- echocardiography
- ECG, holter monitoring
- Cardio exercising

HCM vs Athlete's Heart – wall thickness of 1.5 or greater may be inappropriate for children.

Asymptomatic family members: screening recommendations
- genetic screening: mutation analysis of index pt (parent) 1 degree relatives if feasible
- clinical screening: children < 12 get a ecg & echo?

Risk factors for sudden death – we don't know in adults

Septal myectomy in children
- 56 pediatric pts
- Mean age dx 6.3 5.4 yr
- Age at surgery 2m – 20 yr

Reduced the gradient dramatically, no early deaths, 2 late deaths (1 sudden, 1 after transplant)

96% survival rate.

HCM annual mortality

- Accurate assessment of age-specific mortality is important as surgical findings are unveiled.
- Adults: earliy studies have been done
- Children: early misconceptions; more studies for mortality

Registry in Australia low level but other morbitities existed.

Mortality from US registry (Colan et al), no infant death below 8

Adult HCM has its onset in childhood or adolescence
Infants with HCM respresent 25% of cases
Some adolensence and adult pts have been diagnosed late with inborn errors or mitrochondrial gene.

Treatment plans for children is typical to adults. Although Alcohol Septal Ablation is not recommended for children at this time.

Question: As an adult cardiologist w/pt w/ teenage children. What is the wisdom for an adult cardiologist to see these children with an adult size heart?
Answer: Not good wisdom, but conferring with child / peds cardiologist for recommendation on tests.

Question: What is the definition of an athlete – t-ball vs high school football?
Answer: Competitive sport, levels of concern for standards, but also take the individual process.

11:45 Michael Fowler, Restrictive disease, dilated phase and transplant

Stage D: End-stage Heart failure from HCM.

Relatively rare; definition of the burnt out phase; poor prognosis; treatment

Approximately 3.5% of 1259 consecutive HCM patients over 22 years; LVEF < 50%, range 15 – 49%; age they recognized they had reduced LVEF was 49 y/o

LV remodeling is occurring during the LVEF stages.

Milestones of heart transplantation: 1967 was the first experimental transplant with a dog, Ralphie, in South Africa.

The survival rate has increased over time to be over 10 years.

Cardiac transplantation: What the referring physician needs to know.

When to refer
- worsening symptoms,

Who to refer
- stage D heart failure
- Acute presentation
- Refractory

Adult heart recipients

LUNCH

California ACC chapter president

SUDDEN DEATH IN SPORT – Moderator: Paul Thompson

13:00 – Gary Balady, Incidence and causes of sudden death in sport

Sudden death rates is 0.61/100,000

Study for SD in women by nurses

Dr. Maron's study on causes of Sudden Death in young athletes

- 3% from comodia cordius
- 36% causes of HCM
- 17% coronary anomalies
- Drops from there

Cardiovascular causes of SCD during sport relative to race/ethnicity
- large propensity for non-whites

50% of deaths in Football are cardiovascular; other high levels in basketball, soccer have higher levels of death than others

340 marathons in 2007, 403,000 finishing times
- men 69% > 35 years
- women 55% > 35 years

Summary – the rate of sudden cardiad death during exercise and sport is low
- it's higher in men

Question: why is there a disparity of SD in men & women?
Answer: could be the involvement levels of sports in the prior years. As young women age that are more involved in sports their aging factors could be expressed in closing the gap.

13:15 – Jonathan Drezner, Automatic external defibrillators (AED) in athletic medicine

This topic is a reminder of the fragility of life.

1) Do AEDs provide a survival ratio with athletes?
2) Do AEDs we have data?

There are limited studies and the data shows that the survival rate is quite low.

Its NOT just about AEDs …. EMERGENCY PREPAREDNESS is the important factor for good access, continued maintenance, continued training, awareness of the AED for the improvement of survival of SCA.

National guidelines: Emergency planning and AEDs in Athletics

- NATA position statement on emergency planning in athletics
- Need AEDs available < 3 – 5 minutes from collapse sites.

Sudden cardiac arrest in intercollegiate athletes: detailed analysis and outcomes of resuscitation in nine cases.

- N=9; retrospective cohort

Is there enough data to show that AEDs are effective?

AEDs in US High Schools, methods & study design: Results (36 cases); 17 high school athletes, the rest older adults;

35/36 were SCA cases were witnessed

High school student athletes 0 – 5.75 minutes

9 of 14 Students survived. Overall survival 65%

There are limits to the study, but it is the largest study of emergency planning for SCA in US high schools

If there is a early shock, the survival rate seems to be well over 60%.

HCM was in over half of the college students where as only 21% of the high school students.

Time verses survival rate to defibrillation

Future directions
- continue montitoring > 3400 high schools
- emergency planning
- 2 year study underway.

Conclusion – AEDs should be encouraged in schools

Question: where does that number come from?
Answer: division 1 study of cost of life saved ($10k)

Question: is there an emergency response plane?
Answer: there are several plans in WA and NATA.

Question: do you have an opinion in heath clubs or public venues?
Answer: a recent study by an UW student, was able to provide feedback for the need to have AEDs with large health and fitness facilities with > 2500 membership. The risk and benefits of exercise have been touched on in this issue.

Question: CA legislature for fitness clubs – what about a federal lobbying effort by NATA?
Answer: This is a no brainer for health clubs, but the cost isn't a factor on the private sector, it is by the schools. Legislation is one level.

Question: What is the legal liability for owning and using an AED? The Bethesda guidelines for use of AEDs. It's not just a clinical level, we need to be sure that the legal level of liability.
Answer: We had a situation that ½ the WA schools had AEDs but didn't have a good emergency plan. The need to work with the schools to come to common ground.

Question: What if the cost of the AEDs came down to $150 compared to the fire extinquishers.
Answer: More likely to use the AED than the fire extinquisher. We need to determine the emergency plan as most important to the implementation of AEDs in schools.

13:30 – Paul Zei, Arrhythmogenic right ventricular Cardiomyopathy: an underappreciated killer?

Baseline ECG for a female pt. with many irregularities. Echo presentation as normal.

First description of ARVC – 1736 – Giopvannni Maria Lansisi

The modern day description of pts with CMP, LBB morphology VT

ARVC: Key features originally described
Vt arrhythmias

Clinical presentation in ARVC – most

Structural abnormalities in ARVC – RV enlargement; thinning of the walls

Pathologic and cellular basis; no muscle to speak of

Cellular and molecular basis; desmosome – architechural glue that holds the miocytes together.

ECG: precordial T Wave Inversions, epsilon waves

Much work / studies on ARVC in the Italian studies

Is it a deadly disease – not super high, contrast that with presentation of arrhythmia, is very common?

There is no gold standard for treatment plans. Focusing on the arrhythmia problems as the key to managing this condition.

Scaring could be from MI related to the arrhythmia issues.

Basis for VT in ARVC.

Management – medical treatment, device treatments (ICD), ecapsulations.

Is every VT life threatening? Management of ICD for ARVC studies.

What about catheter ablation? Is it affective, Is it safe? The thin walls to this disease are more at risk for perforation.

Voltage mapping, to assist with determination of treatment for ablation.

Catheter ablation: data, no major complications

Question: What percentage ARVC pts go onto have LV issues?
Answer: No hard data, but it is probably in the low single digits.

Question: What about the 20 – 30% with no need for ICD?
Answer: Never, still don't know if they are really truly high risk. If they are implanted and go many many years without a therapy, should they ever have been implanted?

Question: Uncommon on a HCM practice to find a confirmed ARVC. Pts are minimally asymtopmatic. Should we put them on a beta blocker, medical therapies?
Answer: No gold standard, so until we get a little better testing, we won't have that standard. Use the available screening / testing tools, ECG, Echo, MRI testings.

Question: Young lady (21) had family death (father) and comes in for testing. What kind of testing to offer - MRI?
Answer: Start with minor testing and offer follow up tests as she ages.

Question: Exercise limits?
Answer: based on unique limits per person.

14:00 – Ricardo Stein, Fan heart: the other side of sudden death in sport (not at conference)

14:15 – Mark Estes, A pain in the chest: commotio cordis

Case of the first presentation of commotio cordis. ECG of the young 14 year old boy, from the Emergency responders showing varying levels of the anaomalies to the ECG.

Video of the martial arts blow, the simple impact of the strike that is suspect to commotio cordis

Swine study done to show the impact at the peak of the Twave that causes the VF after the impact.

This then caused a heart block, right at the time of impact.

More and more data about chest wall protectors. Many do not work as with the animal testing that have been done to date.

AED success rate for Commotio Cordis has a good rate of survival.

Panel discussion: Barry Maron, Mark Estes, Jonathan Drezner, Antonio Pelliccia

Question: After finding a young athlete / person with HCM, you take him / her out of their sport of choice. What do you do with them now?
Answer: Maron – we redirect them to golf. Drezner – what are the long term complications to not letting the HCM pts not exercising at all. Maron – we do have recreational guidelines for coronary heart disease, & we use that as a guide for HCM pts.

Question: If we had a recommendation on types of legislation, what would that be?
Answer: Estes - AEDs in all schools, colleges emergency response systems; curriculum for every senior; Drezner – every coach should be trained in emergency response. When working with schools, what is the liability for the schools, ask for broader amunity for the schools with use of AEDs.

Question: What is the Italian perspective?
Answer: Pelliccia – in Europe & Italy, there are studies going on that show the survival is 30%,

Questions/comments: In duty of care needs to be better defined? What to do with the athlete – those who can't do, teach. Many competitive athletes go onto brilliant careers.

Question: What is the response to the deaths related to the benign HCM? Or how many of the deaths show

Question / comments: Get a better drill for emergency response

Question: Why do we not have to register the AED and make sure the "team" is trained? Who is responsible for that?
Answer: In our CO we do have to have the AED registered for several reasons, then the emergency responders know where the AEDs are and the training / follow up is done.

BREAK

Jonathan Drezner: discussion about AED programs going on and how they studies have come about.

Specific question related to Liability for involvement with screening. Answer: each doctor has privileges with hospitals and if they go through the hospital for permission, then the avenue for approval is open for additional volunteers / medical professionals.

GENETICS OF FITNESS, HCM & CHANNELOPATHIES – Moderator: Barry Maron

15:30 – Kelly Osmond, A genetic primer: what the practitioner needs to know.

Pedigrees, review basics of genetics and how this affects the needs for the mutations we are looking for in the HCM infected life.

Sometimes the family doesn't what to know the issues the DNA mutation functions as, but the family may want to know that level of information. A genetic counselor may not go into that level with the family, but the doctor may have to explain this information to the family on certain occasions.

Locus heterogeneity = complicated! Or lots of related problems related to the testing involved.

We are not yet at the point that we have genetic phenotype correlation?

Once we better understand the gene that causes the HCM, there may be more available therapies. Possible processes / drug treatments for the sarcomeres, etc.

Role of the genetic counselor does the risk assessment, history taking, life planning, follow up needs.

Test strategies, test the effective relative first so the results are most informative.

Positive results need medical management

Negative results (may not be negative to HCM).

Variant of Significance – may be reclassified in future studies.

Pts may be more frustrated than when they first started the DNA testing.

What about the kids?

- selecting embryos, costly, not always available with insurance

What about GINA?

- standardized laws with genetic information

Summary: good family history in your practice, make sure you start with the right person, genetic results may not be clear-cut.

There are genetests.org and NCIP,

Question: Is there more information about other GINA for life insurance, long term disability?
Answer: Salberg – no work being done to add that kind of protection.

Question / comment: A lot of families are concerned about the effect of genetic testing on their kids. The families with loss seem to be more impactful in the negative standards of the genetic testing
Answer: Yes, just because their may be some hesitance, the need to encourage the tests are important.

Question: When are where can these counselors be housed?
Answer: The is not limit as there is on need for physical exams, tele-med or internet contact can be included in the contacts.

Question: When we don't have a positive? What do we do?
Answer: Stay connected to the genetic test groups to stay in the changing information.
Answer: the data is rapidly increasing, so the amount of negatives are going down. And the test may be reevaluated down the road.

15:45 – Joshua Knowles, Personalized genomic: the revolution is coming.

What is personalized medicine, exactly? Tailoring medical practices for the patients

The "revolution" has been preceded by years of pain and suffering…
Linkage and candidate gene studies were fruitful in some respects
Not very successful

The HapMap Project: map more SNPs, sequence the genone internationally.

Paradigm shift in genotyping technology:
Arrays developed that could assay 100k 0 1m
SNPs similtaniously.

Genome Wide Association (GWA)

Manhattan Plot – for variances in the genome.

What do we do with this kind of information?
Biology
Risk predictions
Tailoring drug therapies

GWAS results for lipids (HDL, LDL, Trig)
- explain 5 – 10% of the lipid variances

Illuminating Biologic Pathways
There is gold in these discoveries

What about risk prediction?
Still not there yet, as there are only small percentages (<10%) of identified risk predictions.

Variants with larger effects could be done such as HCM.

Pharacogenetics: so fare we have just scratched the surface

Likely that we will find more ways to improve these areas

Lots of sticky issues for research studies are not fully resolved.
Consent control, confidentiality, return of information

Future directions
Educate the public & physicians
Genome sequencing

The ability to sequence the entire genome for $1000 by the end of 2009.

Continue to be educated about this as the process grows / changes.

Question: What is a snip as it relates to HCM?
Answer: A snip is only point or marker for mapping and can occur anywhere in the genome.

Question: Imply that everyone is dying to get this kind of information. How does this related to the HCM issues?
Answer: Yes, that is a concern, but not always definitive.

Question: Micr data is required to be available to the public. Please comment, and how does that apply to studies?
Answer: the NIH is requiring the studies into a repository at the NIH, but the information is more secure and prevent investigators to the data.

Question: The genome.
Answer: Some of the programs will be defined in the future, this is only the start and all those areas need to be approachable.

16:00 – Carolyn HO, Genetics of HCM.

Family example of the history, father and then two brothers died. Last brother had an autopsy and was clearly HCM.

Clinical Genetic testing for the Sarcomere genes. The HCM pheoncopies metabolic storage CMP is done on a lower number of HCM

If there is no family history of HCM, there is only chance of 40% finding the genetic connection. When there is fh, 66%.

About 80% of those identified have the Sarcomere genes.

The original hope was that the genetic test would find 1 or 2 mutations to allow for a broad base testing ability.

Now there are over 900 mutations of the condition.

The clinical diagnosis was done for the family to find 2 more siblings with the condition and ICDs implanted. Then the genetic tests were done for the family and found two children of the siblings to be positive for the gene and asypmtomatic.

Mouse models show that the LVH takes certain levels of the expression of HCM where as the early tests of genetics can show the mice subjects at risk of developing HCM.

Then throughout the weeks prior to expression of HCM, there can be different factors. Early given medical intervention were showing decreased hypertrophy and fibrosis.

Through the data there seems to be a link to calcium expression to LVH.

Not trying to cure HCM in mice, only trying to better understand the expression of HCM in people.

Translation to Human HCM – systolic strain and strain rate seems to increase HCM in study done.

Future goals – proactive management of preclinical HCM

16:30 – Carolyn Ho, ARVC - genetics

Pathological view of the thin walls and electrical instability. EKG changes: epsilon waves

Prevalence is 1:1,000 – 5,000

Familial disease in > 50%

Naxos, Greece is traced back to this island. Autosomal recessive – wooly hair, paloplantar keratoderma, and then ARVC developes in adolescence.

The genetics of the ARVC was described. The mutations cause electrical issues that are known as electrical instability.

Environmental factors (myocarditis, intense exercise) may exaserbate the impared adhesion – hasten the disease progression
Altered intracellular signaling

Invetro example on a study. Frozen cells and how they stick together real well. In contrast other cells that are mutation for ARVC show easy break away factor / not strong.

Genetic testing, no independent determination in many cases.

Question: Is the ARVC ventrical more fragile than others?
Answer: People do go through these procedures, but they are at higher risk of perforation, etc.

16:15 – Colleen Brown, Genetics of LQT and other causes of sudden death.

Colleen.brown@ucsf.edu

Review of the LQTS, ARVC and CPVT as additional cause of sudden death for athletes.

An interesting update in each condition – a pedigree, shows one young man with ECG, showing QTc 525, but family members are clear; continued to have syncope; no mutation was found. A new finding with the type of mutation definitively gave this family some answers.

ARVC tests done to show the reduction of placoglobin. Where in HCM, DCM have no lower level of placoglobin.

CPVT tests of incident & risk factors of arrhythmic events in catecholaminergic polymorphic ventricular tachycardia (CPVT).

- sensitivity of exercise stress tests in asymptomatic relatives: 58%
- no difference in event rate
- authors recommend all mutation carriers be prescribed beta-blockers

Genetic testing yield:
- RVRC 70%
- ?? 5%

Question: How do we improve this information without a national database?
Answer: We need to have a national database, but we need more work to do over the years for the clarification of variances.

Comment: Very few variant coming back in genetic tests. This allows more confidence to families.

16:30 – Paul Thompson, The fitness gene: does it exist?

pthomps@harthosp.org

The exercise performance genes: do they exist?

In mice & men – In mice absolutely; in Men – not so definitive.

Erythrooi Progenitor cells very sensitive to EPO, especially at low leves.

Myostatin – Belgiun Blue Bull (very low birth rate) due to difficult delivery.

If you over express myostratin it expresses in loss of muscle.

Myostatin is over expressed in Hypertrophic Cardiomyopathy.

The problem with performance studies in humans
- cannot do breeding studies
- variablitity of the Phenotype

Phenotype variation
- exercise capacity varioes by training
- laboratory measurements vary by equipment, calibration
- performance varies by multiple factors
- probably multiple genetic pathways to performance.

Multiple genetic pathway
- genes for baseline fitness
- genes for change in performance with training
- genes for motivational to train – high activity genes
- producing a cluster of performance genes

The human gene map for performance and health-related

Animal models of endurance capacity
- exercise models were breed as the high and low exercise models
- after 3 generations the high level was much better
- after 6 generations, the produced lines differing in running capacity by 171%
- now they are up to 17 generations and are using these groups for new studies.
- High performance rats have better cardiac output, muscle area, etc.
- Low performance rats have more fat in their liver, etc.

Genotype score increased prediction 2-3 fold; remarkable improvement