

TRASPLANTE RENAL


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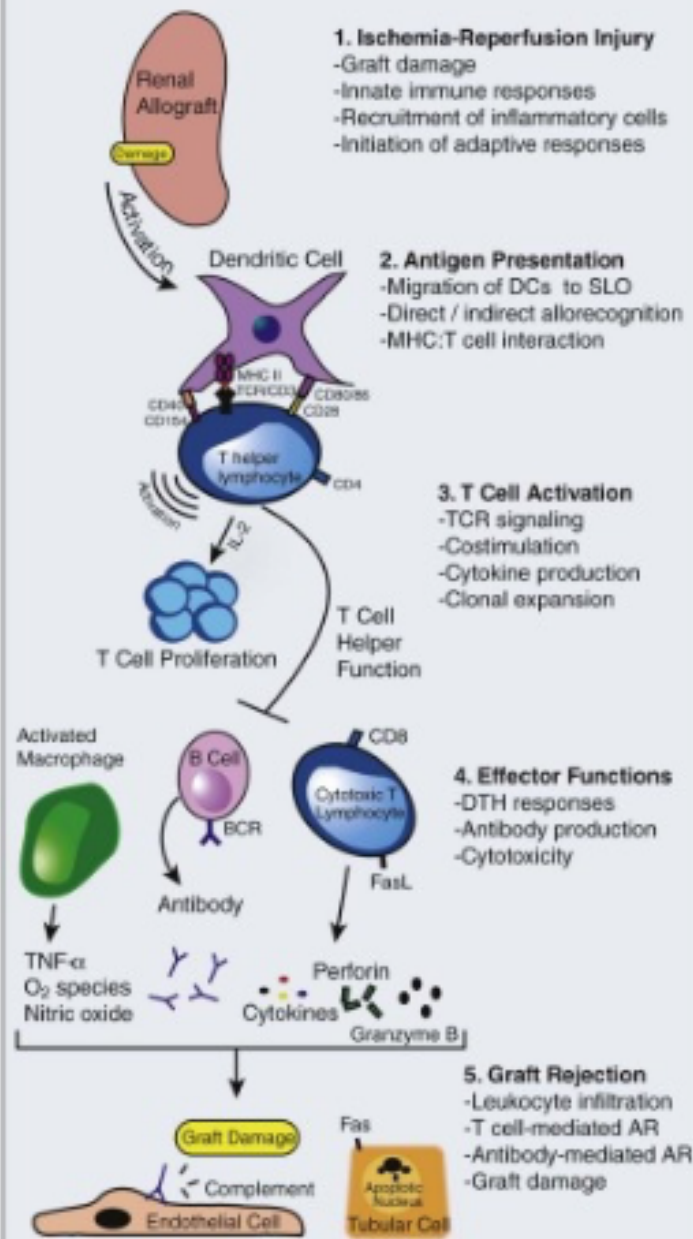
INMUNOLOGÍA DEL TX

- Relación entre los tejidos:
 - Singénica: gemelos idénticos
 - Allogeneica: misma especie
 - Xenogeneica: distinta especie

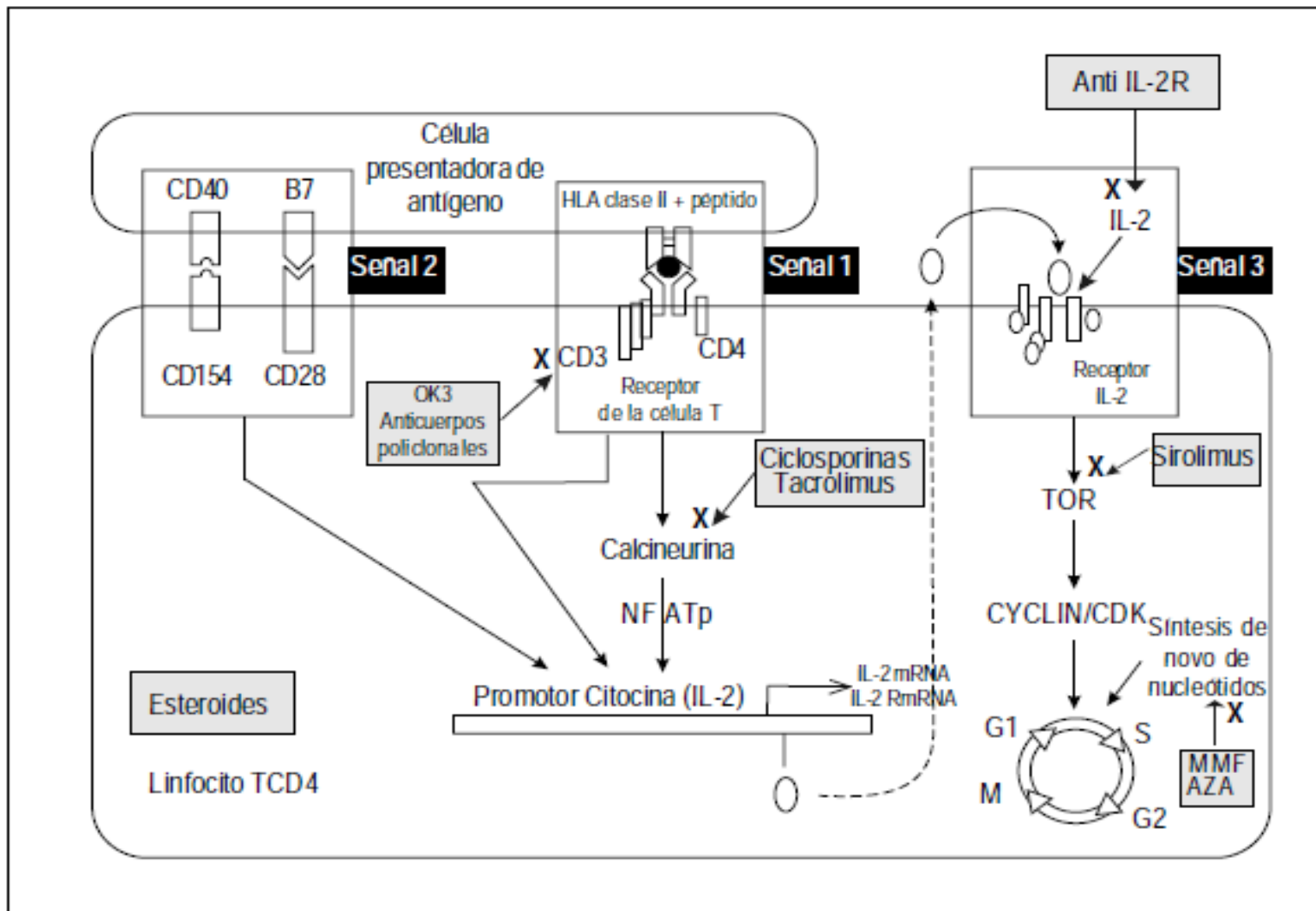
RESPUESTA INMUNE

- Se inicia por activación de CPA a través del sistema inmune innato
- Cél dendríticas del donante y R se activan y migran a órganos linfoides, con activación de linf T naive de memoria, que a su vez activan linf B y producen auto Ac contra HLA del donante
- **Activación T:** modelo de 3 señales
 - Ca-calcineurina
 - Proteinkinasa (MAP kinasa)
 - NF kb
- Linf T activado: expresa IL-2, CD 154, CD 25 (R IL-2).
 - Prolifera y se diferencia a linf T efector  **rechazo**

Generation of Alloimmune Responses



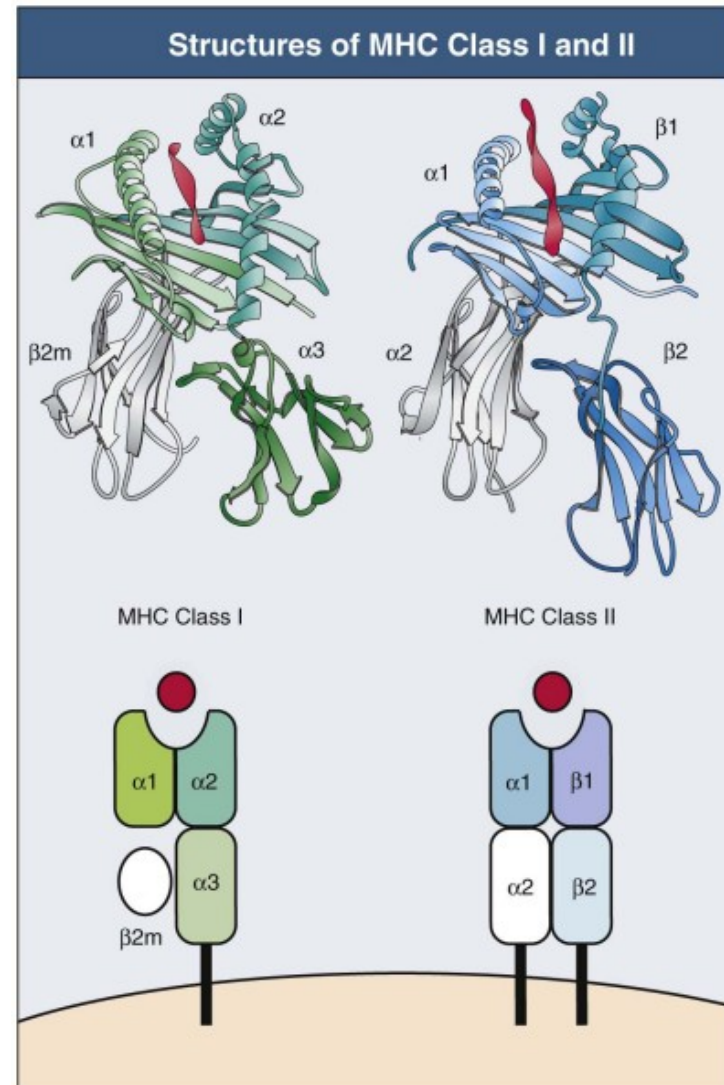
MODELO DE LAS 3 SEÑALES



RECHAZO

- Injuria tisular por rta adaptativa alloinmune
 - Deterioro de Fx del injerto
 - 2 tipos: mediado por células T y mediado por Ac
 - Infiltrado: células T, B, macrófagos, plasmocitos
 - Linfocitos T:
 - CD4 : interactúan con CMH II
 - CD8+: CMH I
 - El injerto induce rta alloinmune por Ag no propios reconocidos por linf T del R, a través de 2 vías de reconocimiento: indirecta (CPA del R) y directa (CPA del donante)

- CMH: HLA
 - 3 clases
 - I: A, B, C
 - II: DR, DQ, DP
 - III
 - Rechazo: A, B, DR
 - Herencia: 1 haplotipo



EVALUACIÓN PRE TX

Contraindications to Renal Transplantation

Current Absolute Contraindications to Transplantation

- Active Sepsis
- Current uncontrolled malignant disease
- Uncontrolled psychosis
- Active drug dependence
- Any medical condition with a severely shortened life expectancy (<1–2 years)
- Positive T-cell CDC cross match

Previous Contraindications to Transplantation

(now acceptable under certain circumstances – see text)

- HIV Infection
- Hepatitis B and C
- Obesity
- Mood disorders
- Age > 60 years
- Previous malignant disease
- Blood group incompatibility

Recipient Evaluation Checklist

History and Examination

Cause of renal failure and risk of recurrence
Sensitization (transfusion, pregnancy, previous transplant)
Past and current infections (TB, hepatitis, HIV)
Immunization (especially hepatitis B)
Malignancy
Cardiovascular risks (smoking, hypertension, diabetes)
Pulmonary, gastrointestinal disease
Genitourinary tract
Psychiatric, psychological history
Surgical issues (weight, iliac vessels, abdomen, previous surgery)

Laboratory and Radiologic Investigations

Viral serology (HIV, CMV, EBV, hepatitis B and C)
Liver function tests
Bone-related issues (PTH, calcium, phosphate)
Chest radiograph
Electrocardiogram
Prostate-specific antigen (for men >50-60 years old)
Mammogram or breast ultrasound
(women >50 years old or with family history of breast cancer)
Pap smear (sexually active women)

Immunologic Investigations

ABO blood group and HLA typing
Screening for HLA antibodies and autoreactive antibodies
Crossmatching

• DONANTES:

– Vivos: relacionados o no

– Fallecidos

- Corazón batiente
- Corazón parado
- Criterios expandidos

– Compatibilidad:

- ABO
- No importa el Rh
- ABO incompatibles? Previa desensibilización
- Mismatch HLA: a > compatibilidad, > sobrevida del injerto
- Crossmatch:
 - Citotoxicidad
 - Citometría de flujo: más sensible
 - Luminex: Ac anti donante

Live Donor Evaluation Checklist: History and Examination

History

Hypertension
 Diabetes (including gestational)
 Infections
 Cancer (including skin lesions)
 Vascular disease
 Renal calculi
 Gout
 Urinary tract
 Family history
 Medications (including NSAIDs, herbs)
 Smoking
 Elicit and intravenous drug use
 Sexual history
 Vocation, sport interests
 Level of physical activity/exercise
 Psychiatric history/psychological factors
 Willingness to donate
 Relationship with recipient

Examination

Blood pressure
 Weight and height, BMI
 Joints, skin
 Cancer (including skin lesions, breast)
 Lymph nodes
 Vascular disease
 Heart and lungs
 Abdomen

Live Donor Evaluation Checklist: Investigations

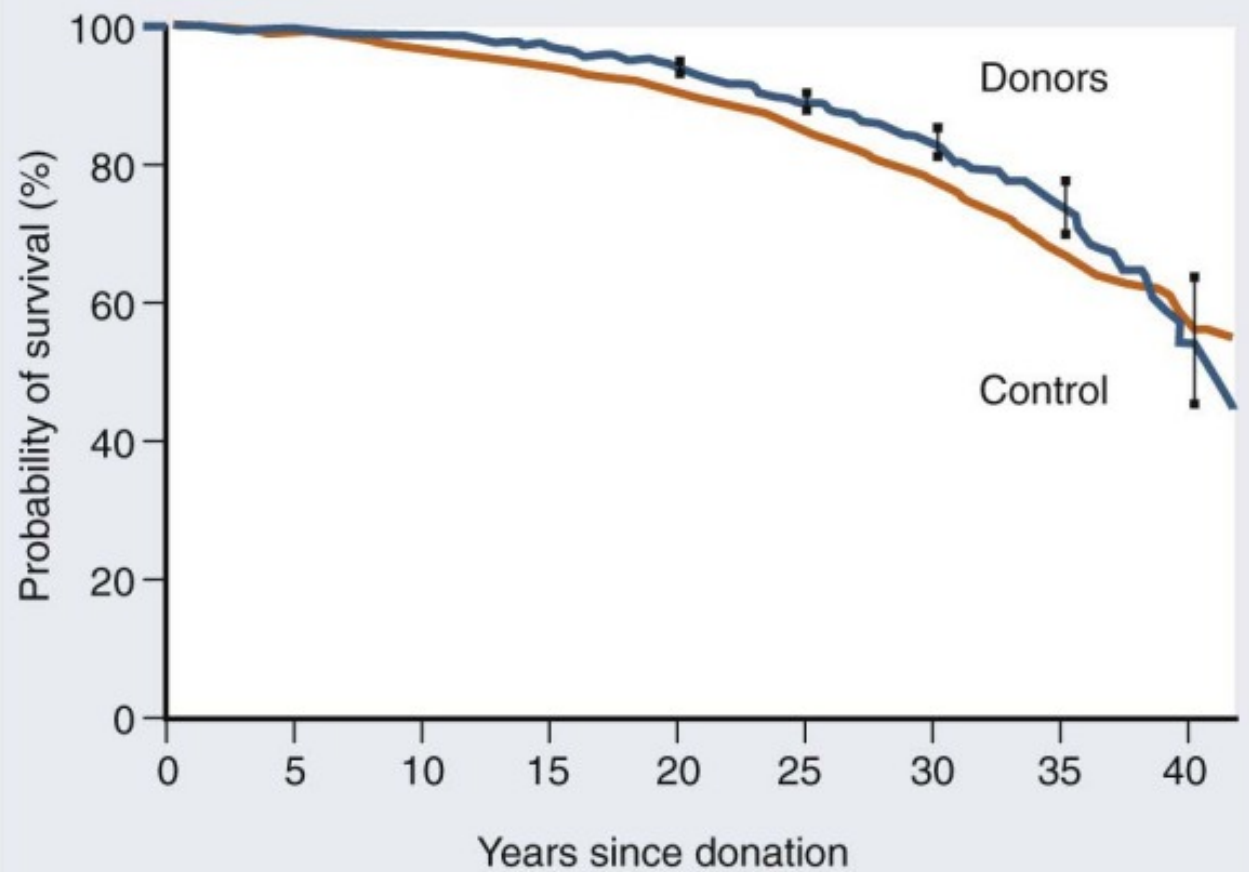
Laboratory and Radiologic Investigations

Urinalysis (blood, protein)
 Urine microscopy and culture (blood, organisms)
 Serum electrolytes, urea and creatinine
 Liver function tests
 Full blood examination
 Fasting blood glucose and/or oral glucose tolerance test
 Fasting lipids
 24-hour urine, creatinine clearance, protein excretion
 (or GFR measurement by other methods, [e.g., iothalamate
 clearance, nuclear GFR by Cr-EDTA, DTPA; protein
 excretion by other methods], [e.g., protein-creatinine ratio])
 Serum uric acid, calcium, phosphate
 Viral screening: HBV, HCV, HIV, CMV, EBV serology
 Syphilis screening (RPR)
 TB screening (PPD)
 Electrocardiogram
 Chest radiograph
 Females: Pap smear, mammography (according to age/family
 history)
 Males: prostate-specific antigen (according to age/family
 history)
 Additional cardiac investigations (where indicated by
 age/history/risk factors)
 Stress test
 Echocardiography
 Ambulatory blood pressure

Renal Anatomy (as per local expertise)

Computed tomographic angiography
 Magnetic resonance imaging angiography
 Catheter angiography

Survival of Kidney Donors and Controls from the General Population



No. of donors
3698
2716
2065
1575
1228
775
410
140
16

INMUNOSUPRESIÓN

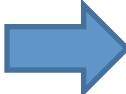




- 2 etapas:
 - Inducción
 - Mantenimiento
- **Corticoides:**
 - VO: prednisona, prednisolona
 - EV: metilprednisolona
 - Antiinflamatorios e IS
 - Mantenimiento y rechazo agudo
 - Seguros en embarazo

- **CIN:**

- Ciclosporina, tacrolimus
- Inhiben calcineurina (activación linf T)
- Nefrotóxicos reversible (VC) e irreversible (hialinosis arteriolar y fibrosis intersticial)
- Inducción y mantenimiento
- Control con niveles plasmáticos
- Útiles en embarazo

- **Azatioprina:**

- Antimetabolito análogo de purinas
- Mantenimiento

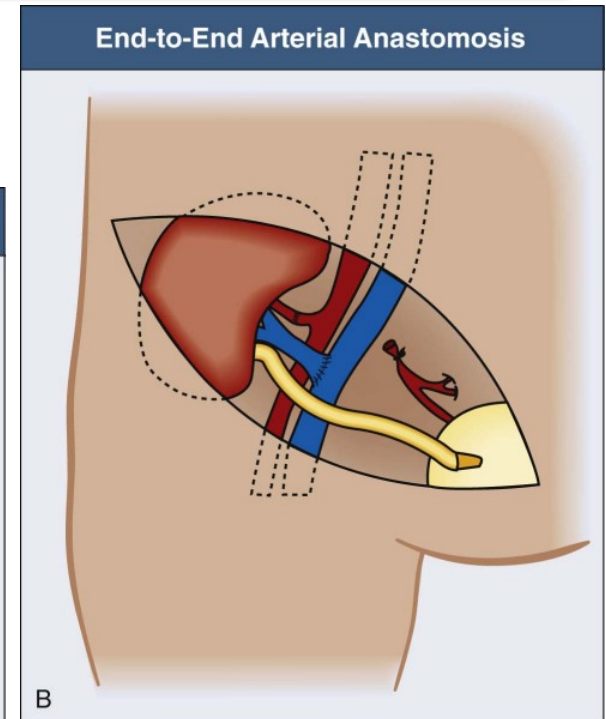
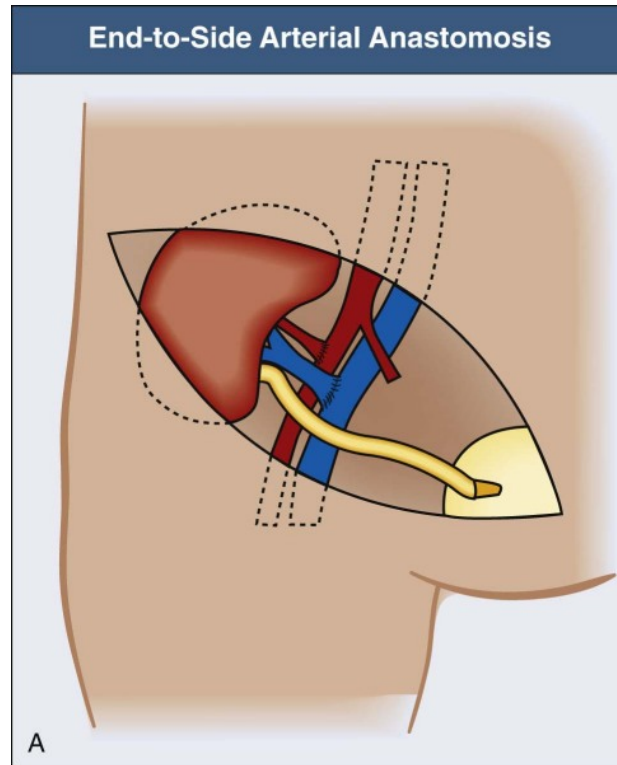
- **Micofenolato:**
 - Mofetil y sódico
 - Inducción y mantenimiento
 - No en embarazo
- **M-tor:**
 - Sirolimus y everolimus
 - Mantenimiento
- **Anticuerpos:**
 - Monoclonales:
 - Anti CD25: Basiliximab, Daclizumab  Inducción
 - Anti CD 20: Rituximab  Rechazo mediado por Ac y desensibilización
 - Belatacept  Mantenimiento
 - Policlonales: timoglobulina  Inducción y tto del rechazo corticoR
 - IVIG  Rechazo humoral, desensibilización

Common Side Effects of Small Molecule Immunosuppressive Medications

	Cyclosporine	Tacrolimus	Mycophenolate	Azathioprine	Corticosteroids	mTOR Inhibitors	Leflunomide
Renal	Nephrotoxicity, type IV RTA, HTN, diuretic resistance, hyperkalemia, hypomagnesemia, hypophosphatemia	Nephrotoxicity, type IV RTA, HTN, diuretic resistance, hyperkalemia, hypomagnesemia, hypophosphatemia			HTN, hypokalemia, diuretic resistance	Synergistic nephrotoxicity with CNIs, delayed recovery from ATN, proteinuria, hypokalemia, HTN	
Gastrointestinal		Diarrhea, abdominal pain	Diarrhea, nausea and vomiting, gastritis, esophagitis, oral and colonic ulcers	Nausea and vomiting, hepatotoxicity, pancreatitis	Peptic ulcers, gastritis, esophagitis, diarrhea, colonic perforation	Diarrhea	Nausea, diarrhea, hepatitis
Hematologic	Thrombotic microangiopathy	Thrombotic microangiopathy	Anemia, leukopenia, thrombocytopenia	Anemia, leukopenia, thrombocytopenia	Leukocytosis, polycythemia	Thrombotic microangiopathy, anemia, thrombocytopenia	Anemia, leukopenia
Metabolic	Hyperlipidemia, hyperuricemia, gout, glucose intolerance	New onset diabetes			Hyperlipidemia, hyperuricemia, hyperglycemia, osteoporosis, vascular necrosis, increased appetite and weight gain	Hyperlipidemia	
Cosmetic	Gingival hyperplasia, coarsened facial features	Alopecia			Hirsutism, acne, cushingoid facies, buffalo hump	Impaired wound healing, oral ulcers	Alopecia
Neuromuscular	Encephalopathy, insomnia, myopathy, tremors	Encephalopathy, insomnia, myopathy, tremors			Psychosis, insomnia, myopathy	Reflex sympathetic dystrophy	
Other	Edema	Myocardial hypertrophy	Viral infections, pulmonary edema in elderly, progressive multifocal leukoencephalopathy		Cataracts	Lymphocele, interstitial pneumonitis, rash, edema	Rash

CIRUGÍA

- Heterotópico en fosa ilíaca contralateral
- Anastomosis venosa con ilíaca externa
- Anastomosis arterial con ilíaca interna o externa
- Anastomosis uréter con vejiga
- Colocación de catéter doble J



Complicaciones Cx

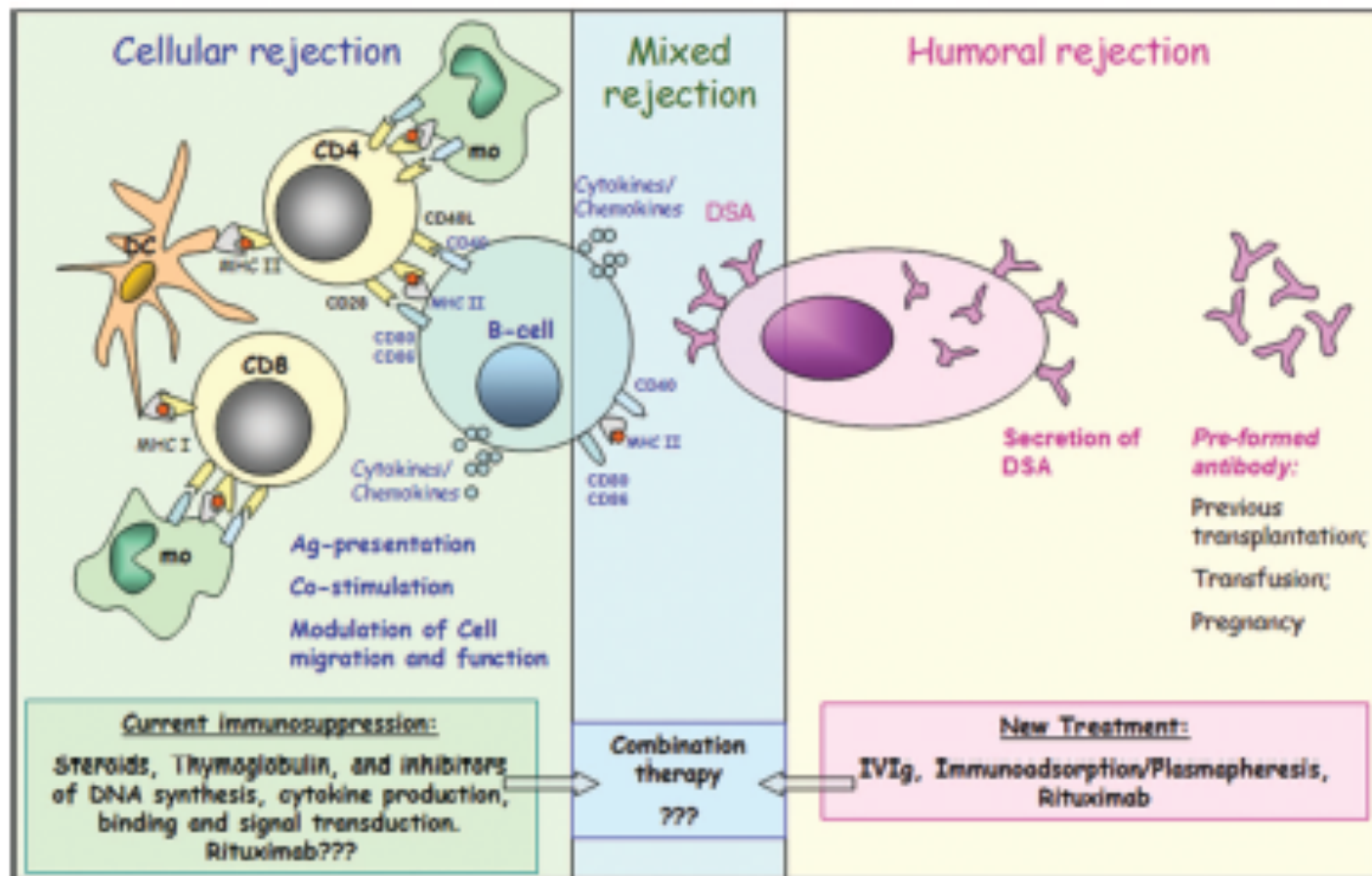
- Infección de la herida
- Sangrado de la herida
- Vasculares:
 - Sangrado del hilio
 - Hemorragia de la anastomosis
 - Trombosis arterial
 - Trombosis venosa
 - Estenosis arteria renal

- Linfocele
- Urológicas:
 - Leaks
 - Obstrucción
- Lesión nerviosa
 - Fémorocutáneo
 - Obturador
 - Sacro
- Lesión arteria testicular

RECHAZO

- TARGET: CMH del donante
- Factores de riesgo:
 - DGF (edad del donante y R, sensibilización, tiempo de isquemia)
 - Afroamericanos
 - < añosos
 - Sensibilización, esp ABO
 - IS: < policlonales, > sin corticoides, > si demora en CIN
- Clínica: AKI. Raro fiebre, dolor, oliguria
- Dx: Eco + Doppler (aumento IR). **BIOPSIA**

Tipos de rechazo



Classification of Rejection

Antibody Mediated

Acute

C4d⁺, presence of circulating antidonor antibodies and acute tissue injury

- I. ATN-like (minimal inflammation)
- II. Capillary and/or glomerular inflammation and/or thromboses
- III. Arterial inflammation

Chronic

C4d⁺, presence of circulating antidonor antibodies and chronic tissue injury

- (1) Glomerular double contours, (2) peritubular capillary basement membrane multilayering, (3) tubular atrophy/interstitial fibrosis, and/or (4) fibrous intimal thickening in arteries

T Cell Mediated

Acute

Mononuclear cell interstitial inflammation and tubulitis and/or arteritis

IA: >25% Interstitial infiltration, 4–10 mononuclear cells/tubular cross section

IB: >25% Interstitial infiltration, >10 mononuclear cells/tubular cross section

IIA: Intimal arteritis, mild to moderate (0%–25% of luminal area)

IIB: Intimal arteritis, severe (>25% of luminal area)

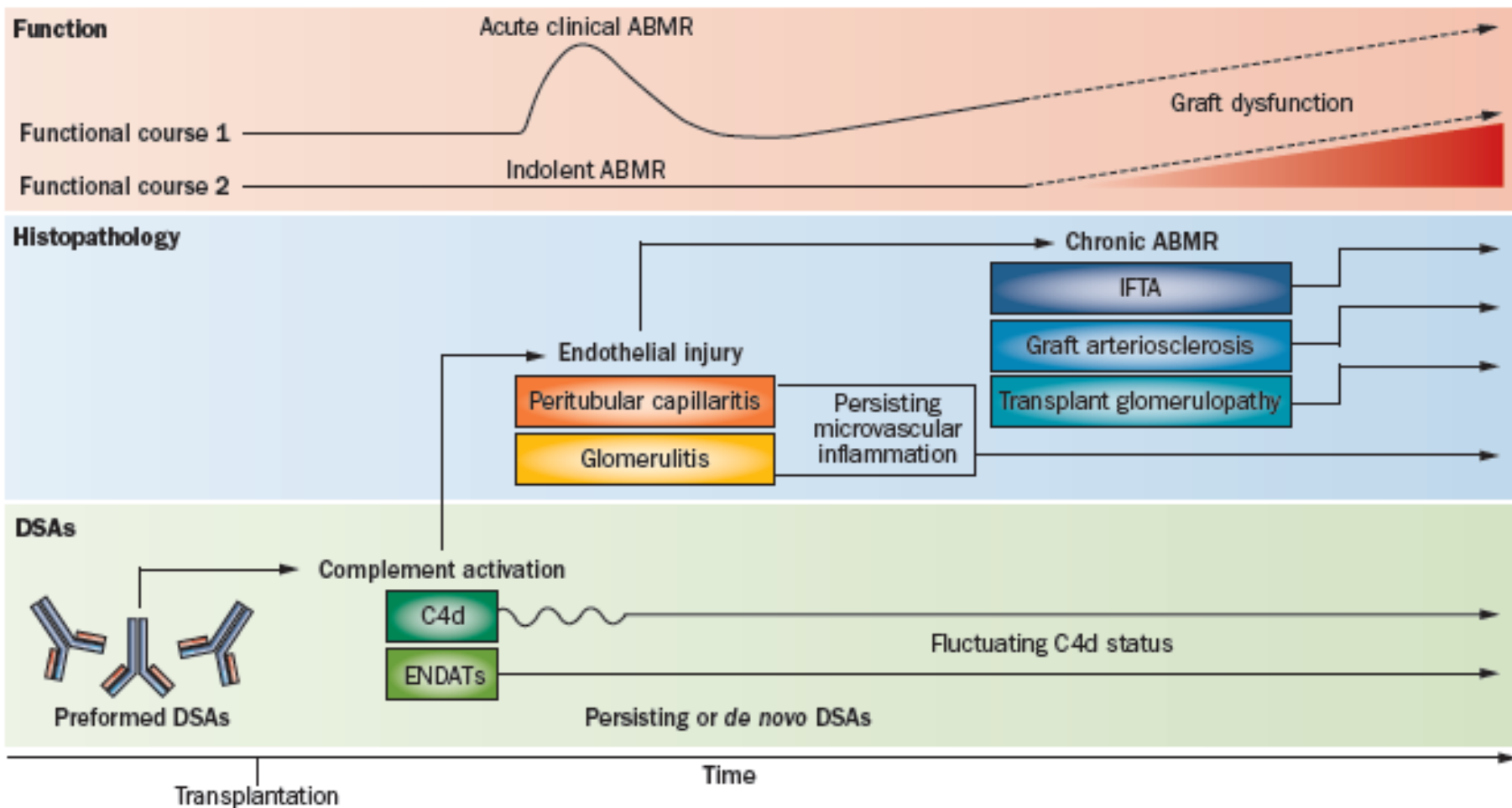
III: Transmural arteritis and/or fibrinoid change and necrosis of medial smooth muscle cells with accompanying lymphocyte inflammation

Chronic

Arterial intimal fibrosis with mononuclear cell infiltration in fibrosis, formation of neointima

Borderline

10%–25% Interstitial infiltration, <4 mononuclear cells/tubular cross section



- Tratamiento:

- Agudo celular: corticoides, timoglobulina
- Mediado por Ac: remover Ac (optimizar IS, PF, IVIG, timoglobulina, Rituximab)
- Profilaxis: CMV, PCP

- Dx dif: nefropatía por virus BK

Complicaciones médicas

- HTA:
 - CIN, corticoides
 - Imp causa de muerte con injerto funcionando la CV
 - No estudios con antiHTA
- DBT:
 - Asociación con HVC
 - Tacrolimus, corticoides
- DLP:
 - Ciclosporina, corticoides, FK, sirolimus
- Obesidad

Infecciones

- 1er mes:
 - Bacterias nosocomiales, Candida, HSV
- 1-6 meses:
 - Virus: **CMV**, HSV, HZV, EBV, HBV, HCV
 - Hongos y oportunistas (PC, Listeria, Aspergillus, Nocardia, Toxoplasmosis)
- > 6 meses: similar a población general, salvo pac con rechazo
- **Virus BK**: viruria, viremia, estenosis ureteral, NTI, nefropatía, rechazo. Imp screening

Malignidad

- Riesgo según IS
- Virus: papiloma y CA cuello uterino, EBV PTLD, HVB-HVC CA hepatocelular, HV8 Kaposi
- Recurrencia de MM, piel no melanoma, vejiga, sarcomas, células claras, mama
- Más común: neoplasias de piel, luego PTLD

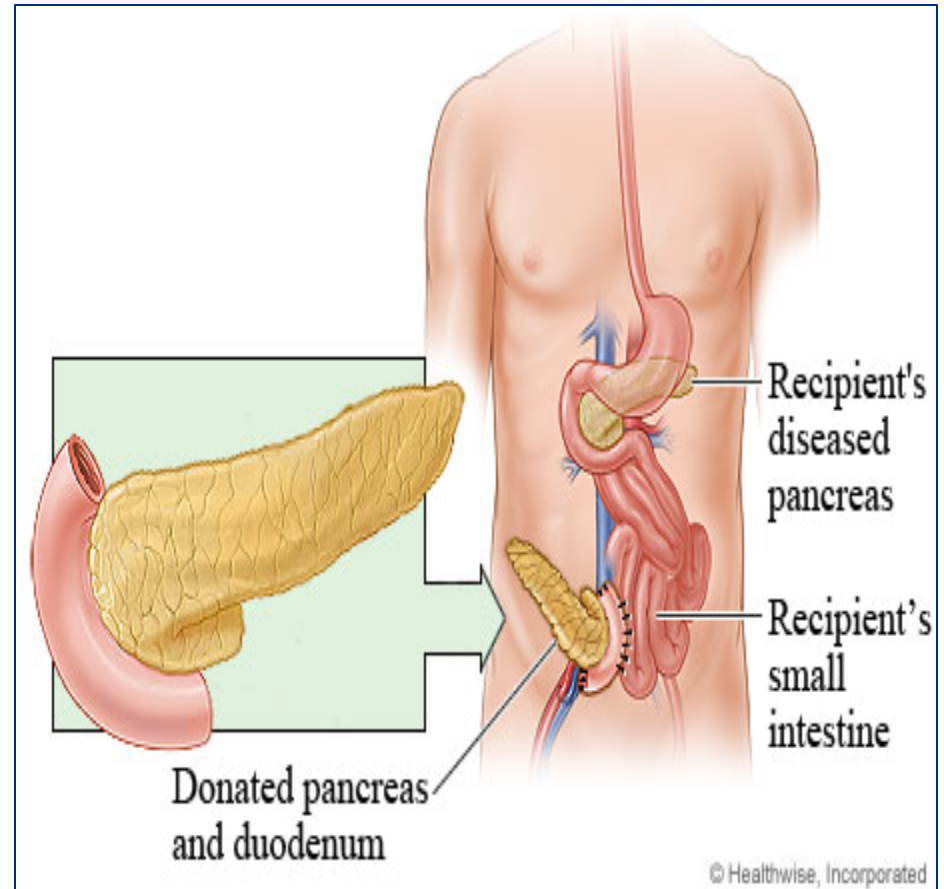
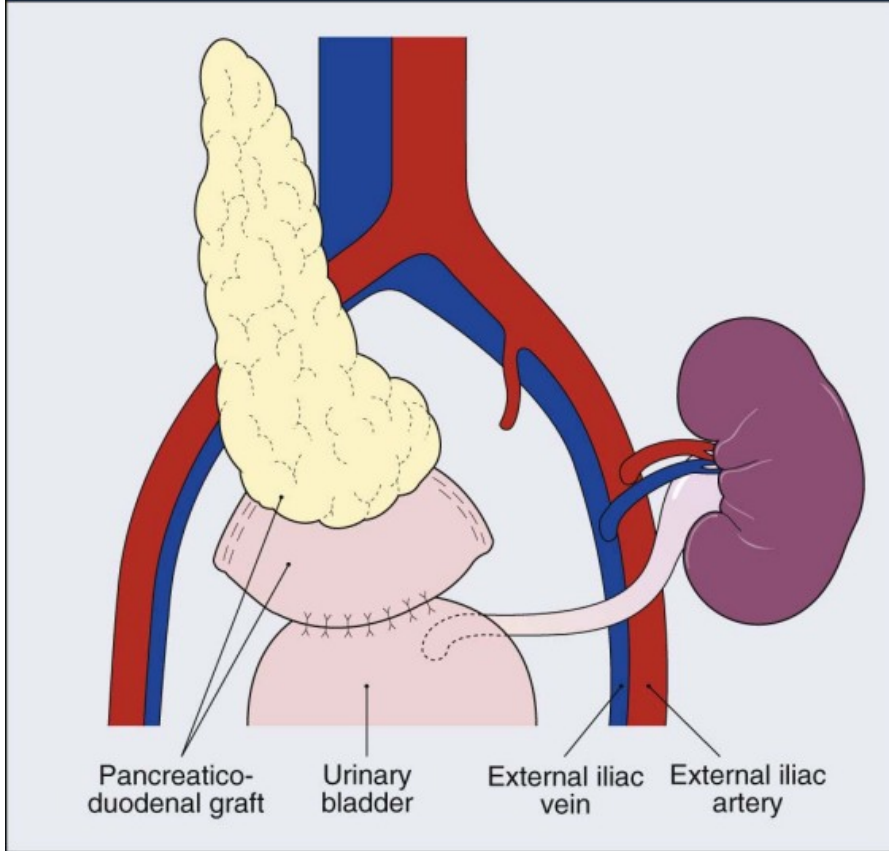
Nefropatía crónica del injerto

- Causa + frec de disfunción crónica del injerto
- AP: FIAT, glomeruloesclerosis, engrosamiento miointimal
- Factores de riesgo: rechazo agudo, C4d+, mismatch, CMV, Tx previos, jóvenes, toxicidad CIN, cadavéricos, DGF, tipo de donante, HTA, DLP, TBQ, proteinuria
- Dx: HTA, IRC, proteinuria. Bx renal

Trasplante de páncreas

- DBT IR con complicaciones (nefropatía, retinopatía, neuropatía)
- DBT con hipoglucemia inadvertida
- Rol no claro en DBT tipo II
- < 48 años (< 55?)
- Primer Tx, no sensibilizados, isquemia < 12 hs
- Tx doble o páncreas dps de riñón

Pancreatic Transplant with Bladder Drainage



Evolución

- Mejor control metabólico
- Retinopatía variable
- Mejoría de neuropatía
- Mejor control de HTA y menor progresión de enfermedad macrovascular