 64: 967, 1957.
- 3- Groth, C.G.: Landmarks in clinical renal transplantation. *Surg. Gynecol. Obstet.*, 134-323, 1972.
- 4- Hume, D.M., Merrill, J.P., Miller, B.F., and Thorn, G.W.: Experiences with renal homotransplantation in the human; Report of nine cases. *J.Clin. Invest.*, 34: 327, 1955.
- 5- Keown, P.A., and Stiller, C.R.: Control of rejection of transplanted organs. Chicago, Year Book Medical Publisher, 17-46, 1986.
- 6- Keown, P.A.: The Canadian Transplant Study Group. Examination of parameters influencing the benefit: detriment ratio of cyclosporine in renal transplantation. *Am. J. Kidney Dis.* 5:328, 1985.
- 7- Keown, P.A., Stiller, C.R.: Kidney transplantation. *Surg. Clin. North Am.*, 66:(3) 517-535, 1986.
- 8- Kissmeyer-Nielsen, F.: Matching of HLA.: Kidney transplantation: Principles and practice. London, Academic Press, 107, 1979.
- 9- Leary, F.J., and De Weerd, J.H.: Living donor nephrectomy. *J.Urol.*, 109: 947-948, 1973.
- 10- Murray, J.E., Merrill, J.P., Dammin, C.J., et al.: Kidney transplantation in modified recipients. *Ann. Surg.*, 156:337, 1962.
- 11- Moore, F.D.: Transplant. New York, Simon and Schuster, 1972.
- 12- Murray, J.E., Merrill, J.P. and Harrison, J.H.: Renal homotransplantation in identical twins. *Surg. Forum*, 6: 432, 1955.
- 13- Murray, J.E., Lang, S., Miller, B.F. and Dammin, G.J.: Prolonged functional survival of renal autotransplantation in the dog. *Surg. Gyenc. Obstet.*, 103:15, 1956.
- 14- Murray, J.E., Merrill, J.P., and Harrison, J.H.: Kidney transplantation between seven pairs of identical twins. *Ann. Surg.*, 148:343, 1985.
- 15- Murray, J.E., Merrille, J.P., Dammin, J.F., et al: Study on transplantation immunity after total body irradiation: Clinical and experimental investigation. *Surgery.* 48: 272, 1960.
- 16- Murray, J.E., and Wilson, R.E.: The role of organ transplantation in biological research. *Ann.N.Y.Acad. Sci.* 129,1: 585, 1966.
- 17- Opelz, G.: Results of the international study on renal transplantation. presented at the second Dutch Congress on cyclosporine, Maastricht, Netherlands, 1985.
- 18- Opelz, G., Sengar, D.P.S., Mickey, M.R., et al: Effect of blood transfusion on subsequent kidney transplants. *Transplanr. Proc.* 5:253, 1973.
- 19- Simonsen, M., Bremann, J. Gammeltaft, A. et al: Biological incompatibility in kidney transplantation is dogs. *Acta. Pathol. Microbiol. Scan.* 32:1, 1953.
- 20- Steinmuller, D.R.: Evaluation and selection of candidates for renal transplantation. *Urol. Clin. North Am.*, 10:217-229, 1983.
- 21- Wener-Favre, C., Jeannet, M. Harder, F., et al: Blood transfusion, cytotoxic antibodies, and kidney graft survival. *Transplantation.* 28: 343, 1979.