The Thymus Gland In Health and Disease

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THE THYMUS GLAND IN HEALTH

- LYMPHOID ORGAN OF THE IMMUNE SYSTEM
- T-CELLS DEVELOP WITHIN THE THYMUS AT AN EARLY AGE
- SELF VS. NONSELF DETERMINATION
- STROMAL CELLS AND CELLS OF HEMATOPOIETIC ORIGIN (THYMOCYTES)
- THYMOCYTES ARE DERIVED FROM THE BONE MARROW RESIDENT HEMATOPOIETIC STEM CELLS
BASIC ANATOMY

- LOCATED IN THE ANTERIOR SUPERIOR MEDIASTINUM BEHIND THE STERNUM AND IN FRONT OF THE HEART

- 2 IDENTICAL LOBES

- SIMPLE BLOOD SUPPLY WITH ARTERIAL SUPPLY FROM IMA AND SUPERIOR POLE BRANCHES FROM THE INFERIOR THYROID ARTERY. VENOUS DRAINAGE TO THE INNOMINATE VEIN.
THE THYMUS GLAND IN DISEASE

- DiGEORGE SYNDROME
- MYASTHENIA GRAVIS
- ATHYMIA
- THYMOMA
- MALIGNANT THYMOMA
WHAT IS THE MOST COMMON INDICATION FOR THYMIC RESECTION?

CONGENITAL HEART SURGERY IN NEONATES
WHY NEONATES?

THE USUAL REASON FOR A THYMECTOMY IS TO GAIN ACCESS TO THE HEART TO CORRECT CONGENITAL HEART DEFECTS IN THE NEONATAL PERIOD.

THYMECTOMY MEANS THE SURGICAL REMOVAL OF THE THYMUS.

THE THYMUS IS LARGE IN THE NEONATAL PERIOD AND TENDS TO REGRESS OVER OUR LIFETIME.
WHAT IS THE CONSEQUENCE OF NEONATAL THYMECTOMY?

- J THORAC CARDIOVASC SURG 1998 May; 115(5): 041-6
  Wells WJ et al.

- OBJECTIVE: to determine if thymectomy in newborns have a negative effect on immune function.

- 25 neonates prospectively studied

- Samples drawn at 3 months and 12 months

- At followup patients asked about infection
At 12 months, all T cells (CD3) were significantly less then in control groups (48% vs. 64%).

At 12 months, T helper cells (CD4) were significantly less then in controls (31% vs. 46%).

At 12 months, T suppressor cells (CD8) were unchanged relative to controls.

At 12 months, all studies of immune function were normal including lymphocyte blastogenesis to phytohemagglutinin and tetanus toxoid and antibody to tetanus toxoid.
No patient required readmission for infection and there were the expected number of minor infectious events.

CONCLUSION: Thymectomy in neonates results in a modest but significant decrease in T-lymphocyte levels, but there is no compromise in immune function.

• 19 children heart surgery in first months of life

• 19 children aged 5-16 years

• Same results as prior study with reduced total lymphocytes reflected in lower number of T-cells but not B-cells.

• Furthermore, significantly lower CD3 and CD4 cells (all T cells and T-helper cells).
Cytotoxic T-cells (CD8) were not significantly lower. Additionally, the level of neutrophils in peripheral blood was significantly higher in the study group. The reduction of CD3 T cells did not reach the critically low level of approximately 20% which has been associated with a significant increase in clinical infections. Trend towards increased natural killer cells (CD16 and CD56).
My Conclusions

- I was trained to perform total thymectomy in neonates but rarely do.
- Perform subtotal thymectomy whenever possible
- I await results on immune function in adult congenital patients after thymectomy associated with congenital heart surgery as neonates or infants.
Myasthenia Gravis and Thymectomy

- Autoimmune disorder whereby autoantibodies reduce the number of acetylcholine receptors at the neuromuscular junction.
- Diagnosed by Tensilon test and confirmed by elevated acetylcholine receptor antibody titers.
- Medical therapy includes mestinon and corticosteroids.
"Treatment of myasthenia gravis with physostigmine"

“Mrs. M.”

Walker MB. Lancet 1934;1:1200-1
Myasthenia Gravis and Thymectomy

- Concept of thymic involvement in myasthenia gravis based on clinical observation.
-Observed in young patients, that thymus either hyperplastic or contains thymoma in up to 80% of cases (Buckberg et al, 1967).
- Antibodies to acetylcholine receptors (Almon et al, 1974) demonstrated in the thymus of patients with myasthenia.
THYMECTOMY FOR MYASTHENIA GRAVIS IN CHILDREN

- Over 12 years 8 children under 16 treated for MG
- 6 girls and 3 boys
- 3 underwent tracheostomy because of severe respiratory insufficiency preop
- Clinical deterioration or no improvement despite increasing doses of medication
Thymectomy in all after average of 12 months (range 4-17 months)

Postop no morbidity, mortality or thymoma

Dramatic amelioration with eventual complete recovery was seen in 6 with an average followup of 7.3 years. Two are less then 1 year post and improving.
First thymectomy for thymoma and MG performed by Alfred Blalock and associates in 1939 in a young woman. Her MG improved and they subsequently performed 6 more thymectomies on MG patients without thymoma.

Consensus opinion suggests results are superior when thymectomy is performed earlier in the course of disease.
Alfred Blalock
The man who inspired me most, I think, was Dr. Alfred Blalock, who was professor of surgery at Johns Hopkins. He was a rather simple man with a burning curiosity. It was through his curiosity that he made many real contributions to medical science.

— Deatton Cooley
DiGeorge Syndrome

Normal → Deletion → DiGeorge
DiGeorge Syndrome

- All patients at Sunrise Childrens Hospital with significant congenital heart disease have chromosome analysis and FISH study for chromosome 22 microdeletion which defines DiGeorge Syndrome.

- These patients require special care and special blood products. Specifically Packed RBCs need to be irradiated and CMV negative.

- The risk is to the undefined DiGeorges

- Severe DiGeorges will get graft vs host disease with improper transfusion technique. Basically WBCs in blood will attack recipient of blood transfusion.
Synonyms

1. Chromosome 22q11 deletion syndrome.

2. CATCH 22.
   - Cardiac anomalies.
   - Abnormal facies.
   - Thymic hypoplasia.
   - Cleft palate.
   - Hypocalcemia.
DiGeorge syndrome

- More frequent cleft lip/palate
- Small jaw
- Small upper lip/mouth
- Eyes slanted upward or downward
- Low-set and/or abnormal folding of ears
- Short stature, mild to moderate learning difficulties
- Underdeveloped parathyroid and thymus
- Cardiac malformations
History

- Described by Angelo DiGeorge, in 1965.
  - Thymic hypoplasia.
  - Congenital cardiac anomalies.
- Kinouchi et al, in 1975 described the
  - Conotruncal anomalies face.
- Shprintzen et al, in 1977 described.
  - Velocardiofacial syndrome (VCFS).
Pathogenesis

The result of this deletion is:

1. Defective migration of the neural crest cells during the fourth week of embryogenesis.

2. Developmental field defect involving the third and fourth pharyngeal pouches portions of:
   - The heart.
   - Head and neck.
   - Thymus.
   - Parathyroid.
DiGeorge Syndrome and Conotruncal Defects

- 50% interrupted aortic archs
- 35% truncus arteriosus
- 16% tetralogy of Fallot
- 5% DORV
- 0% transposition
- 2 of 6 posterior malignement VSD

JACC 1998; 32(2): 492-498