Where We began, Where We Are Now, and Where We Are Headed

Gerald A. Beathard, MD, PhD, FASN

Where We Came From
Concerns over vascular access for dialysis

Beginning of Modern Hemodialysis

- 1943 - First practical model for hemodialysis Dr. Kolff
- 1950s - First commercially available dialysis machine
- Early enthusiasm for this new therapy was dampened by technical problems associated with vascular access

Next Advance

- 1956 - "twin coil" artificial kidney
- Hemodialysis more easily available to more patients
- Vascular access still a major problem
- Cut down or by cannulation with large bore needles
The Great Solution

• 1960 – Schribner shunt made chronic dialysis a reality
• These devices would sometimes go for several weeks without a complication
• Bleeding, infection, sclerosis of vessels, frequent thrombosis
• Nephrologists did thrombectomies, taught patients how to do them

The Great Solution

• In 1966, Brescia, Cimino, Appel and Hurwich reintroduced the arteriovenous fistula
• Brescia, Cimino and Hurwich were from “Renal Service”

First Fistula Angiogram

First Fistula Angiogram

Performed by nephrologist in 1968

Problems

• 1972 – Initiation of ESRD program under Medicare
• Rapid expansion of hemodialysis as a standard of care began
• Vascular access really became a major issue
• Less than 50% of the patients were felt to be candidates for a Cimino fistula

The Next Solution

• 1974 - Bovine grafts were introduced

• These worked but had problems
  – Became aneurysmal
  – Infection was a problem

The Great Solution – PTFE Graft

Mid 1970s

“Its availability, ease of handling and significant decrease in cost make the PTFE graft ideal as a means of access for chronic hemodialysis”

Grafts Predominate

- Many Advantages
  - Wide applicability
  - Use early
  - Works well
  - Large cannulation area
- But turned out to be a double edged sword

Training Programs

- Devoid of active training in dialysis vascular access
- True for
  - Nephrology
  - Surgery
  - Radiology
- Felt to be a simple procedure not worthy of special consideration
- Low priority
- No one available to do training in some instances

Where We Were

- Attitude toward vascular access was:
  - Disorganized
  - Fragmented
  - Uninformed
  - Non-analytical
  - Unscientific
- Nephrologists were not involved
- As a result, both quality of patient care and economy were largely ignored

Beginnings of Interventional Nephrology

- Makes no mention of vascular imaging in patient evaluation
- States that first choice for access should be a radial-cephalic fistula, but as a second choice it lists 4 alternatives. The first three are grafts, the fourth is a fistula
- “When an AV fistula occludes salvage attempts are often unproductive, we usually prefer to insert a forearm graft if possible”

Trend In Medicine

- There has been a definite movement toward specialization in medicine
- Internal Medicine is an excellent example of this trend
  - There are 18 subspecialties within IM
  - There are subspecialties within subspecialties
  - 5 perform interventional procedures
Requirements for the Emergence of A New Subspecialty

Requirements

- Need
- Interest and opportunity
- Academic involvement

Requirement #1 - Need

- There has to be a need for a particular service or activity
- Related to, but outside of or on the periphery of basic specialty
- Reasonably well defined
- Potential for development and growth

Nephrology

- Multidimensional speciality which offers a home to eclectic interests
  - Clinical nephrologist
  - Experts in dialysis
  - Transplantation medicine
  - Immunology
  - Hypertension

Nature of Nephrology Private Practice

- The practice of nephrology is primarily involved with the care of dialysis patients
- Historically the nephrologist has cared for all of the various problems presented by these unique patients
  - Social, nutritional, hematology, endocrinology, cardiovascular, GI, etc
- All problems except vascular access
  - Delegated to a consultant
Vascular Access 1980s – 1990s

- Major morbidity and mortality
- 1 billion dollars/year
- Excessive reliance on synthetic grafts
- Excess use of catheters
- High hospitalization rates
- Inordinate amount of time dealing with problem

Requirement #1 - Need

- There was certainly a need to do something
- Actually nephrologists were already getting concerned with vascular access
  - Fistula % was increasing slowly
  - Access treatment was slowly moving to outpatient facilities
- NKF – DOQI practice guidelines were published in 1997

Requirements

- 1. Need
- 2. Interest and opportunity
- 3. Academic involvement

Requirement #2 – Interest & Opportunity

- An individual or group of individuals with an interest in development
  - Establish standards of practice
  - Develop practice guidelines
  - Develop a body of supportive literature
  - Develop training programs
- An opportunity to develop subspecialty
  - Department, Division, Practice support
  - Hospital regulations
  - Relations with other specialties with similar interest

Austin Diagnostic Clinic

- I was at the Austin Diagnostic Clinic
- We were caring for about 700 dialysis patients and were seeing the same types of vascular access problems as everyone else
- At a medical meeting in early 1980s, images were shown of stenotic lesions that were found in dialysis patients
- First publication of angioplasty treatment of vascular access in 1980

Early Efforts

- I was fascinated by the idea of diagnosing venous stenosis in these patients
- I started taking patients across the hall to our radiology department with their dialysis needles in place and making still images of their veins
- We saw a lot of pathology
- I was interested, but the surgeons weren’t
Perspective
• 1964 – First angioplasty Charles Dotter (Oregon, USA) – used graded catheters
• First balloon catheter – 1975 - Andreas Gruentzig (Zurich, Switzerland)
• 1977 – First coronary angioplasty
• 1978 – First US balloon patent
• 1980 – First reports of angioplasty for dialysis access
• My interest started in about 1983 or 84

Next Step
• In about 1985 a new cardiologist joined our Clinic
• The first to perform coronary angioplasty in our area
• Our group convinced him to treat some of the access lesions that we were seeing
• He did a few and then got too busy and lost interest

My Development
• My interest was piqued and I thought that this approach was worth while
• Another much more collegial cardiologist joined our clinic and he was willing to be a proctor
• I was able to convince the hospital to allow me to have temporary privileges with a proctor
• I started doing cases
• I was proctored on the first case, after that I was on my own
• There were no established techniques or standard protocols to follow
• I learned by doing
• I worked in the general angiographic suite of the hospital where all of the interventional procedures were done
• I had a wide variety of tools and supplies to use and a group of excellent trained technicians to assist
• I learned a great deal from these technicians

Status at the Time
• At this time the value of prospective treatment of venous stenosis in the dialysis vascular access was not established
• It was considered controversial

Entry Into Science
• Medicare published a letter stating that angioplasty of dialysis “shunts” would not be paid
• I contacted our political representative for Texas nephrologists – Dr Allen Hull
• He called back a couple of weeks later and stated that he could not support the issue
  – Talked with vascular surgeon who said it was of no value
  – Talked with interventional radiologist who said he had not heard of it being done
First Publications

- I started collecting data on our cases
- Abstract accepted at ASN – they didn’t have a session to assign it to (Today they have multiple sessions)
- Paper published in Kidney International in 1992 reporting data on 536 procedures with a 94% success rate
- Randomized controlled stent study – 1993 – Hand made stents
- Mechanical thrombectomy – 1994

Growing Interest

- As we began to present and publish our data, interest among nephrologists began to grow almost exponentially
- We started having request from nephrologists all over the US and outside of US to come to Austin and train
- We began to accept trainees on a regular basis

Support

- My associates were supportive as long as it didn’t affect call schedule
- Radiologists at hospital were supportive
  -- Busy, had no interest in this area
- Surgeons were permissive
  -- Did not think activity of any value
- Able to get privileges at hospital
  -- I was chairman of the credentials committee

Formation of ASDIN

- Ash, O’Neill, Work and Beathard discussed starting a national organization in a bar in Miami in 1999
- Further discussions in bar in Memphis
- Plans finalized
- 1st Annual Business Meeting held in New Orleans on Feb 20, 2001
- 1st Annual Scientific meeting held in Scottsdale, AZ on Feb 12, 2005

Special Note

- Should note that Steve Ash had started peritoneal dialysis training for nephrologists late 1970s early 1980s
- Charles O’Neill begun renal ultrasound activity in early 1990s

Professional Organizations

- Both American Society of Nephrology and Renal Physicians Association adopted policies of support for Interventional Nephrology in early 1990s
- When NKF put together their DOQI committees to develop practice guidelines two interventional nephrologists were asked to be on the committee dealing with vascular access
Requirement #2 – Desire & Opportunity

• The desire was there as well as the opportunity
• The necessary groups were very supportive
• Support was not universal however
• Turf issues were a major issue
  – Locally
  – Nationally
  – Internationally

Requirement #3 – Academic Involvement

• Typically, new specialties typically begin in academia
• Interventional nephrology could not because of turf and political issues
• Attempt was made at Duke – political problems
• IN arose in the private sector and developed there primarily although there were several academicians that certainly did play critical roles

Requirements

• 1. Need
• 2. Interest and opportunity
• 3. Academic involvement

Why Is Academic Involvement Critical?

• Credibility
  – Practitioner who takes short course to gain new skill is looked upon with skepticism
    • Totally foreign area
    • Training done outside of academic institution
  – Fellowship trained much easier to accept
• Create body of scientific literature
• Develop dedicated training programs

What is the Current and Future Status of Interventional Nephrology?

Scott D. Trerotola
Department of Radiology, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

“As indicated in the title, I believe interventional nephrology is headed in the right direction.”

“A challenge was laid down and the interventional nephrology community rose to it.”

“In an article recently published by Beathard et al., aggregated data ... were published. The authors compared their results to the K/DOQI recommendations as well as published literature and found that their outcomes met or exceeded those standards. ... the results are compelling.”

Semin Dial. 18:370, 2005

Commentary

Interventional Care of the Hemodialysis Patient: It’s About Quality

— John E. Trerotola, MD, Robert J. Caputo, MD, Michael Rosen, MD, and Yoel D. Shinem, MD

…a very small group of nephrologists “borrowed” from our well-recognized name and began calling themselves “interventional nephrologists.”

“...it is likely that with the proliferation of poorly trained physicians performing these procedures will come an increase in adverse outcomes and complications including radiation injuries...”

2001

2005

2005
Contributions of Interventional Radiology

- Because of overlap with IR, we have realized great benefits from their contributions
- Several academic IR have had special interest in dialysis vascular access
  - Major contributions

Problems With Development of Academic Training Program

- Need dialysis patient population large enough to develop a dedicated facility
- Most of dialysis patient population in US is being cared for in private practice setting and primarily in small to medium sized practices
- Very few academic nephrology programs have large dialysis populations
- Inavailability of faculty

Where Are We Going

The Road Ahead Is Clear ???

- It would be nice if the road ahead was clear
- The only thing that is clear is that we are going to continue to face difficult problems
- I have no doubts that we will be able to find solutions

Arenas of Concern

- Science
- Credibility
- Economic
- Political

Arenas of Concern

- Science
- Credibility
- Economic
- Political
Problem
• The dialysis vascular access literature is replete with what can only be referred to as “junk science”
• In 2010 we still do not have sound scientific evidence to support many of the most basic things that we do
• We need to increase our efforts toward evidence based practices

Our Goal
• Our goal must be to do what is best for the individual patient
• To achieve this goal we need to use both individual clinical expertise and the best available external evidence, and realize that neither is sufficient alone
• We must be careful in selecting the best external evidence to use
• We must be diligent in our efforts to generate the best external evidence possible

Evidence Based Pyramid

Arenas of Concern
• Science
• Credibility
• Economic
• Political

Mechanisms for Assuring Credibility
• Exert care in advancing professional activity
• Prudent self referral
• Approved fellow programs—ACGME
• Specialty board certification - ABMS

Mechanisms for Assuring Credibility
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• Specialty board certification - ABMS
Advances In Professional Activity

• We are seeing new areas being proposed for Interventional Nephrology
• Every advance in professional activity must be accompanied by appropriate training criteria
  — Standardized training requirements
  — Standardized certification requirements

Nature of Interventional Nephrology

• Most Interventional Nephrologist work in POS 11
• Most of these centers are owned by the physician’s practice
• These centers care for the practice’s patients

Solution

• We can not ignore this concern
• We have an obligation to address it directly
• This can be done by:
  — Increased levels of accountability
  — Diligent adoption of clinical practice guidelines
  — Standardization of coding practices
  — Documentation of quality outcomes and complications combined with overall cost savings
  — Accreditation of Access Centers

Mechanisms for Assuring Credibility

• Exert care in advancing professional activity
  • Prudent self referral
  • Approved fellow programs – ACGME
  • Specialty board certification - ABMS

Self-Referral

• Health care costs are higher in the United States than in any other country in the world, and imaging services have been growing much more rapidly than other services
• Studies have shown a tendency for increased utilization of services, including imaging services, when referring physicians have ownership interest in the services
• This has engendered concern among those who pay for health care


Mechanisms for Assuring Credibility

• Exert care in advancing professional activity
  • Prudent self referral
  • Approved fellowship programs – ACGME
  • Specialty board certification - ABMS
Board Certification

• We have had ASDIN certification since 2003
  – We need to progress in our certification requirements
• It is time to begin the process
  – Approved fellowship programs—ACGME
  – Specialty board certification - ABMS

Arenas of Concern

• Science
• Credibility
• Economic
• Political

Economic Concerns

• As interventional nephrologists we can provide the best possible and most economical medical care to our patients and do it with a high level of patient satisfaction
• However, in order to continue to do this we must be economically viable
• This will be one of the challenges of the future

Procedure Reimbursement Trend

• More restrictions were proposed for 2010 than were enacted
• Restrictions that would have reduce revenue by an additional estimated 15%
• This was averted through a collaborative effort
  – The Public Policy Committee of ASDIN played a major role
Bundling of Codes

- New code for 2010 – 36147
- Bundles 36145 and 75790 as well as several other less used codes
- New code given a 3XXXX designation
  - Payment is depreciated when used with other 3XXXX codes
- Bundling will continue
- All of this has a greater impact on Interventional nephrologist because of site of service

Speciality Benefits Management Companies

- Contract with carriers to develop criteria for privileging for various types of procedures
- These criteria determine whether the carrier will pay for procedures performed by an individual physician
- Radiological Benefits Management –
  - Deals with imaging procedures and modalities
  - Basically do not recognize a nephrologist doing US procedures in POS 11
- Many national payers (Aetna, Cigna, etc.) use these in an effort to improve quality and control utilization of imaging services

Arenas of Concern

- Science
- Credibility
- Economic
- Political

Importance of Political Issues

- What we as nephrologists are permitted to do
- Where we can do it
- What we get paid to do it
- All affected by and dependent upon politics
- We need to recognize this, acknowledge it and deal with it

Coping With Issue

- Get more involved with the politics of medical practice – must have a voice at the table
- The committees that control a great deal of what happens are actually committees of the AMA
  - CPT committee
  - RVS Update Committee – RUC
- Politics determines who has a voice at the table
  - Based upon numbers

Vascular Access Costs By Physician Specialty

- Graph showing vascular access costs by physician specialty from USRDS 2008
Specialities Performing Angioplasties (2006)

Role of ASDIN

- We have a very active Public Policy Committee
- It is critical that we facilitate their efforts
  - Consistency and uniformity in coding
  - Join ASDIN
    - Work through RPA – 50% rule
      - Join RPA
      - Dependent upon AMA membership – 50% rule
        » Join AMA

Interventional Nephrology’s Impact

The Future of Interventional Nephrology

- I really can’t predict what the future will be like for interventional nephrology except to say that I feel it definitively has a future
- I think it will be nephrologists caring for their patients just like today but perhaps with a greater array of tools, procedures and approaches
- This subspecialty has arisen because of a definite need and we are meeting that need

- What we do has been good for patient care and has been good for nephrology
- There is absolutely no reason to feel that the future for this newly developed and developing subspecialty will be anything other than continued progress

- However, we must remember that the future will belong to those that prepare for it today
- We still have a great deal of work that will need to be done
- When it comes to the future, there are three kinds of people: those who let it happen, those who make it happen, and those who wonder what happened
- We need to make it happen
Effects of catheter Lock Solutions on Infection and Patency

Stephen R. Ash, MD, FACP
Past President* and Editorial Chief, ASDIN
Past President ASAIO
Secretary Treasurer of IFAO

Clarian Arnett Health and Wellbound Inc.
Ash Access Technology and HemoCleanse, Inc.
Lafayette and West Lafayette, Indiana

Catheters - Bacterial Highways

What happens to injections of lock solution equal to one catheter volume?

Fluid follows parabolic flow down the center of catheter lumen:

As a result 15-20% of the injected volume goes out the tip of the catheter immediately*

*Polaschegg HD, Shah C., ASAIO J. 2003
**Outcome of Vanc-Ceftaz lock protocol in catheter-related bacteremia**

- **Success**: 15%
- **Persistent fever**
- **Pos surv BC**: 70%

Poole et al, NDT, 2004

**Active Component(s) Name Formulation Product Risks Sites**

1. **Taurolidine and Citrate**
   - Neutrolin (US) and TauroLock (Europe)
   - 1.35% taurolidine and 4% citrate
   - None known at these concentrations even with overdose

2. **Concentrated Citrate**
   - Citra-Lock 23-30% citrate
   - Safety issues at 46.7% but lower concentrations are safe and effective.

3. **Citrate, methylene blue, parabens**
   - AAT, Zuragen
   - 7% citrate, 0.05% methylene blue, X&Y
   - None known at these concentrations even with overdose.

4. **EDTA and minocycline**
   - A0.3% minocycline, Contains antibiotic which Raad, MD
   - 3.0% disodium EDTA creates antimicrobial resistance risks.

5. **tetrasodium EDTA**
   - 4.0% tetrasodium EDTA
   - None known at this concentration.

6. **Ethanol and citrate**
   - Ethanol 30% ethanol and 4% citrate
   - Ethanol could degrade catheter materials. Weak antibacterial effect.

7. **Gentamicin and citrate**
   - gentamicin and citrate
   - Contains antibiotic which creates antimicrobial resistance risks.

8. **Hypertonic saline**
   - Hypertonic saline
   - Weak bactericidal effect. No anticoagulant activity.
   - Density causes efflux from catheter unless bubble placed.

**Non-antibiotic Catheter Locks Recently Studied for Infection Prophylaxis**

- **CRB rate per 1000 catheter days:**
  - 0.6 vs 5.6
  - Allon, CID, 2003

- **CRB rate per 1000 catheter days:**
  - 0 vs 2.1
  - Betjes, NDT, 2004

**Isopropyl alcohol (70%) lock prevents CRB**

- **Subcutaneous dialysis device (Lifesite)**
- **CRB rate per 1000 catheter days:**
  - 1.3 vs 3.4
  - Schwab, KI, 2002

**30% citrate lock prevents CRB**

- **Preliminary report compared 30% citrate lock to heparin.**
- **CRB rate per 1000 catheter days:**
  - –1.3 vs 3.4

Allon, 2005
Gentamicin lock prevents CRB

CRB rate per 1000 catheter days:
0.3 vs 4.2
Dogra, JASN, 2002

0.3 vs 4.0
McIntyre, KI, 2004

But gent/citrate lock increases frequency of antibiotic-resistant Staph epi

Guerraoui et al, ASN abstract, 2004

EMERGENCE OF GENTAMICIN-RESISTANT BACTEREMIA IN HEMODIALYSIS PATIENTS RECEIVING GENTAMICIN LOCK CATHETER PROPHYLAXIS

Stephen Sweet¹, Stephen Gobeille³, Gregory Braden. ¹ Renal Division, Baystate Medical Center, Springfield, MA; ³ Division of Infectious Disease, Baystate Medical Center, Springfield, MA; ² Western New England Renal and Transplant Associates, Springfield, MA.

NKF Presentation, March, 2009

Over a 4 year period, beginning in October 2002, we initiated a gentamicin/heparin lock (GHL) protocol in 1488 chronic hemodialysis patients receiving dialysis through a tunneled catheter in 8 outpatient units. CRI rate decreased from 17 to 3.7 events per 1000 catheter days.

Beginning 8 months after initiation of the GHL protocol, febrile incidents occurred in 17 patients with 26 episodes of coagulase negative Staphylococcus aureus resistant to gentamicin. Over the 4 years of GHL use, an additional 8 patients developed 10 episodes of gentamicin-resistant CRI...

Due to these events, the GHL was discontinued in 2006. While the use of a GHL effectively lowered the CRI rate in our dialysis population, within 8 months gentamicin-resistant CRI emerged.
Published Clinical Use of Citrate

- Used in blood products and plasmapheresis and infused with no adverse events
- Even at lower concentrations 1% to 4%, citrate is as effective as heparin as an anticoagulant
- Numerous catheter lock studies with concentrations of 1% to 46.7% reported no significant adverse events
- One 10 ml injection of 46.7% solution resulted in severe cardiac arrhythmias.

Symptoms of Citrate Infusion Beyond Optimum Dose- Animal Studies

Trisodium Citrate 4%: maintains catheter patency better than heparin

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Heparin</th>
<th>Citrate 4%</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVC exchange</td>
<td>2.98/1000 days (HP) vs 1.65/1000 days (CP) (P = 0.01);</td>
<td></td>
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<tr>
<td>TPA use</td>
<td>5.49/1000 (HP) vs 3.3/1000 days (CP) (P = 0.002)</td>
<td></td>
</tr>
<tr>
<td>Anticoagulant</td>
<td>81 vs 79</td>
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</table>

CVC exchange 2.98/1000 days (HP) vs 1.65/1000 days (CP) (P = 0.01);
TPA use 5.49/1000 days (HP) vs 3.3/1000 days (CP) (P = 0.002)

Or is equal to heparin in maintaining patency...

Or at least doesn’t cause systemic anticoagulation...

The rate of flow-related catheter exchange was not different during the two periods (1.81 vs 1.88 per 1000 catheter days, P = 0.89).
Falsely elevated INR values were eliminated with citrate
Rate of rt-PA treatments was similar during the two periods (4.1 vs 3.23 per 1000 catheter days respectively, P = 0.07).
The number of bacteremias was similar during the two periods (0.77 vs 0.94 per 1000 catheter days respectively, P = 0.36)

Antibacterial-Antithrombotic Catheter Lock-Design Objectives

Desired properties:
- Anticoagulant properties comparable to heparin.
- Components previously approved for IV administration
- Safety for use prophylactically, with infusion of both lumen volumes.
- Ability to kill planktonic bacteria and fungal strains within 60 minutes.
- Ability to kill sessile bacteria in biofilm.
- No known bacterial resistance to components.
- Not an antibiotic
Relative density of 1.040 which is ≈ to blood of a typical dialysis patient (sodium citrate 7%).
Zuragen® Lock (an investigational device)

- Sodium Citrate 7%, Methylene Blue 0.050%, and 0.165% parabens.
- Density same as blood, 1.040.
- To be used as routine catheter lock instead of heparin.
- In vitro data showing eradication of all planktonic and biofilm bacteria in one hour.
- Similar solution (methylene blue/4% citrate) has been used for catheter salvage for 5 years in our practice, acceptable results.

Properties / Mode of Action

Methylene Blue

- Antiviral / Antimicrobial activity; a weak antiseptic
- Photosensitizer – light enhances antimicrobial properties
- Red-ox potential - can alter respiratory mode in bacteria
- May increase the permeability of cell wall and change the potassium flux of bacteria

Published Clinical Uses of Methylene Blue

<table>
<thead>
<tr>
<th>Disease Treated</th>
<th>MB Dose</th>
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<tbody>
<tr>
<td>Hepatopulmonary syndrome</td>
<td>3 mg/kg for 15 min</td>
</tr>
<tr>
<td>Post-cardiac bypass hypotension</td>
<td>2 mg/kg</td>
</tr>
<tr>
<td>Septicemia with hypotension</td>
<td>2 mg/kg</td>
</tr>
<tr>
<td>Hemodialysis patients w/hypotension</td>
<td>1 mg/kg bolus</td>
</tr>
<tr>
<td>Parathyroid gland identification</td>
<td>5-7.5 mg/kg</td>
</tr>
<tr>
<td>Methemoglobinemia acute and chronic</td>
<td>1-2 mg/kg up to 7mg/kg</td>
</tr>
<tr>
<td>Pelvic surgical procedures (identify ureters)</td>
<td>1 mg/kg</td>
</tr>
</tbody>
</table>

Dose range for 70kg patient: 70 mg-490 mg
Zuragen – 0.05% MB in 5 ml: 2.5 mg

Properties / Mode of Action

Parabens

- Broad spectrum activity against yeasts, molds and bacteria
- Provides synergistic effect by enhancing antimicrobial efficacy
- Changes the bacteria membrane ions efflux
- Alters the permeability of cell membrane
- Upsets the osmotic gradients in bacteria

Synergistic Effect of Citrate, Parabens, Methylene Blue

Zuragen kills all planktonic organisms in presence of albumin and medium.

Comparison of Antimicrobial Effectiveness between Heparin and AAT-023
Biofilm Antimicrobial Effectiveness: S. aureus Colonization Inhibition and Elimination.

And physically eliminates biofilm from plastic surfaces

Figure 4 - Scanning Electron Microscopy (SEM) of P. aeruginosa biofilm on polycarbonate coupons before (left) and after (right) one hour of Zuragen™ treatment.

Figure 6 - Fluorescence Microscopy (FM) of S. aureus biofilm with LIVE/DEAD® BacLight™ bacterial viability dye staining. Dense biofilm with mainly live cells (green, shown on left) was drastically reduced after 1 hour Zuragen™ treatment. Remaining cells are stained red (right) indicating the anti-biofilm efficacy of Zuragen™.

Changes in the biomass contents and average thickness of S. aureus biofilm over first 60 minutes of treatment with Zuragen™

Clinical Trial Summary (Zuragen)

- Prospectively Randomized study, 415 patients with Chronic CVC, 23 centers
- Comparison lock was 5000 units (total per lumen)
- 6 months followup (mean, 3 months)
- Endpoints
  - Incidence of CRBSI (Concordant Culture from catheter and peripheral blood)
  - Incidence of catheter patency failure-catheter removal after 25% decrease in Qb<200.
- Enrollment finished 12/07, final data collected 6/08
- Findings: Statistically significant decrease in CRBSI and fewer catheter occlusions, using Zuragen

AZEPTIC™ Analysis: Time to CRBSI Events

Kaplan-Meier survival curves reinforce the statistically significant (p<0.0290) efficacy Zuragen™ Solution has in the prevention of CRBSI vs. heparin.
AZEPTIC™ Analysis: Time to Patency Failure

Kaplan-Meier survival curves reinforce the significant (p=0.0423) difference of Zuragen™ Solution in preventing catheter patency failures.

AZEPTIC™ Final Analysis

Conclusions:
- CRBSI: 69% (Definite + Concordant + Suspected) statistically significant and clinically relevant reduction with Zuragen™ injection
- Patency: No Zuragen™ failures vs. 4 Heparin failures
- Adverse Device Events: No significant concerns related to Zuragen™ therapy observed
- Deaths: 78.5% Relative Reduction in favor of Zuragen™
- Composite Endpoint Analysis: p=0.0002 favoring Zuragen™

The Prospective Final Data Analysis Demonstrates Statistically Significant and Clinically Relevant Results In Favor Of Zuragen™

Note on Heparin Lock Concentrations

- 5000 unit/ml heparin has a lower incidence of catheter clotting and tPA use
- 1000 unit/ml heparin has a lower incidence of systemic bleeding
- The lower dose is now recommended for Fresenius and Satellite Units, and is the most common choice
- Position paper by ASDIN in 2008 favors the lower heparin concentration, with 4% sodium citrate as alternative (Semin. Dial. 2008 (5), Sep-Oct)
- Allergic responses were to a contaminant, now there are ongoing evaluations for purity, but with these the cost of heparin is higher

Conclusions: catheter lock options for tunneled CVC for dialysis in 2009

- Routine catheter lock-1000 units/ml heparin
- Catheters with flow problems-5000 units/ml heparin and tPA intermittently
- Salvage of catheters with apparent CRBSI-heparin/antibiotic or 4% citrate/antibiotic
- Prevention of CRBSI if rate in unit is high- Implement KDOQI catheter care recommendations
- For patients at high risk CRBSI-heparin/antibiotic or 4% citrate/antibiotic may be recommended
- Heparin sensitive patients-4% sodium citrate
- Near Future-Zuragen™ may be a routine catheter lock option

Thanks for the attention....
The Effect of Catheter Coatings on Infection and Patency

Amy Dwyer, MD
Assistant Professor of Medicine
Director, Interventional Nephrology
University of Louisville

Catheter Statistics
- Almost 21% prevalent dialysis patients in the US use a catheter as their only vascular access
- Use of catheters within first 90 days 60%
- Relative risk of death is 3 times greater with a catheter compared to an AV fistula
- Complications due to dialysis catheters cost more than $1 billion annually

Causes of Catheter Failure
- Infection
- Thrombosis
- Fibrin Sheath

Biofilm Formation
- Attachment of Bacteria
- Bacteria Proliferation
- Secretion of Polysaccharide Matrix
- Attachment of Other Organisms

Chan and Nuñez, Advances in Nephrology, September 2009
Manierski and Besarab, Advances in Chronic Kidney Diseases, 2006
Allon AJKD, 2004
Rayner et al. AJKD, 2004
Centers for Disease Control and Prevention
Pathology of a fibrin sheath

- Smooth muscle cells
- Collagen
- Endothelial cells
- Bacteria
- Fibrinogen
- Lipoproteins
- Albumin
- Coagulation factors
- Inflammatory cells

Chan, Seminars in Dialysis, 2008

Catheter Coating Types

- Antibiotic
  - Minocycline/Rifampin
  - 5-Fluorouracil

- Antiseptic
  - Chlorhexidine + heparin
  - Silver sulfadiazine
  - Silver or other metals

- Antithrombotic
  - Heparin

Critical Care Catheters

- Minocycline/Rifampin
  - ½ life = 25 days

- Chlorhexidine-Silver Sulfadiazine
  - ½ life < 14 days

Critical Care Literature

- Systematic review 37 randomized, controlled trials involving 11,568 patients
- Coated vs. non-coated catheters
- Coated vs. coated catheters
- Do coated CVC reduce:
  1. CRB?
  2. Bacterial colonization?

Gilbert and Harden, Curr Opin Infect Dis, 2008

Forest plot of meta-analysis showing the effect of impregnated or coated cvc on CRB
Study Conclusions

- For central venous catheters in ICU patients, best options for reducing infection—
  - Heparin coated catheters
  - Antibiotic coated catheters

In addition...

- Cost effective
  - If the incidence of bloodstream infections > 3.3/1000 catheter-days
- For every 300 catheters used
  - Approx $60,000 would be saved
  - 7 CRB and 1 death prevented

Coated hemodialysis catheters?

Coated, non-tunneled hemodialysis catheters

ARROWGard Blue®
• 12 and 14 French
• 13, 16, 20 and 25 cm
• Chlorhexidine-SS
- Exterior of catheter only

Heparin Coated
• 12 French, 16 cm
• Heparin bonded
• Internal & external surfaces

No clinical trial data using these catheter coatings in dialysis patients.

Coated, tunneled hemodialysis catheters

Chatzinikolaou et al., 2003
minocycline/rifampin (Cook Medical)

- 130 Patients
- 66 patients minocycline/rifampin (treatment group)
- 64 patients non-coated catheter (control group)
- Followed until catheter removed

+0 episodes bacteremia
• 13 (20%) colonizations

7 (11%) episodes bacteremia
16 (25%) colonizations

CONCLUSION:
Minocycline/rifampin coated catheters decreases risk of catheter-related infection (p = 0.006).
Trerotola et al., 1998 Silvergard® (MedComp)

91 Patients

47 patients silver-coated catheter (treatment group)
44 patients non-coated catheter (control group)

Followed until catheter removed/exchanged.

4 episodes bacteremia (0.16 infection/100 catheter days)
1 exit site infection
8 colonizations

CONCLUSIONS:
Silver coating does not confer a benefit against clinical infection or colonization.

Kakkos et al, 2008

HemoSplit® (CR Bard) vs. Palindrome Ruby® (Kendall / Tyco Healthcare)

14.5 Fr Hemodialysis Catheter

Followed until catheter removed/exchanged.

32% HemoSplit catheters inserted into femoral vein
9% Palindrome catheters inserted into femoral vein

HemoSplit® vs. Palindrome Ruby®

100 Catheters in 163 Patients

100 catheters HemoSplit (control group)
100 catheters Palindrome Ruby (treatment group)

68% Internal Jugular Vein
31% Femoral Vein

Patients followed for 9,765 catheter days

32% HemoSplit catheters
18% Palindrome Ruby

Kakkos et al, 2008

• case-controlled study
• new placements/exchanges

HemoSplit® vs. Palindrome Ruby®

100 catheters HemoSplit (control group)
100 catheters Palindrome Ruby (treatment group)

68% Internal Jugular Vein
31% Femoral Vein

Patients followed for 11,173 catheter days

Jain et al, 2009

Decathlon® vs. Uncoated MedComp

14.5 Fr Hemodialysis Catheter

No clinical trial data using Emerald or Sapphire catheter coatings.

No clinical trial data using Emerald or Sapphire catheter coatings.

Decathlon® vs. Uncoated MedComp

86 catheters MedComp (non-coated)
89 catheters Decathlon (Heparin-coated)

Retrospective Data collected:
• Time to catheter removal, failure, exchange
• Infection rates
• IPA instillations
• Blood flow rates
Coated Catheters: Conclusions

- Catheter coatings are a new technology
  - Antimicrobial, antiseptic and antithrombotic
- Data supports the use of surface treated catheters in the ICU
- They may decrease complication rates and improve catheter survival in dialysis patients
- Randomized, controlled trials of all coating types are needed determine their full effectiveness
We need the damn devices, but.....

- 2-3 X increased risk of death
- 5-10 fold risk of serious infection
- Increased hospitalizations
- Decreased likelihood of adequate dialysis
- Increased number of procedures
- Serious ongoing risk of the procedures
- $1 to 1.5 Billion cost per year – direct cost of catheters is 10%

Catheters are expensive...

- 2-3 X increased risk of death
- 5-10 fold risk of serious infection
- Increased hospitalizations
- Decreased likelihood of adequate dialysis
- Increased number of procedures
- Serious ongoing risk of the procedures
- $1 to 1.5 Billion cost per year – direct cost of catheters is 10%

Catheter Technologies

- Curves and Lengths
  - Precurved; Straight; various lengths
- Coatings
  - Heparin; silver; none
- Tips – Tips with different “sizes” vary, shortest; longest (oval or round)

A Catheter for everyone, to suit every palate and preference

- Centros; Arrow
- Configurations
  - Antegrade; retrograde
- Content/Material
  - Polyurethane; Carbothane; Silicone;

Tunneled Dialysis Catheters

- Bard
  - Equilumen – Hemopet
  - Hemoray (precurved)
- Medcomp
  - Split CathII – Bioflex Tessio
- Angiodynamics
- Canto
  - Next Step – Samsung – Canon (retrograde)
  - Edge (antegrade)
- Covidien
  - Mahurkar – silicone
  - Mahurkar Maxid – Quinton Permcath – silicone
  - Tal Palindrome – silicone

What constitutes the Ideal Catheter?

- Ease of insertion/removal
- Durable and reliable, with flows of 400 ml/min for extended periods of time.
- No infection/fibrin sheath/thrombosis/stenosis
- Inexpensive

All catheters are designed to tweak flow and reduce incidence of infections, thrombosis and recirculation......

But.......???
How do Devices come to Market?

- 1976 Medical Device amendment to Food, drug, and cosmetics act
- Class III – Pose a serious level of risk. Needs a regulatory submission before can be marketed and for new devices or with significant modifications requires PMA (pre-market approval) submission
- Purpose – Demonstrate – Device is “substantially equivalent” to a predicate device (one that is FDA “cleared” or marketed before 1976)

How do Devices come to Market?

• 510(K) Approval - Compares and contrasts the “subject” and “predicate” explaining why any differences between them, if any, should be acceptable.
  - Human (clinical) data not required for 510(K) approval
  - Lab data is always required
  - FDA “clears” devices; does not “approve” in 30/90 d
- Pre Market Approval – raises the bar to demonstrate that the device (new/significantly modified) is safe and effective
  - Human data is required
  - FDA “approves” the devices
  - Manufacturers have less leeway in modifying PMA devices than they do for 510(K) approval

510 K Approval Process for Class III Devices

- Implement a Quality management system that meets the FDA Quality System Regulation (QSR) as found in 21 CFR Part 820
- Develop Clinical trial protocol and obtain Investigational Device Exemption (IDE) approval from FDA
- Conduct clinical trials, then submit to FDA for completeness review
- Prepare and submit 510(K) application and pay fee (and prepare and submit FDA submission fee)
- FDA reviews 510(K) app within 90 days and PMA app within 180 days
- Register company and all devices inocked at www.fda.gov that identifies devices released for commercial distribution
- Subject to random FDA inspection for QSR compliance

Most Tunneled Catheters are approved without the need for a clinical trial!!

How do we handle new information thrown at us?

- “All Catheters are the same – Evil”

Emotional Honesty

- “All Catheters are the same – Evil”
Scientific Honesty

- Randomized prospective trials comparing flows – 2 studies (Trerotola et al - 1999, 2002)
- Randomized prospective Trials comparing recirculation – The same 2 studies
- Randomized Trials comparing coatings – None
- Randomized Trials comparing ease of insertion – None
- *Post Approval Systematic Data Tracking Systems
- *Process improvement with redesign after 1-2 yrs

Steps for Catheter Design Improvements

- Study current catheters to determine incidence of infection, flow, recirculation, etc.
- What is the cause of failure
- Define a design that would minimize failure
- Design and construct lab prototypes
- Invitro testing – benchtop hydraulic system; computational flow dynamics or particle flow velocity measurements
- Medical Advisory Board – design review, patient benefits, anticipate problems

Steps for Catheter Design Improvements

- Production prototypes
- Test the production catheter and validate production techniques
- FDA approval – to market and test product
- Conduct pilot trial
- Randomized, prospectively, controlled trial
- Obtain early feedback
- Market to beta sites followed by larger launch
- Plan for design change 1-2 yrs after launch

The Real Technology Partnership

Catheters are Bridging and (only in some instances) Salvage Devices

Strategies for Catheter reduction
Catheters are Salvage Devices

- Catheter “dependent” patients
  - 2483 HD Patients - prevalent patients in Dallas in 2009
  - 364 patients with Tunneled Catheters
  - 114/364 patients deemed catheter dependent
- Central and peripheral venograms done on 85/114 patient at time of insertion or revision of catheters
- 24/85 had complete central occlusions on their last catheters – translumbar, azygous, JI, Femoral
- 61/85 patients had viable anatomy for AV access placement – referred for surgery

How to Implement New Technologies

Interventionalist’s Vantage Point

- Ask for scientific rigor in studies
- Flow rates over time – more than 30 days, if available
- Don’t accept – “It always works” or “Why don’t you call Dr. Soandso” or “Success is guaranteed”
- Questions to ask of yourself
  - Why am I putting the catheter in?
  - Do I have a plan in place?
  - How long is the catheter going to stay?
  - Am I doing the right thing?
- Cost Considerations

Marketing New Technologies

Can we apply lessons from the best marketing companies?

3 Basic Principles of Brand Marketing:

1. Brand Positioning and Target Grouping
2. Moving from “Product Features” to “Consumer Benefits”
3. Moving from “Product Marketing” to “Experience marketing”

Stop talking about “Product Features” talk about “Patient Benefit”

<table>
<thead>
<tr>
<th>Brand</th>
<th>Product Feature</th>
<th>Consumer Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pampers</td>
<td>Super Absorbent keeps dry longer</td>
<td>Baby sleeps soundly so does Mom</td>
</tr>
<tr>
<td>Nike</td>
<td>Superior cushioning</td>
<td>Makes you an athlete</td>
</tr>
<tr>
<td>Apple</td>
<td>Superior operating software</td>
<td>Think Different</td>
</tr>
<tr>
<td>Catheter A</td>
<td>Coating</td>
<td>Reduces infections (and insurance premiums)</td>
</tr>
<tr>
<td>Catheter B</td>
<td>Coating/bonding</td>
<td>Less infection and fibrin sheath</td>
</tr>
</tbody>
</table>

Top brands never talk about Product Features, they only talk about Consumer Benefits.

Even though you are selling to a technical audience (doctors) you should talk about eventual Patient benefit for greater communication impact – what is good for the patient is eventually good for the Doctor.
**From “Product” to “Experience Marketing”**

- Research confirms that consumers significantly prefer the taste of the same coffee in a Starbucks branded cup compared to a Plain cup. *The same coffee!*
- Providing a website/support materials (e.g. pamphlets, hotline, etc.) for patients that clearly explain the working of the device with a support group, etc. can improve the “total experience”

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**Requirements for Successful Function of a Tunneled Dialysis Catheter**

- High blood flow rates at moderate pressure drops, with few instances of outflow failure and pressure alarms regardless of patient fluid status and relationship to vein wall.
- Minimal trauma to the vein intima to avoid thrombosis and venous stenosis.
- Resistance to occlusion by fibrous sheathing.
- Prevention of bacterial migration around the catheter after placement.
- Avoidance of contamination of the catheter lumen.
- Avoidance of seepage of the outside of the catheter during bacteremia.
- Avoidance of clotting at the tip or within the catheter.
- Biocompatibility of the catheter surfaces, avoiding removal of white cells or platelets.
- Avoidance of bacterial colonization under negative pressure.
- Avoidance of kinking of catheter segments at points of bending.
- Physical strength and integrity to avoid breaks or disconnections of any component (ability to replace broken connectors is desirable).
- Resistance to antiseptic agents that might be applied at the skin exit site.
- Radiopaque appearance on X-ray for evaluation of location during placement and after use.

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**Overview of current trends in access angioplasty**

A Q Urbanes, MD  
RMS Lifeline Vascular Access  
ASDIN 6th Scientific Meeting  
20-21 February 2010
Overview

- inflation times
- conventional vs HP vs UHP angioplasty
- parallel-wire technique
- cutting balloon
- laser-assisted angioplasty
- radiofrequency recanalization

inflation times

- How long does one keep balloon inflated once effacement has been achieved?
- Does it make a difference?

inflation times and technical success

- Trerotola, 2005
  - 230 accesses (85 AVF, 138 AVG, 7 hybrid)
  - 102 PTAs (66 patent, 36 thrombosed)
  - negative association between residual stenosis and duration of inflation

- Forauer, 2008
  - 48 patients with 76 stenoses
  - 1 min vs. 3 min inflation times

<table>
<thead>
<tr>
<th>outcome</th>
<th># of stenoses</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>technical success</td>
<td>1 min (n=40)</td>
<td>3 min (n=36)</td>
</tr>
<tr>
<td>technical failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>elastic lesion</td>
<td>30 (75%)</td>
<td>32 (89%)</td>
</tr>
<tr>
<td>resistant lesion</td>
<td>62</td>
<td>62</td>
</tr>
</tbody>
</table>

- multivariate analysis (patient age, sex, access age)
  - PTA 4.7 times more likely to be successful in 3 min inflation than 1 min (p = 0.03)

inflation times & success

- nominal or working pressure
  - the pressure at which the balloon reaches it’s labeled diameter

- rated burst pressure (RBP)
  - pressure at which the manufacturer has 95% confidence that 99.9% of the balloons will not burst at or below upon single inflation
How much pressure does one need?

UHP vs. HP PTA

- 22% with 110 PTA procedures for vein-graft anastomoticstenoses
- 96% technical & clinical success

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>UHP</th>
<th>HP</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean access blood flow pre-PTA (ml/min)</td>
<td>723 ± 261</td>
<td>696 ± 243</td>
<td>0.75</td>
</tr>
<tr>
<td>mean access blood flow post-PTA (ml/min)</td>
<td>960 ± 325</td>
<td>1246 ± 376</td>
<td>0.76</td>
</tr>
<tr>
<td>mean Δ in access blood flow (ml/min)</td>
<td>264 ± 357</td>
<td>524 ± 383</td>
<td>0.14</td>
</tr>
<tr>
<td>stenosis pre-PTA (%)</td>
<td>63 ± 12</td>
<td>63 ± 16</td>
<td>0.83</td>
</tr>
<tr>
<td>stenosis post-PTA (%)</td>
<td>25 ± 11</td>
<td>16 ± 11</td>
<td>0.68</td>
</tr>
</tbody>
</table>

Pressures needed to efface waist

<table>
<thead>
<tr>
<th>Type of lesion</th>
<th># patients</th>
<th>mean # balloons</th>
<th>mean (range) pressure (atm) to efface waist</th>
<th>&gt; 15 atm (%)</th>
<th>&gt; 20 atm (%)</th>
<th>&gt; 30 atm (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVG</td>
<td>85</td>
<td>1.4</td>
<td>15.2 (2-38)</td>
<td>59</td>
<td>20</td>
<td>9</td>
</tr>
<tr>
<td>AVG</td>
<td>138</td>
<td>1.4</td>
<td>15.4 (4-35)</td>
<td>53</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Hybrid</td>
<td>7</td>
<td>1.8</td>
<td>17.1 (12-20)</td>
<td>57</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>All</td>
<td>230</td>
<td>1.4</td>
<td>15.8 (2-38)</td>
<td>55</td>
<td>8</td>
<td>3</td>
</tr>
</tbody>
</table>

Trerotola. JVR 2005; 16: 1613-1618
pressures needed to efface waist

• In our hands, UHP PTA is most often needed in – cephalic arch – vein-vein anastomoses (eg, proximal swing segment of BVT)

Is there a price to pay for UHP PTA?

• 1,985 HD access interventions with 75 ruptures in 69 patients

<table>
<thead>
<tr>
<th>type</th>
<th>type to compare</th>
<th>( \rho ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVF, overall (5.6)</td>
<td>AVG (2.8)</td>
<td>0.002</td>
</tr>
<tr>
<td>AVF, transposed (10.7)</td>
<td>AVG (2.8)</td>
<td>0.0001</td>
</tr>
<tr>
<td>AVF, in situ (3.8)</td>
<td>AVG (2.8)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>AVF, in situ (3.8)</td>
<td>AVF, transposed (10.7)</td>
<td>0.001</td>
</tr>
</tbody>
</table>


Response of rupture to treatment

<table>
<thead>
<tr>
<th>type</th>
<th>treatment success</th>
<th>treatment failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVG (n = 36)</td>
<td>26 (72%)</td>
<td>10 (28%)</td>
</tr>
<tr>
<td>AVF, overall (n = 29)</td>
<td>27 (89%)</td>
<td>12 (41%)</td>
</tr>
<tr>
<td>AVF, transposed (n = 20)</td>
<td>14 (70%)</td>
<td>6 (30%)</td>
</tr>
<tr>
<td>AVF, in situ (n = 19)</td>
<td>13 (68%)</td>
<td>6 (32%)</td>
</tr>
</tbody>
</table>


How was rupture treated?

<table>
<thead>
<tr>
<th>access type</th>
<th>successful treatment requiring stents</th>
<th>successful treatment requiring only balloon tamponade</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVG (n = 28)</td>
<td>14 (54%)</td>
<td>12 (44%)</td>
</tr>
<tr>
<td>AVF (n = 27)</td>
<td>5 (19%)</td>
<td>21 (78%)</td>
</tr>
</tbody>
</table>


treatment failure

<table>
<thead>
<tr>
<th>type</th>
<th>treatment failure rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVG (n = 36)</td>
<td>10 (28%)</td>
</tr>
<tr>
<td>AVF, overall (n = 29)</td>
<td>12 (41%)</td>
</tr>
<tr>
<td>AVF, transposed (n = 20)</td>
<td>6 (30%)</td>
</tr>
<tr>
<td>AVF, in situ (n = 19)</td>
<td>6 (32%)</td>
</tr>
</tbody>
</table>


before the cutting balloon

• was the parallel wire technique
• use guidewire as an “atherotome”
parallel-wire technique

self-reversed parallel-wire technique

Fukasawa. JVIR 2002; 13: 943-945.

available endovascular options

- stents and stent-grafts
- peripheral cutting balloon (PCB)
- laser-assisted angioplasty
- radiofrequency perforation

Fukasawa. JVIR 2002; 13: 943-945.

self-reversed parallel-wire technique

Fukasawa. JVIR 2002; 13: 943-945.

peripheral cutting balloon

- first used for dialysis-access work in 1995
- has four atherotomes 0.127mm high x 1.0 cm long
- limited sizes (up to 8mm diameter and 2cm length)
- uses a 0.018” guidewire
- differences between PCB and conventional angioplasty balloon
  - low pressures (6-10 atms)
  - short lengths (positioning)
  - slow inflation and deflation
  - multiple inflations with rotation of balloon

peripheral cutting balloon
Is PCB PTA superior to conventional PTA?

- prospective, randomized study of 340 AVG patients
- 6 mo. primary patency end-point

Where might the PCB be most useful?

- AVF stenoses tend to require higher pressures than AVG stenoses
- desire to reduce barotrauma
- most benefit when used in AVF rather than AVG?

PCB in AVF

- Singer-Jordan, 2005
  - prospective, non-controlled, non-randomized
  - 29 patients with 42 stenoses
    - 20 (69%) brachiocephalic
    - 5 (17%) brachiobasilic
    - 4 (14%) radiocephalic
  - 6 mo. primary patency 76%
PCB in AVF

• Guiu, 2007
  – retrospective, non-randomized, historical controls
  – 29 patients, all with stenoses > 2cm. long; 28/29 AVF

PCB in AVF

• Kariya, 2007
  – prospective, non-randomised, historical controls
  – 62 PCB and 52 conventional PTA patients

PCB in AVF

• Wu, 2008
  – retrospective, non-randomised, historical controls
  – 70 stenoses resistant to conventional PTA up to 24 atm
  – PCB vs. UHP (30 atm)

### Table

<table>
<thead>
<tr>
<th></th>
<th>PCB (n = 35)</th>
<th>UHP PTA (n = 35)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean procedure time (mins)</td>
<td>38.2 ± 14.6</td>
<td>35.8 ± 16.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Success rates (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Procedure success</td>
<td>100</td>
<td>97.1</td>
<td>0.99</td>
</tr>
<tr>
<td>Anatomical success</td>
<td>100</td>
<td>97.1</td>
<td>0.99</td>
</tr>
<tr>
<td>Clinical success</td>
<td>100</td>
<td>97.1</td>
<td>0.99</td>
</tr>
<tr>
<td>6 mo. primary patency rate (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Target lesion</td>
<td>71.4</td>
<td>42.9</td>
<td>0.009</td>
</tr>
<tr>
<td>Access</td>
<td>65.7</td>
<td>40.0</td>
<td>0.009</td>
</tr>
</tbody>
</table>

Wu. JVR 2008; 19: 877-883

role of PCB

• more prospective, randomized and controlled studies
• AVF stenoses most likely to benefit

laser-assisted angioplasty

• conventional lasers require high energies to remove tissue
  – generates heat; harm to surrounding healthy tissue
• Excimer
  – excited dimer
  – diatomic molecule usually of an inert gas atom and a halide anion which are bound in excited states only
  – very short lifetimes
  – dissociate releasing the excitation energy through UV photons
radiofrequency (RF) perforation

- has been used in cardiac and hepato-biliary applications
- novel application in vascular recanalization
- few case studies showing benefit
- need more studies addressing safety and specific indications for vascular recanalization
Summary

• high-pressure and ultra-high pressure PTA have resulted in clinical and technical success
• new technology or new application of existing technology needs to be systematically examined for lesions resistant to UHP PTA
• the role for cutting balloon, laser-assisted and radiofrequency-assisted angioplasty/recanalization remains to be elucidated

•MAIN SAT 09

Mapping Prior to HD Access
- Types of permanent HD access
- Comprehensive ultrasound examination
- Discuss our success with the technique
- Future directions

2 Types of Permanent HD Access
- Native arteriovenous fistulas (AVF)
  - AVF longevity > 5 yrs.
- Synthetic arteriovenous grafts (graft)
  - Graft longevity = 18 mo. – 2 yrs.
  - (Catheter)
Preferred Order of Access Placement

- Non-dominant arm, dominant arm
- AVF: Forearm, upper arm
- Graft: Forearm, upper arm
- Thigh graft
- Only six potential sites

AVF Types

- Forearm: Radial a.
  - Cephalic v.
  - Ulnar, dorsal or volar v. transposition

- Upper arm: Brachial a.
  - Cephalic v.
  - Basilic v. transposition

FA Cephalic Vein AVF

UA Cephalic Vein AVF

UA Basilic V. Transposition AVF

Graft Types - Forearm Loop

- Brachial a. ⇒ Antecubital v.

Graft Types - Upper Arm

- Upper arm straight
  - Brachial a. ⇒ Basilic v.
- Upper arm loop
  - Axillary a. ⇒ Axillary v.

Thigh Graft: SFA ⇒ GSV, CFV
U.S. Hemodialysis Patients

- 49% fistulas
- 24% grafts
- 27% catheters

Spergel, Semin Dial 2008 Nov-Dec;21(6)550-2

Surgical Pre-operative Evaluation

- Based on physical exam
  - Visible or palpable vessels
  - Arm size
  - Probability of success

US Assessment

- Feeding arteries: Size, stenosis, spectral waveform, calcification
- Potential draining veins: Size, stenosis, thrombus
- SCV, IJ Doppler waveforms
  - Central abnormality

Vascular Mapping - Arteries

- Evaluate brachial, radial arteries
  - Caudal 1/3rd
  - Look for stenosis
  - Measure diameter
  - Assess degree of calcification

Vascular Mapping Technique - CV

- Place tourniquet mid forearm (FA) (tight)
- Percuss wrist area for 2 minutes, concentrating on cephalic vein
- Measure caudal FA cephalic vein diameter

Vascular Mapping Technique - CV

- Move tourniquet cranial FA
- Measure cephalic vein diameter
  - Mid FA
  - Cranial FA
### Vascular Mapping Technique - CV
- Move tourniquet cranial upper arm (UA)
- Measure UA cephalic vein diameter
  - Caudal
  - Mid
  - Cranial

### Vascular Mapping Technique - BAV
- Leave tourniquet on cranial upper arm
- Measure basilic vein diameter
  - Caudal UA
  - Mid UA
  - Cranial UA
  - 4 cm caudal to antecubital fossa

### Cephalic Vein Not Palpable
Vascular Mapping Diameter Criteria

- Artery ≥ 2.0 mm
- Vein ≥ 2.5 mm for AVF
- Vein ≥ 4.0 mm for graft


Early Results - 52 Accesses Placed

- Δ’d surgical procedure in 16/52 (31%)
- Neg. explorations ↓ to 0/52 (11% prev.)
- BCV and/or SVC stenosis 3/5 (60%)


Vascular Mapping Long Term Results

- 217 vascular accesses / 17 months
- 139 AVF, 78 grafts
- 64% had AVF placed vs. 34% prev. (p< 0.0001)

147 Patients Known Outcomes

- Primary access failure (access never usable for dialysis)
  - 46% AVF vs. 21% graft ($p < 0.001$)

Vascular Mapping - Summary

- Double # of pts. dialyzing with an AVF
  - from 16 - 34%
- Substantially changed surgical practice
- Role in $\approx 80\%$ of all access surgery

Multicenter Trial AVF Failure Rate

- 60% failure to mature
  - Infection
  - Inadequately sized vessels
  - Inadequate arterial inflow
  - Undetected vein stenosis/ sclerosis
  - Undetected central occlusion

Future Research Needed - Function

- Assess arterial inflow
  - Measure blood flow rate
  - Ability to dilate
- Assess venous distensibility

Future Research Needed - Function

- NIH multicenter study just beginning: Hemodialysis Fistula Maturation Study (HFM)
- Observational trial of pts getting AVFs
- Evaluating variety of preoperative mapping criteria, among many other factors
- Stay tuned!

Future Research Needed

- AVF may not always be best access choice
- Grafts may be better
  - Elderly
  - Patients with short life expectancy
- More research needed!


Are We Crazy?

Jeffrey Packer, D.O., FACOI, FASN
Co-Site Director
University of Arizona / College of Medicine
Interventional Nephrology Program
AKDHC
Phoenix, AZ

Please, Don't Shoot the Messenger.....

Not a lead vest!
The Problem.....

- Prevalence of AVF in the US
  - Nationally 54.4% as of November 2009*
  - Fistula First Goals
    - 66% by 2010*
  - How can we get there?

Solutions?

- Programs like Fistula First
  - Educate those performing the procedures now

More exposure to AVF creation during surgical training
- Cannot mandate demographics or population at specific center

Mean Estimated Number of AVFs and Grafts Placed by Operator*
During Training

*Prevalence of AVF in the US

- Fistula First Website

Solutions?

- Some communities lack
  - Surgeons with vascular training
  - Surgeons with adequate understanding of dialysis
  - Surgeons with adequate dedication and focus
  - Is K/DOQI misleading?*

Have those already dedicated learn
- Interventional Nephrology, by definition, is dedicated to the vascular access!
  - Allegedly understand dialysis
  - Know the anatomy
  - Already called upon to "fix" problem AVF

*Fistula First Website

- Packer, J. "Unconventional Fistula Creation. Is K/DOQI Misleading?". ASDIN, February 2010

*DOPPS II, restricted to operators placing >1 AVF or graft in prior year
State of AVF Creation in US

- Problems with training?
  - Is learning to create a connection between an artery and a vein the only necessary skill involved?
  - Rhetorical question

- Is ongoing experience and exposure to dialysis access creation a necessary component for successful AVF creation?
- Another rhetorical question

Do some of our surgical colleagues understand the issue and are they sufficiently creative?
- Sometimes successful AVF creation requires “thinking outside the box”*
- “The ‘simple’ AV fistula is all but simple and a great challenge even for the experienced access surgeon” **
- Another rhetorical question!

---

Mean Estimated Number of Accesses Placed by Vascular Access Surgeon During Training, by Country

*restricted to surgeons who made > 1 AVF or graft in prior year;

Saran et al, Annals of Surgery

---

Average Number of Access Surgeons Per Facility and Per 100 Patients

*Packer, J. “Unconventional Fistula Creation. Is KDOQI Misleading?”. ASDIN, February 2010

**Konner, K, ASDIN, February 2008

---

State of AVF Creation in US

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- Sometimes successful AVF creation requires “thinking outside the box”*
- “The ‘simple’ AV fistula is all but simple and a great challenge even for the experienced access surgeon” **
- Another rhetorical question!
One Might Conclude:
- Some of our surgical colleagues lack sufficient training
- Some of our surgical colleagues do not perform many vascular access procedures annually

Our Solution
- Nephrologist creating AVF
  - Unusual concept in the US*
  - Not unusual in Europe and other locations

*Packer, J. "Fistula Creation by Interventional Nephrologists, the Next Generation." February, 2008

Our Solution
- Nephrologist creating AVF
  - History
    - RM
    - JP
    - SW
    - GS

Perspective*

Perspective
- Outcomes
  - 89% fistula creations are working at 2 week post-op*
  - 78.5% develop into mature fistulae suitable for cannulation*
- Nephrologist created AVF outcomes are at least equivalent to those of vascular surgeons

*Derived from Personal Communication

Nephrology versus Vascular surgery success
- 205 pts with AVFR as first access
- This represented only 69% of those mapped
- Primary success 64%

**Perspective**

- As Interventional Nephrologists:
  - We are dedicated to the Vascular access
  - We know the anatomy
  - We understand the dialysis process
  - We are called upon to deal with vascular access problems

**Training Models**

- Go to Europe *
- Be a Surgeon first (SW)
- Train with US Surgeon (RM)
- Nephrologist train Nephrologist ** (JP)

*Sreenarasimhaiah, V and Ravani, P Semin in Dial 18: 6, 2005
**Packer, J. “Fistula Creation by Interventional Nephrologists, the Next Generation.” February, 2008

**Prerequisites - My Opinion**

- Must Have “Chops”
  - Hard to define
  - Interventional skills
    - Ligation accessory vein
    - Tunnel Catheter procedures
    - + / - PD Catheter procedures

**Prerequisites - My Opinion**

- Be An Interventional Nephrologist
  - Knows the need
  - Knows the anatomy
  - Knows the physiology
  - Has seen the problems

**Prerequisites - My Opinion**

- Desire
- Commitment

**Training - What’s Needed**

- Literature review / ongoing
- Observe AVF creation
- “Learn Loupes”
- Scrub / Assist AVF creation
- Perform AVF creation under supervision
Ongoing

- Follow-up
  - Imperative that the operator follow post-op course
  - Only by assessing outcomes can one evolve
- Continuing education

Future

- ASDIN Certification?
  - We should be taking a lead role
  - Standardized practices
  - Standardized outcomes for QA

Proposed ASDIN AVF Certification Requirements*

- Basic AVF (100-150 cases)
  - Variety of simple cases
  - Distal/proximal/high forearm anastomoses
  - Evidence of creative vein/artery use
- Advanced AV Access (additional 50-100 cases)
  - Ligation /banding (? part of IN procedures)
  - Transpositions / Superficializations
  - Patch angioplasties
  - PTFE graft
  - Native vein interposition

Conclusion

- “There are known knowns. These are things we know that we know. There are known unknowns. That is to say, there are things that we know we don’t know. But there are also unknown unknowns. There are things we don’t know we don’t know.”
- Donald Rumsfeld 2002

So……..

Are we crazy?
From Training to Practice: What are the Practical Steps and Pitfalls

Jan Bijan Tawakol, MD
Dialysis Access Specialists

**Contents**

- Surgical Procedures
- Training Opportunities
- Challenges
- Obtaining Privileges
- Complications

**Surgical Procedures**

- AVF creation
- AVG placement
- Aneurysm/pseudoaneurysm surgery
- Access and/or arterial ligation
- Flow reduction surgery
- Patch grafting

**Training opportunities for AV access surgery**

- Vascular surgeon willing to train a nephrologist
- Access trained nephrologist training another nephrologist
- Access training outside of the US (France, Germany, Italy, UK)

**Challenges for the Nephrologist**

1. Limited basic surgical training and experience
2. No surgical fellowship
3. No vascular surgery fellowship
4. Limited knowledge of vascular anatomy
Surgical back-up challenges
- Vascular Surgeon back-up willing to intervene if complications occur
- Vascular surgeon willing to operate on patient previously operated on by a nephrologist
- "Turf" issues - Surgeons others than back up surgeon

Anesthesiology coverage
- Anesthesiologist must agree to sedate patient while you operate, even if you have hospital privileges

Obtaining Privileges
- Procedures performed in hospital
- Procedures performed in private access center

Obtaining Hospital Privileges
- No certification or recognition of training by societies or universities
- Credentialing based on experience, number of procedures and complications
- To be reviewed by surgical credentialing board

Complications
- Select your patients and procedures
- Pre-op and post op clinic
- Start with Radio-cephalic Fistulas and advance as you feel comfortable
- Go as far as you can handle them

Why aren’t we doing them
- Training time out of your practice
- Isolation from surgeons
- Low reimbursement
- Low confidence
- Lack of back up
- Lack of certification
Arterial Interventions

Arif Asif, M.D.
Professor of Medicine
Director, Interventional Nephrology
University of Miami, Miami, FL

Arterial Interventions

• Vascular access dysfunction
• Hand ischemia
• Renal Artery Stenosis

Asif et al: Kidney Int 2005
Arterial Stenoses

- A significant number (8-10%) of patients presenting with dialysis access dysfunction have a **pure arterial lesions**


Pathophysiology of Hand Ischemia

- Stealing of blood

Arterial stenoses

- By increasing resistance arterial stenoses can severely limit distal blood flow in a system

Arterial Stenoses and hand ischemia

- Underlying obstructive arterial stenoses as a cause of peripheral ischemia in HD patients has been documented
- Using comprehensive arteriography, these studies have reported the incidence of arterial stenosis to range from 62-100%

Does Arterial Angioplasty Work?

- Arterial Angioplasty
  - A retrospective study of arterial angioplasty in dialysis access included 10 patients with severe limb ischemia
  - 8/10 became symptoms free after the application of PTA


Hand Ischemia

- Prospective study
- Chronic dialysis patients with signs and symptoms of arterial steal syndrome were referred to interventional nephrologists
- History and physical examination was performed
- Arteriography
- Decision regarding the application of corrective treatments was based on the findings of angiography
- Both surgical and percutaneous approaches were used


<table>
<thead>
<tr>
<th>Number of patients</th>
<th>n=12</th>
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<tbody>
<tr>
<td>Age years</td>
<td>52±11</td>
</tr>
<tr>
<td>Sex</td>
<td>7 (58%)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>7 (58%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1 (8%)</td>
</tr>
<tr>
<td>Others</td>
<td>4 (33%)</td>
</tr>
<tr>
<td>Type of access</td>
<td></td>
</tr>
<tr>
<td>Atherosclerosis</td>
<td>6 (46%)</td>
</tr>
<tr>
<td>Trauma</td>
<td></td>
</tr>
<tr>
<td>Arteriovenous Fistula</td>
<td>6 (46%)</td>
</tr>
<tr>
<td>Renal artery</td>
<td>4 (33%)</td>
</tr>
<tr>
<td>Brachial Dissection</td>
<td>3 (23%)</td>
</tr>
<tr>
<td>Extirpating</td>
<td>2 (16%)</td>
</tr>
<tr>
<td>Cause of end stage renal disease</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>4 (33%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3 (23%)</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>3 (23%)</td>
</tr>
<tr>
<td>Polycystic kidney disease</td>
<td>1 (8%)</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± SD.
Hand Ischemia

- Degree of stenosis
  - (Pre PTA: 66±14%; range:50-90%)
  - (Post PTA: 12±10%; range: 0-40%)
- Axillary (n=1)
- Brachial artery (n=5)
- Arterial lesions just above the anastomosis (n=4)


Hand Ischemia

- Overall, 8/12 treated with PTA and 4/12 underwent surgical intervention
- All became symptoms free immediately after the treatment
- 11/12 are receiving dialysis using the same access
- All remain symptom free with a mean follow-up of 8.3±4 months
- There were no procedure-related complications


Generalized Arterial Disease

Cannulation

- Trans access approach
- Femoral artery approach
- Brachial artery approach
- Radial artery approach


Cannulation

- Trans access approach
- Femoral artery approach
- Brachial artery approach
- Radial artery approach
High Complication Rate

- 12% (12/103)
- Four required surgery
- Eight were minor: Four required ultrasound guided compression
- What is the long term consequences of brachial artery trauma? *Subsequent stenosis?*

Manninen et al: Radiology 2001

Radial Artery Approach

- Cannulated in a retrograde fashion.
- Has been highlighted to allow access to both radiocephalic, brachiocephalic fistulas and to the entire arterial tree of the upper extremity

Braun SD: Radiology 2001
Arterial Angioplasty Precautions

- Do not oversize the balloon
- Do not undersize the stent
- Do not use a longer balloon than you need
- Always keep the wire across the lesion, even when retracting the balloon
- Never intervene before giving anticoagulation
- Never inflate over burst pressure
- Never retract a partially inflated balloon
- Do not use bony landmarks alone to locate a stent
- Do not allow air into the arterial system

Courtesy of Alexander Yevzlin
Renal Artery Stenosis: An Interventional Nephrologist’s Perspective

Alexander S. Yevzlin, M.D.
Assistant Professor of Medicine (CHS)
Director, Interventional Nephrology
University of Wisconsin, Madison

Road Map
• Background
• Defining the Controversy
• The Nephrologists’ Perspective
• Future Directions

Background - Epidemiology
Up to 40% of selected hypertensive patients with end-stage renal disease (ESRD) have RAS.

Background – Pathophysiology of RAS
• Activation of the renin-angiotensin-aldosterone (RAA) system produces renal and systemic vasoconstriction, salt retention, and activation of the sympathetic nervous system.
• Other actions of angiotensin II (Ang II) promote pressor mechanisms, vascular remodeling, cardiac dysfunction, and tissue fibrosis.

Background – Progression of Disease
• RAS > 50% ≠ Ischemic Nephropathy (no fibrosis resulting from hemodynamic changes)
• Ischemic Nephropathy ≠ RAS > 50% (small vessel disease)
The Controversy

• To intervene or not to intervene? – that is the question… And when?

Medical Therapy

Intervention

The Controversy

• Recent guidelines from professional organizations lend support to the application of interventional-vascular procedures into the renal arteries and inclusion of renal arteriography as part of coronary angiographic procedures.*


The Controversy

• CMS commissioned an analysis of published information regarding the benefits of revascularizing the kidney for atherosclerotic RAS by the Agency for Healthcare Research and Quality.

• The results of this analysis were published in December 2006: “The available information is insufficient to support benefits regarding mortality, progressive kidney disease, or cardiovascular events.

• “Thus, the published literature cannot support the observed, massive expansion of endovascular intervention.”*


The largest portion of this increase derives from procedures undertaken by cardiologists.*


The Controversy

• During the same time interval, at least four prospective, randomized trials for atherosclerotic RAS (ASTRAL, STAR, RAVE, CORAL) were started to examine the role of medical therapy alone as compared with medical therapy plus stent revascularization.

• In the United States, the National Heart, Lung, and Blood Institute of the National Institutes of Health is funding the Cardiovascular Outcomes for Renal Atherosclerotic Lesions (CORAL) trial. *


<table>
<thead>
<tr>
<th>Study</th>
<th>1996</th>
<th>2000</th>
<th>2005</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac</td>
<td>500</td>
<td>2000</td>
<td>8000</td>
</tr>
<tr>
<td>Surgery</td>
<td>300</td>
<td>800</td>
<td>1800</td>
</tr>
<tr>
<td>Other</td>
<td>200</td>
<td>400</td>
<td>600</td>
</tr>
<tr>
<td>Total</td>
<td>1000</td>
<td>3600</td>
<td>11600</td>
</tr>
</tbody>
</table>

The largest portion of this increase derives from procedures undertaken by cardiologists.*

Why Are Nephrologists Averse to RAS Intervention?

- Nephrologists have moved toward a more conservative clinical stance in recent years, perhaps as a pragmatic counterweight to enthusiastic interventional specialties.*


Current Limitations of Our Knowledge

- It is not clear why some patients deteriorate after renal revascularization.
- The selection of patients for revascularization is controversial because of uncertainty regarding the likely outcomes.
- There is no good test to predict whose GFR will decline and whose will improve.
- Misconceptions about the natural course of CKD progression.

Risk Factors for Outcomes

- Pre-intervention GFR
- Initial size of the treated kidney
- Vascular resistive index
- Patient age
- Lateralization to the affected kidney

New Algorithm

Case Presentation: RAS

- 62 yo female with DM, RCC s/p right nephrectomy, CKD, CAD, now requiring CABG. Sent for evaluation of RAS found on MRA. Cr = 2.2.
Wire Choice

3 stages of progression of the atherosclerotic lesion:
1. Fatty streak
2. Simple atheromatic plaque
3. Complicated plaque

Anticoagulation

Coagulation cascade:
- Tissue factor
- Plasma clotting cascade
- Prothrombin
- Thromboxane A2
- ADP
- Aspirin
- Ticlopidine
- Collagen
- Platelet cascade
- Prothrombin
- Thrombin
- Fibrinogen Fibrin
- Thrombus
- Conformational activation of GPIIb
- Taciopidin
- Clopidogrel
- GPIIb/IIIa inhibitors
- LMWH
- Antithrombin
- Heparin
- Bivalirudin
- Hirudin
- Argatroban
- Thrombolitics
Advances in AVF Maturation

ASDIN 2010 Annual Meeting
Orlando, FL

Jeffrey Hoggard MD FACP FASN
Capital Nephrology Associates
Raleigh, NC

Objectives

Definition of mature AVF
Physiology of AVF maturation
Endovascular interventional procedures to improve maturation
Study of Size and Flow

- If fistula diameter was 0.4 cm or greater, the chance that it would be adequate for dialysis was 89% versus 44% if it was less.
- If fistula flow was 500 ml/min or greater, the chance that it would be adequate was 84% versus 43% if it was less.
- Combining the two variables, the chance that it would be adequate was 95% versus 33% if neither of the criteria were met.
- Experienced dialysis nurses had an 80% accuracy in predicting the ultimate utility of a fistula for dialysis.

KDOQI 2006

Rule of 6’s

- Access flow of >= 600 ml/min
- Depth of <= 6 mm from skin surface
- Fistula vein diameter of >= 6 mm
- 6 weeks after creation

What defines a mature fistula?

- Enough blood flow to avoid recirculation
- Distal limb perfusion must be maintained
- Cannulatable segment should be straight, thick-walled, superficial, adequate caliber
- Unimpeded drainage into the central veins

% Prevalent AVF as of May 2009

Fistula First Change Concepts

1. Routine CQI review of vascular access
2. Timely referral to nephrologist
3. Early referral to surgeon for "AVF" only
4. Surgeon selection
5. Full range of surgical approaches
6. Secondary AVF’s in AVG pts
7. AVF evaluation in all catheter pts
8. Cannulation training
9. Monitoring and maintenance
10. Continuing education
11. Outcomes feedback
How does one achieve a mature/functional fistula?

Preoperative plan
- Vein preservation
- Clinical exam
- Vascular mapping

Operative/surgical issues
- Surgical expertise and center effects
- Pharmacology

Postoperative follow-up/intervention

ASDIN Recommendations for venous access in CKD pts
- Use dorsal hand veins for peripheral access and phlebotomy
- Use the Internal Jugular vein for central access
- Avoid the Subclavian vein
- Avoid PICC’s (peripherally inserted central catheters)


Which CKD 3 patients need vein protection?

Relationship Between Predicted Creatinine Clearance and Proteinuria and the Risk of Developing ESRD in Okinawa, Japan

The Case for Using Albuminuria in Staging Chronic Kidney Disease

Relationship Between Kidney Function, Proteinuria, and Adverse Outcomes
JAMA 303: 423-429, 2010

Preoperative Strategy

Preservation of veins – important
Semin Dial 21: 186-191

Vascular mapping – imperative
Robbin et al. Radiology 225: 59-64, 2002
Robbin et al. Radiology 217: 63-68, 2000
Asif et al. Semin Dial 18: 239-242, 2005

Duplex sonography

Plethysmography
Comparison of Morphological and Functional Characteristics Evaluated by Duplex Sonography Before AVF Construction Between Two Groups

<table>
<thead>
<tr>
<th></th>
<th>Group A (n = 93)</th>
<th>Group B (n = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Artery baseline examination</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IDA (cm)</td>
<td>0.264 ± 0.065*</td>
<td>0.162 ± 0.066</td>
</tr>
<tr>
<td>Thickness of artery wall (cm)</td>
<td>0.0273 ± 0.015</td>
<td>0.0302 ± 0.016</td>
</tr>
<tr>
<td>QA (ml/min)</td>
<td>54.50 ± 22.81*</td>
<td>24.11 ± 16.83</td>
</tr>
<tr>
<td>RI</td>
<td>1.15 ± 0.13</td>
<td>1.16 ± 0.13</td>
</tr>
<tr>
<td><strong>Artery at RH</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IDA (cm)</td>
<td>0.294 ± 0.075*</td>
<td>0.171 ± 0.073</td>
</tr>
<tr>
<td>QA (ml/min)</td>
<td>90.52 ± 45.90*</td>
<td>3169 ± 26.82</td>
</tr>
<tr>
<td>RI</td>
<td>0.50 ± 0.13*</td>
<td>0.70 ± 0.17**</td>
</tr>
</tbody>
</table>

RI = Resistance Index  
RH = Reactive hyperemia  
N = 116

Success Rate of Newly Constructed AVFs in Patients Grouped by Morphological and Functional Characteristics of Vessels Established Before Surgery

<table>
<thead>
<tr>
<th>Vessel Characteristics</th>
<th>No. of Patients</th>
<th>Success Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IDA (cm)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;0.16</td>
<td>91 (78)</td>
<td>85/91 (93)†</td>
</tr>
<tr>
<td>≤0.16</td>
<td>25 (22)</td>
<td>8/25 (32)</td>
</tr>
<tr>
<td><strong>RI at RH</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;0.7</td>
<td>85 (73)</td>
<td>81/85 (95)†</td>
</tr>
<tr>
<td>≥0.7</td>
<td>31 (27)</td>
<td>12/31 (39)</td>
</tr>
</tbody>
</table>

† = P<0.01
RI = Resistance Index  
RH = Reactive hyperemia

Forearm Venous Distensibility Predicts Successful Arteriovenous Fistula
Joke van der Linden et al. AJKD 47:1013-1019, 2006

Measured with strain gauge plethysmography
Choice of surgeon and surgical center:


Pharmacological Dialysis Access Consortium (DAC)
887 pts RCT (multi-center, double-blinded) of clopidigrel (Plavix) 75mg daily x 6wks vs placebo

<table>
<thead>
<tr>
<th></th>
<th>Thrombosis</th>
<th>Suitability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clopidigrel</td>
<td>12.2%</td>
<td>61.8%</td>
</tr>
<tr>
<td>Placebo</td>
<td>19.5%</td>
<td>59.5%</td>
</tr>
</tbody>
</table>


AV Fistula

Primary failure rate

40%

Physiology of maturation

Blood flow in artery baseline: 60 cc/min
One day after avf creation: 400 cc/min
30 days after                       500 800cc/min
90 days                                   same

Robbin et al. Radiology 225: 59-64, 2002

When to intervene

KDOQI 2006 update: CPG 3.2

“At a minimum, all newly created fistulae must be physically examined by using a thorough systematic approach by a knowledgeable professional 4 to 6 weeks postoperatively to ensure appropriate maturation for cannulation.”

Causes of fistula immaturity or “early failure”

Arterial Disease and Stenoses
Juxta-anastomotic lesions
Venous Disease and Stenoses
Thrombosis
Accessory veins
Vein is deep or tortuous
Surgical Salvage options

1. Excision of stenotic lesion with simple primary vein re-anastomosis
2. Patch or interposition vein segment
3. Prosthetic segment
4. Penumilization of arterial inflow
5. Superficialization
6. New AVF in a new location

See references

Endovascular Salvage procedures for immature avf

<table>
<thead>
<tr>
<th>salvage rate</th>
<th>primary patency rate</th>
<th>multiple patency rate</th>
<th>pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beathard 2003</td>
<td>82%</td>
<td>75%</td>
<td>78%</td>
</tr>
<tr>
<td>Nassar 2006</td>
<td>83%</td>
<td>65%</td>
<td>73%</td>
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<tr>
<td>Clark 2006</td>
<td>88%</td>
<td>34%</td>
<td>42%</td>
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<tr>
<td>Falk 2006</td>
<td>74%</td>
<td>nana</td>
<td></td>
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<tr>
<td>Song 2006</td>
<td>95%</td>
<td>28%</td>
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<tr>
<td>Miller 2009</td>
<td>96%</td>
<td>39%</td>
<td>na</td>
</tr>
</tbody>
</table>

Endovascular Interventional Procedures

Angioplasty
PTA of stenoses
BAM (balloon angioplasty maturation)
Stents
Thrombectomy
Coil embolization or ligation of accessory veins
Flow re-routing

Aggressive approach to salvage non-maturing avf:
A retrospective study with follow-up.

Sheathless access
Staging procedures
Long balloon lengths (8-10 cm)
Controlled arterial inflow to limit extravasation

Highlights:
118/122 successful fistula maturations
1.6-2.6 mean # procedures/per fistula
Secondary patencies 72-77% at 12 months

Percutaneous dilation of the radial artery in nonmaturing autogenous radial-cephalic fistulas for hemodialysis

74 consecutive patients: 2002-2008, single center France
69% DM
23% resolvers
64% CAD
46% PAOD
32% lower limb amputations

102 pts excluded had arterial anastomotic lesions = surgical revision
321 pts excluded had only venous stenoses or thromboses.
Highlights

Technical success 73/74 cases
PTA ruptures 11 (17%)
2 mean repairs
Hand ischemia 5 (7%) distal radial artery ligation
Assisted patency 12 months
96% 94%

Highlighted:

No sedation, only local lidocaine
90% diluted contrast for 6 pts not on dialysis
Brachial and radial arterial cannulations were the most common accesses for the procedures
6F sheaths
No anticoagulant
Frequent saline flushes
Tourniquet to decrease arterial pressure

"All arterial stenoses dilated to 4mm at 25atm"
- cutting balloon PTA refractory lesions
Mean artery stenosis length 6.8 cm

Juxta-anastomotic stenosis

Percutaneous transluminal angioplasty

Post Angioplasty
Figure 1. A sample of two vascular lesions that were encountered during salvage procedures on “failing to mature” arteriovenous fistulas (AVF).

Mid cephalic vein fistula severe stenosis

Post Angioplasty

Accessory vein

Catheter in place

Coil in place
Final Result

Immature RC AVF

Stenosis resolved

Radial artery stenosis

PTA of the radial artery

Stenosis resolved
Conclusion and Summary

AVF: Primary Failure Rate 40%

Pre-operatively:
- continued vein preservation strategy
- better refinement of our mapping

Operative/Surgical:
- new drug/molecules therapies (pancreatic elastase—induces vein dilatation by promoting breakdown of collagen)

Post-operatively:
- endovascular interventions when applied appropriately and judiciously can be very successful in converting the immature fistula into a functional HD access

Fistula First: Impact on AVF, AVG and Catheters
An Update

Anil K. Agarwal, MD, FASN, FACP
Professor of Internal Medicine
Director, Interventional Nephrology
The Ohio State University College of Medicine and Public Health
Columbus, Ohio
Objectives

- Provide background of Fistula First Breakthrough Initiative
- Discuss improvement in AVF rates with FF
- Describe impact of FF on AVG and Catheters
- Has FF increased catheter rates?
- Consider strategies to achieve goals of ‘Fistula First and Catheter Last’


Fistula First: History

- FF Breakthrough Initiative sponsored by CMMS
- Also known as National Vascular Access Improvement Initiative (NVAII)
- Developed in 2003, launched in 2004 through 18 ESRD networks nationwide

FF: Key Recommendations

- Autogenous AVF is the most optimal access for hemodialysis (HD)
- FF did not advocate ‘Fistula for All’, only a consideration and placement of AVF when feasible
- FF ‘Change Concepts’ included catheter reduction strategies, recommending:
  - ‘AVF placement in patients with catheters when indicated’
  - It was the expectation that the AVF will increase, and the catheters will be reduced

FF: Impact on AVF

- Achieved goal of 40% prevalent AVF in 2005- ahead of 2006 schedule
- In first 4 years of FF initiation, by January 2008, AVF prevalence increased by ~50% (from 32% to 49%)
- New stretch goal of 66% prevalent AVF by 2009- considered conservative in comparison to many other developed countries
- Prevalence of AVF is continuing to rise with some variation among the networks

Fistula Rates By Network: 2002 and 2008
Prevalent AVF: Nov 2009 (FF Dashboard)


State of Access:
August 2009 (FF Dashboard Summary)

Incident Catheters: USRDS 2009 Report

Incident Accesses: 2008 (FF Dashboard)

Tunneled Catheter: No TIME safety
Central Vein Stenosis & Infection
Has the Fistula First Breakthrough Initiative Caused an Increase in Catheter Prevalence?

Lawrence M. Spergel, Clinical Chair, A-V Fistula First Breakthrough Initiative
Dialysis Management Medical Group, San Francisco, California

Seminars in Dialysis
Vol 21, No 6 (November-December)
2008 pp. 550–552

Catheter Rates Around FFBI Inception

Continuing Impact of FF On Access Type

Barriers to Catheter Reduction

SPECIAL ARTICLE

Balancing Fistula First With Catheters Last

Eduardo Lacson Jr, MD, MPH, J. Michael Lazarus, MD, Jonathan Himmelfarb, MD, T. Alp Ikizler, MD, and Raymond M. Hakim, MD

American Journal of Kidney Diseases, Vol 50, No 3 (September), 2007, pp 379-395
Suggestions to improve AVF rates

• Focus on early creation of AVF in late CKD
• Early salvage of ‘non-maturing’ AVF
• Maintenance of AVF by dialysis staff and the interventionalist if needed
• Creation of Secondary AVF
• Avoidance of placing catheters
• Removing the catheters as soon as possible
• Use of alternative ‘bridges’ to AVF- PD, AVG

SUMMARY

• FFBI has significantly impacted the culture of vascular Access in US
• AVF rates have increased and continue to improve across all the networks
• AVG rates have decreased
• Catheter rates have remained stable
• Reinforced strategies- including pre- dialysis AVF placement, early intervention for non- maturing AVF and placement of secondary AVF will be needed to improve AVF rates further

SUMMARY

• Emphasis on catheter reduction is becoming the new focus in conjunction with improving AVF utilization
• Strategies for ‘Fistula First’ must continue to be balanced with ‘Catheter Last’ approach

MAIN SAT 16
Vascular Access & Mortality

Monnie Wasse, MD, MPH
Emory University
Renal Division & Interventional Nephrology

Financial disclosure: None

Vascular Access & Mortality

- Cause of death
  - infection
  - cardiovascular
  - all-cause
- Other factors to consider

Infection-related death by vascular access type

- CVC vs. AVF: OR=3.0
  - Diabetics: CVC vs AVF: OR = 10.1
  - CVC vs. AVG: OR=2.2
  - AVF=AVG

2002, Pastan et al: Network 6, n=7500 prevalent patients

Infection-related death by vascular access type

- CVC’s are associated with significantly greater risk of infection & infection-related hospitalization than AVF and AVG
- AVG vs. AVF:
  - AVG infection rate 9.5% vs. 0.9% in AVF (p<.001) ¹ in retrospective study n=1700
  - AVG infection-related hospitalization is greater than AVF²
- Non-diabetic AVF and AVG patients have similar risk of infection-related mortality

¹ Schild, 2008, J Vasc Access; ² Pisoni, 2009, AJKD
Catheters are associated with increased infection-related hospitalization & death

Cardiovascular-related death by vascular access type: Incident patients

- At Dialysis initiation
  - AVF = CVC
  - AVG = CVC
  - Lack of association likely due to high rate of death within first 90 days from other causes

- 90 days after dialysis start
  - AVF vs CVC: HR = 0.69
  - AVG = CVC
  - Possibly related to reduction in systemic inflammation

2008, Wasse et al, USRDS CPM data, n=4854 incident patients

Cardiovascular-related death by vascular access type: Prevalent patients

- Non-diabetic
  - CVC vs AVF: RR = 1.38
  - AVG = AVF

- Diabetic
  - CVC vs AVF: RR = 1.85
  - AVG vs AVF: RR = 1.35

2001; Dhingra et al, USRDS n=5500 prevalent patients

Cardiovascular-related death by vascular access type

- Incident ESRD patients
  - CVC use increases risk of CV-related death 90 days after dialysis start
  - No difference in CV-death between AVF and AVG

- Prevalent ESRD patients
  - CVC use has greatest risk of CV-related death, followed by AVG use among diabetics
  - No difference in CV-death between non-diabetic AVF and AVG users

Vascular access & all-cause mortality

- Non-diabetic
  - CVC vs AVF: OR = 1.7
  - AVG = AVF

- Diabetic
  - CVC vs AVF: OR = 1.54
  - AVG vs AVF: OR = 1.4

2001; Dhingra et al, USRDS n=5500 prevalent patients

Vascular access & all-cause mortality

- CVC vs AVF: 40% greater risk of death
- CVC vs AVG: 30% greater risk of death
- AVF = AVG
- Diabetics had no increased risk of all-cause death

2002, Pastan et al: Network 6, n=7500 prevalent patients
Vascular access & all-cause mortality: Older patients

- CVC vs. AVF:
  - OR=2.15 (90 days)
  - OR= 1.85 (6 months)
  - OR= 1.70 (1 year)
- CVC vs. AVG: 46% increased risk of death
- AVF=AVG

2003, Xue et al; Medicare incident, n=66,600 ESRD patients > 67 yo

Vascular access & all-cause mortality

- CVC vs AVF: RR 1.32
- AVG vs AVF: RR 1.15 (P<.001)

Pisoni, 2009, DOPPS data, 28,200 ESRD patients

What about change in vascular access & all-cause mortality?

- Change from CVC to permanent access
  - When transitioning from CVC to either AVF or AVG, reduced mortality by 21%
  - Change from AVF or AVG to CVC increased risk of mortality by more than 2-fold (HR 2.12, P < 0.001)

2009 Lacson et al, Fresenius n=79,500 ESRD patients

Vascular access & all-cause mortality

- CVC patients have increased risk of infectious, cardiovascular and all-cause death compared with AVF and AVG users
- Change from CVC to permanent access reduces all-cause mortality
- AVG vs AVF patients?
  - Diabetics with AVG have greater all-cause mortality than AVF patients
  - No difference in patients > 67 yo

Additional factors to consider: QOL

- Quality of life
  - Random sample 1563 incident ESRD patients
    - AVF, AVG QOL > CVC QOL
    - Better health perception, energy, sleep and lower burden of ESRD on daily life with AVF vs. CVC
    - Better energy, lower burden ESRD on daily life among patients with AVG vs. CVC
    - No significant differences in QOL between AVF and AVG patients

1Wasse et al, CJASN, 2007

Additional factors to consider: cost

- 2010 USRDS Annual Data Report
  - per person per year total costs
    - CVC $79,364
    - AVG $72,729
    - AVF $60,000
Conclusion

Vascular access type influences mortality; CVC’s are worse in every metric
AVF and AVG are comparable in cardiovascular mortality among non-diabetics, QOL

Academic collaborations

Bryan Neil Becker, MD, MMM, FACP
For the annual meeting
American Society of Diagnostic and Interventional Nephrology
2010

Disclosures

• President, National Kidney Foundation
• Funding, National Institutes of Health

OBJECTIVES

Understand a framework for looking at academic societies and other specialty organizations
Examine value of collaborative efforts between specialty or other healthcare society organizations
Identify obstacles that alter the potential effectiveness of specialty or other healthcare society organizations in collaboration
Review possible approaches to collaboration that focus on success—“win-win” situations for the collaborating groups

Professional organizations in healthcare

Different missions
Different organizational structures
Different foci
Different people
Where collaboration might not work

Leadership-specific agendas

Super sub specialty issues

Complex issues

Contradictory goals and objectives

How collaboration might start?

Organizations address an issue

Organizations assess the issue

Organizations look for partner groups who might share perspective

Organizations determine whether they are aligned
ASDIN:
To promote the appropriate application of new and existing procedures in order to improve the care of patients with kidney disease.

NKF:
Enhancing the lives of everyone with, at risk of or affected by kidney disease

HOW IT MIGHT WORK

Collaboration

Successful collaborations
Keeping a 30,000 foot perspective even as we focus on the road
Find areas of alignment
Recognize inter-group differences and respect them
Maintain professionalism
There will be another issue tomorrow

• MAIN SAT 17
LOBBYING EFFORTS AND COALITION BUILDING

Edward R Jones, MD
President, Renal Physicians Association

DEFINITION

- **Lobbying** is an attempt by an individual or an organization to influence public policy decision.

- **Coalitions** refer to bringing organizations and groups together to develop a consensus on topics common to each group.

Examples of Success

- Radiologists in ‘60s avert designation of hospital services.
- Averting the double digit cuts in Medicare reimbursement
- Funding for demonstration projects for Patient Centered Medical Home
- The dialysis organization pilgrimage to get an annual update
- MIPPA legislation including CKD education benefit and statutory annual update to dialysis reimbursement

BARRIERS

- Physicians not trained to lobby or build coalitions
- Physicians mistrust politicians and lobbyists
  - Considered peddling or “special interest groups”
  - Concern that politicians are not physician friendly
- A *General misunderstanding of the political process*
- Doctors in aggregate: disorganized compared to insurance lobby, hospital, lawyers etc.
- “Circle the wagons and fire inward” approach
  - PCP and specialists, Proceduralist vs. cognitive physicians, and coalition members with self interest
  - Results in divide and conquer approach by congress, the agency and others
- Reluctance to make financial contributions or make visits to legislators
- Generally, knowledge deficit on some critical policy that affect physicians
  - only 30% of medical directors understand bundling
  - only 30% of young nephrologists understand need to engage in political process
CURRENT COALITIONS, Lobbyists AND PACS
- Kidney Care Partners is a coalition of over 30 organizations from the renal community.
  - Utilize Lobbyists and Marketing and a PAC to accomplish goals
  - Successful in writing legislation and accomplishing goals: CKD education, increased reimbursement, quality agenda, etc
- Vascular access coalition
- RPA PAC successful and has opened doors
- AMA
- ACP

ATTRIBUTES OF LOBBYING
- Provide access to legislative and regulatory agencies—should be able to get appointments, etc
- Education of policy makers about issues and constituent views.
  - Provide data, technical information and statistics
- Act as Effector arm of organization—gather information on what is happening and can be influence e.g. MIPPA legislation, bundling of drugs, etc

EFFECTIVENESS
- Core ideology with palpable intensity of devotion.
- Critical to form a strong consensus e.g. KCP and Access Coalition vs. AMA
  - CMS and Congress will divide and conquer.
  - Can agree to disagree but can’t politic for it
- Need leadership particularly by physicians
- Must relate to quality and access
- Personalize the message.
- Patients role is underestimated
- Must develop relationships over long haul
  - Use of direct and indirect lobbying

COALITIONS
- Have demonstrated success e.g. KCP
- Require strong lobbyist and marketing effort
- Require leadership to bring consensus
- Can be recognized as resource to legislative, regulatory and executive agencies
- RPAs political footprint enhanced by lobby effort and coalition participation
  - Recognized as “go-to” organization on quality and reimbursement in the renal community

Methods of Lobbying
- Direct Lobbying
  - Direct communication with policymakers
  - Must be knowledgeable about topic—do homework and be prepared
  - Must understand the political process, legal nuances pertaining to the group’s issues and in public relations
  - As or more important to meet with staffers—they are more knowledgeable e.g. Grassley, etc

INDIRECT LOBBYING
- Grass roots effort to mobilize individual outside policy-making community
- Generate influence in the home districts
- Direct meeting on local level, emails, Cap wiz but not mass correspondence
- Use of media, editorial writing, etc
- Sponsoring events in home districts
SUCCESS FACTORS

- Must meet with policy makers or their staff both in DC and at local level
- Develop long term relationship
- Recognize importance of preventing unwanted legislation vs. new policies e.g. AMA
- Insertion of language that is favorable for future action is a success e.g. language re ACO.
- Financial contributions critical PACs are necessary
  - One study: ROI of 200%
  - e.g. MIPPA-dialysis reimbursement

FAILURES

- Can’t be episodic
- One tract emphasis on reimbursement not tied to quality — real or perceived
- Not being prepared when meet with policy makers
- Fragmentation within Coalition

SUMMARY

- Lobbying, Coalitions and PAC are not dirty words
- Nephrologists and all physicians must engage in the process visits necessary
- Long term relationships, personalized message and talk about more than reimbursement
- Financial contributions directly or through a PAC are critical

Messages from the best lobbyist for their wants and needs

- Maddie “Pop, I want a new doll”
- Kyle “Poppi more toys”
- Dad “tuition fund”

•MAIN SAT 19
Nephrology Focused Practice and Subspecialty Options
Stuart Linas M.D.
Chair, Nephrology Board ABIM
February 2010

Certification Exam Pass Rates
(for first-time takers)

<table>
<thead>
<tr>
<th>Year</th>
<th>N</th>
<th>Percent passing</th>
</tr>
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<tbody>
<tr>
<td>2004</td>
<td>377</td>
<td>91%</td>
</tr>
<tr>
<td>2005</td>
<td>395</td>
<td>92%</td>
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<tr>
<td>2006</td>
<td>421</td>
<td>93%</td>
</tr>
<tr>
<td>2007</td>
<td>399</td>
<td>92%</td>
</tr>
<tr>
<td>2008</td>
<td>402</td>
<td>91%</td>
</tr>
</tbody>
</table>

Mean Equated Scores by Program Director Rating

2008 Nephrology Certification Exam – first-time takers

First-year Nephrology Fellows by Gender

- Female
- Male

First-year Nephrology Fellows by Medical School

- Osteopathic
- International
- U.S./Canadian

2009-2010 ABIM Subspecialty Board on Nephrology

- Arnie Berns
- Connie Davis
- David Ellison
- Fernando Fervenza
- Alp Ikizler
- Stu Linas (Chair)
- Biff Palmer
- Mark Perazella
- Elaine Worcester
Certification Exam Pass Rates

First-time taker Pass Rate by Medical School

![Graph showing pass rates for US/Canadian and IMG/DO medical schools.]

Maintenance of Certification (MOC) Exam Pass Rates
(for first-time takers with valid 10-year certificates)

<table>
<thead>
<tr>
<th>Year</th>
<th>N</th>
<th>Percent passing</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
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<td>90%</td>
</tr>
<tr>
<td>2005</td>
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<td>88%</td>
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<tr>
<td>2006</td>
<td>284</td>
<td>85%</td>
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<tr>
<td>2007</td>
<td>162</td>
<td>86%</td>
</tr>
<tr>
<td>2008</td>
<td>207</td>
<td>86%</td>
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</table>

Computer-Based Testing Satisfaction Survey Responses

Fall 2008 Certification and Maintenance of Certification Examinations
Percentages are sums of negative ratings (Strongly Disagree + Disagree)

<table>
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<tr>
<th>Statement</th>
<th>All Exams (N=12,445)</th>
<th>Nephrology (N=556)</th>
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<td>1. Scheduling a test center seat with Pearson was easy</td>
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<td>1%</td>
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<tr>
<td>2. The distance I had to travel to the test center was reasonable</td>
<td>7%</td>
<td>8%</td>
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<td>3. The test center was easy to find</td>
<td>8%</td>
<td>8%</td>
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<td>4. The test saddles and seats were comfortable</td>
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<td>7%</td>
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<tr>
<td>5. The test environment was quiet</td>
<td>8%</td>
<td>7%</td>
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<tr>
<td>6. The test environment was comfortable</td>
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<td>7%</td>
</tr>
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<td>7. The test environment was studious</td>
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<tr>
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</tr>
<tr>
<td>9. The exam was too long</td>
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<td>12. The on-site assistance was adequate</td>
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<tr>
<td>13. The tutorial was easy to use</td>
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<td>0%</td>
</tr>
<tr>
<td>14. The navigation throughout the examination was easy</td>
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<td>0%</td>
</tr>
<tr>
<td>15. The examination was a fair assessment of clinical knowledge in this discipline</td>
<td>0%</td>
<td>0%</td>
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</tbody>
</table>

Additional Nephrology ‘recognition’

Process for Approving New Nephrology Subspecialties

- Request submitted to ABIM from specialty society or other external group
- ABIM Nephrology Board
- ABIM BOD
- ABMS BOD
- ABMS Assembly
- ABMS Committees on Certification, Subcertification, and Maintenance of Certification (COCERT)

Note: Input from external stakeholders (e.g., relevant societies, other ABMS Boards) is sought throughout the proposal development and review process. Revisions to the application may be required in order to be forwarded to the next stage of approval.

Process for Exploring New Disciplines within Nephrology

- Review by the ABIM Subspecialty Board on Nephrology. If the Nephrology Board approves the proposal, it is then forwarded to the ABIM Board of Directors.
- ABIM would seek support from the Nephrology and Internal Medicine communities at large.
- With community support and approval by the ABIM Board of Directors, the new discipline would then need to be approved by the American Board of Medical Specialties (ABMS). Minimum 1 year.
Criteria for Recognition as Subspecialty Certification

- Requires a unique body of knowledge that cannot be fully incorporated into the “parent” discipline
- Has clinical applicability to be practiced in a form distinct from the “parent” discipline
- Contributes to the scholarly generation of new information, and advances research in the field
- There is an important social need for the discipline and evidence that its practice improves patient care

continued...

Criteria for Recognition as MOC Focused Practice

- Body of knowledge is a component of the “parent” discipline (nephrology)
- Large numbers of nephrologists focus their practice in the discipline, while others may not practice the discipline at all
- There is an important social need for the discipline and evidence that its practice improves patient care

continued...

Subspecialty vs. Focused Practice

<table>
<thead>
<tr>
<th>Criteria for Subspecialty Certification</th>
<th>Criteria for MOC Focused Practice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basis for Certification or MOC Focused Practice</td>
<td>Practice is distinct from the parent discipline</td>
</tr>
<tr>
<td>Practice Adds Value</td>
<td>Large numbers of diplomates focus practice in the new field that may not focus at all</td>
</tr>
<tr>
<td>How Competence is Acquired</td>
<td>Requires supervision and direct observation of competence</td>
</tr>
<tr>
<td>Technology or Site of Care</td>
<td>Requires demonstration of self-directed, continuous learning and self-evaluation of practice over time</td>
</tr>
<tr>
<td>Impact on Parent Discipline</td>
<td>No formal training beyond initial certification requirements</td>
</tr>
</tbody>
</table>

Technology or Site of Care: Involves same technology and sites of care used by the broad discipline
Impact on Parent Discipline: The positive benefits outweigh the negative impact on the parent discipline

Certification Models for Nephrology Disciplines

“Third-Tier” Subspecialty Training Model:

- 2 years Nephrology training
- Nephrology certification
- At least 1 year sub-subspecialty training
- Certification in Nephrology sub-subspecialty

Focused Practice Model:

- 2 years Nephrology training
- Nephrology certification
- At least 3 years post-fellowship practice experience in focused practice area
- MOC in Nephrology with focused practice

Criteria for Recognition as Subspecialty Certification (cont.)

- Achieving competence requires supervision and direct observation provided in formal training settings
- Requires a minimum training period of 12 months
- The positive value of certification in the new discipline must outweigh any negative impact on the practice of, or education in, general internal medicine or an existing subspecialty
Questions?

**MAIN SAT 20**

A National Database for Dialysis Access Procedure Outcome Benchmarking

The ASDIN Access Procedure Outcomes Registry

Timothy A. Pflederer, MD
Medical Director
Renal Intervention Center
Morton, IL

Adjusted inpatient vascular access placements, by age

Total PPPY physician/supplier costs for vascular access

USRDS 2009

USRDS 2009
Per person per year vascular access costs, by physician specialty

Questions
- Where are my colleagues doing dialysis access procedures?
- Am I doing quality work?
- Is it safe to do these invasive procedures in elderly, ill patients in my facility?
- How can I answer when payors want to know how they benefit from my center?
- Is my center’s QIP in compliance with accreditation requirements?

Registry Goals
- Promote Quality
- Provide Benchmarks
- Promulgate Data
  - Useful for individual centers and in public policy advocacy
- Protect Patient Access
  - To the highest quality and most efficient access procedures

Survey Details
- Open to everyone — no requirement for ASDIN membership
- Voluntary participation
  - Must register your participation
  - “Registry membership”
- Everyone submits their own de-identified data
- No patient level data involved (HIPPA compliant)
- Confidentiality and security assured
- Only those who participate will have access to the data reports

Survey
- Quarterly data submission
  - Easy format
  - Limited questions
- Quarterly data reports
  - National aggregate data reported to all participants
  - Participants can benchmark their own data against the national data
  - Custom reports related to specific questions

Survey Contents
- Demographics
- Patient safety
- Procedure Complications
- Procedure Outcomes

We will be seeking participant input into additional data collection and modifications as the registry proceeds.
Demographics

- Procedure/billing location
- Physician specialty
- Population served
- Procedure volume
- Coding practices

Patient Safety

- Patient medical acuity, co-morbidity
  - ASA classification
- Adverse events
  - Patient fails
  - Wrong site surgery
  - Moderate sedation complications
  - Medication errors
- Hospitalization rates

Procedure Complications

- ASA/N Classification System

  - Type I – Access site hematoma
  - Type II – Vascular rupture
  - Type III – Arterial complication
  - Type IV – Stent complication
  - Type V – Catheter complication
  - Type VI – Adverse med rxn
  - Type VII – 02 sat, apnea
  - Type VIII – BP related
  - Type IX – Cardiac arrhythmia
  - Type X – Clinical status

  - Grade 1
    - nominal, unplanned increase in service
  - Grade 2
    - minor, percutaneous therapy
  - Grade 3
    - moderate, surgical therapy or hospitalized
  - Grade 4
    - severe, long term sequelae

Procedure Outcomes

- Immediate success
  - Left the facility with a successful procedure and functional access
- Functional success
  - Able to use the access for its intended purpose for at least 1 dialysis treatment after the procedure

Future

- Data collected can change as needed
  - Response time
  - Access prevalence
  - Patency rates
  - Costs
- Qualified physician quality reporting initiative (PQRI) database
- Research collaboration
- Pay for performance metrics
Steps Toward Device Innovation
Bart Dolmatch, MD
UTSW Medical Center
Dallas, TX

The "Steps"
1. Identify a problem
2. Propose a solution
3. Use the scientific method
4. Protect your concepts
5. Get money
6. Make money

Disclosure
- Bard Peripheral Vascular (Consultant, Royalties, Speaker)
- Endovascular Forum (Advisory Board)
- Vital Access (Advisory Board)
- VASA (Board of Directors)

There are widgets and there are solutions.
These are widgets...

Man's Milk

Day Dream

Chop Stick

Fan

Your innovation (device) will solve a problem...

Charles Dotter (1920 -1985)

The “father” of catheter-delivered therapies

PROBLEM: Bad toes due to focal atherosclerotic arterial occlusion required morbid bypass surgery.

SOLUTION: Angioplasty

Transluminal Treatment of Arteriosclerotic Obstruction:
Description of a New Technic and a Preliminary Report of Its Application

By Charles T. Dotter, M.D., and Melvin P. Jenkins, M.D.

Circulation, Volume XXX, November 1965

Dotter designed the tools and technique, then tested them in vivo.
He showed how angioplasty solved the problem

PROBLEM: How to keep arteries “open” after angioplasty?

SOLUTION: The Stent

**Transluminal Expandable Nitinol Coil Stent Grafting: Preliminary Report**

Charles T. Dotter, M.D.
Robert W. Bandyk, F.A.C.
Montgomery K. McKittry
Jared Reisch, M.D.

A method is described for the percutaneous delivery of a new expandable nitinol coil stent for the nonoperative restoration and maintenance of patency in internal flow pathways, especially the lumen of blood vessels and biliary ducts.

Index terms: Arteries, transluminal angioplasty, endovascular and catheterization, instrumentation: Nitinol

Radiology 155:239-240, April 1980

1. What problem do you see?
2. What solution do you propose?

- Has anyone tried to solve the problem?
- Time to revisit old solutions?
- Can you think of new solutions?

3. Apply Scientific Method

- Question: What’s the problem?
- Research: What’s been tried already?
- Hypothesis: What solution do you propose?
- Experiment: Test your idea(s)
- Data: Did your solution work?
- Conclusion: Are you on to something?
4. Protect your concepts

- Document your ideas - write them down
  - Concept
  - Time
  - Witness
- Beware of disclosure^
- Non-disclosure agreement when sharing your conceptual information.

^except to your dog?

Intellectual Property (IP)

YOUR GREAT IDEA IS WORTH LOT’S MORE WHEN THERE’S “IP”

- Patent Attorney $$
- Professional Patent Search $$

Who has rights to “your” IP?

- You
- Your employer
- Your University
- Your State

I’m at UTSW - University and State!

Start thinking “ATTORNEY”

5. Show me the money!

- Your own cash?
- Venture or other investors
- Collaborate with deeper pockets and know-how

GET A (GOOD) ATTORNEY!!!
You will NOT regret this - trust me

You are your best advocate

- Make friends
- Be bold and brave
- Don’t be stupid and unyielding
- Read the tea leaves
6. Make money

- Relationships are everything: Be sure you like (and trust) people with whom you work.
- Your financial success is based upon whatever "agreements" you and your attorney worked out earlier with others.

Why me?

The year: 1993
Arterial stents had been around 5 yrs: since 1988

The problem: How to prevent instent restenosis in 5-12mm dia. blood vessels.

MY IDEA to PREVENT RESTENOSIS:
ADD A BARRIER TO THE STENT

Scientific Method

- Question: Can covering halt in-stent restenosis?
- Research: What "coverings" were available?
- Hypothesis: Covering will stop in-stent restenosis in medium sized blood vessels.
- Experiment: In vivo studies of different devices
- Data: Yes, this works for certain devices.
- Conclusion: I'm on to something!!!

2 Coverings: PET and ePTFE

PET: Polyethylene Terephthalate
(PET or POLYESTER - "DACRON")

Used for 50 years as an aortic bypass conduit.
PET COVERED STENTS

- Prototype devices
- Animal implants
- Gross specimens, angiograms, and histology

Dacron-covered stent: INFLAMMATORY!!!

INFLAMMATION

This was a problem!!!
PET COVERED STENTS

• BAD IDEA
• Walk away to fight another day!

ePTFE COVERED STENTS

• PROTOTYPES
• Stent on inside of graft
• Stent on outside of graft
• Bare stent (control)
ePTFE Covered Stents

- Not inflammatory
- Subtle luminal neointima forms when stent is not on luminal surface

I’m on to something!!!

But I couldn’t make ePTFE covered stents

Porcine ePTFE covered stent at 6wk

Who needs a covered stent?
Impra made ePTFE for AV Grafts. Bare stents in AV Grafts stenosed. Use ePTFE covered stents in AV Grafts.
The Flair (Bard Peripheral Vascular*)
- ePTFE encapsulated Nitinol stent
- Straight and end-flared configurations
  - 6-9 mm in diameter
  - Flare 4 mm
  - 30, 40, 50mm length

*Bard acquired Impra along the way.

The Delivery System
- A lot more stuff to deliver than a bare stent
- CR Bard catheter technology

Subtle neointimal healing
but no stenosis

Feb 10, 2010

Stent Graft versus Balloon Angioplasty for Failing Dialysis-Access Grafts

Steps to device innovation?

The longest journey starts with the first step.

- A wise woman
  (My mom and others)

Overview

- Vascular research.
- What makes a “good” grant?
- Funding opportunities from non-profit and government organizations.
Steps to follow to get a grant
• Prior research in vascular access.
• Excellent data base.
• Excellent background on the filed of your research.
• It is best to have peer review manuscripts in top medical journals regarding your research.
• Excellent grant writing.

Why do I want to do research in vascular access?
• My mentor/Chair told me to do it.
• Getting promoted sounds like a good idea
• I need to get out of this place and buy my way into somewhere else.
• It would look good on my CV.

There is only one good reason!
I am interested in vascular access and want to acquire the knowledge needed to improve or change the current practice.

Research requires: INTELLECTUAL CURIOSITY
• Follow up on every unusual case you see as an interventionalist.
• View adverse events as an opportunity to learn.
• Question every vascular access “guideline”.
• A good source for a vascular access research topic is the K-DOQI guidelines.

Research requires: TIME
• Solution 1: Do research on nights and weekends. Less time for family.
• Solution 2: Protected research time.
  Accept 20% pay cut in lieu of protected research time.
  – Academics: Negotiate with your Division Director protected time for research.
  – Private practice: Negotiate with your group practice protected time in exchange for research (e.g., 1 research day per week).

Ask yourself questions about your field of interest: fistulas
• Why don’t fistulas mature?
• Can we predict which fistulas won’t mature?
• What is the optimal time and test to assess immature fistulas?
• Which immature fistulas can be salvaged by specific interventions, and what is the nature and optimal timing of the intervention?
• Can pharmacologic interventions improve fistula maturation?
• Pathophysiology of stenotic lesions.

Ask yourself questions about your field of interest: grafts
• Does graft monitoring/surveillance with preemptive angioplasty improve graft outcomes?
• Is any method of monitoring/surveillance superior for detecting stenosis?
• What are the cellular mechanisms that lead to neointimal hyperplasia?
• Can pharmacotherapy prevent graft stenosis/thrombosis (either primary or after PTA)?
• Stent outcomes.
Ask yourself questions about your field of interest: catheters

- What is the preferred treatment for catheter thrombosis?
- Which catheters with low dialysis blood flows require thrombolytic therapy?
- What is the optimal management of catheter-related bacteremia?
- How can catheter-related bacteremia be prevented?
- Outcomes of new coated catheters.

IRB issues

- If you want to analyze an existing access database, you can apply for expedited IRB review
  - Exempt from consent
  - HIPAA waiver
- If you want to do a prospective study, you need a full IRB application with consent form and HIPAA form.

You will need: A computerized access database

- Keep it simple—someone has to enter all the data!
- Use consistent terminology.
- Data entered promptly.
- Only 1-2 people enter data.
- Use it for scheduling, not just recording.
- Periodic review of entries.

You will need: an access coordinator

- Liaison among nephrologists, surgeons, radiologists, and HD staff
- Schedule all access procedures.
- Maintain computerized records.
- Identify new access issues.

Computerized entry for access procedures

<table>
<thead>
<tr>
<th>Pt name</th>
<th>Jane Doe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Med Rec #</td>
<td>123</td>
</tr>
<tr>
<td>Date of birth</td>
<td></td>
</tr>
<tr>
<td>Date of procedure</td>
<td>2/7/09</td>
</tr>
<tr>
<td>Service</td>
<td>Surgery / IR or clinic</td>
</tr>
<tr>
<td>Procedure</td>
<td>New LUA fistula / angio / declot</td>
</tr>
<tr>
<td>Indication</td>
<td>S/P failed LFA graft</td>
</tr>
<tr>
<td>HD unit</td>
<td>unit</td>
</tr>
<tr>
<td>Nephrologist</td>
<td>Dr. K</td>
</tr>
<tr>
<td>Was the procedure done?</td>
<td>No</td>
</tr>
</tbody>
</table>

Access history for a patient

<table>
<thead>
<tr>
<th>Date</th>
<th>Service</th>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/1/08</td>
<td>IR</td>
<td>Place permcat</td>
</tr>
<tr>
<td>1/6/08</td>
<td>US</td>
<td>Preop VM</td>
</tr>
<tr>
<td>1/18/08</td>
<td>Surg</td>
<td>New LFA fistula</td>
</tr>
<tr>
<td>2/26/08</td>
<td>US</td>
<td>Postop US</td>
</tr>
<tr>
<td>3/5/08</td>
<td>Surg</td>
<td>Ligate accessory veins</td>
</tr>
<tr>
<td>5/20/08</td>
<td>Neph</td>
<td>Remove permcat</td>
</tr>
<tr>
<td>10/4/08</td>
<td>IR</td>
<td>PTA of fistula stenosis</td>
</tr>
</tbody>
</table>
Analysis

- Must include EVERY patient.
- Each patient can only be counted ONCE.
- Must account for EVERY access event (some may have been done by a surgeon, radiologist or IN).
- Statistical analysis: use simple tools and go from there.
- T-test, Chi square, Kaplan-Meyers survival curves. Post-test following two-way ANOVA. Hard ratios and confidence intervals.

Basic statistical tests (free website): http://www.graphpad.com/calculators/

Write your first manuscript

- Have a mentor.
- Organize your thoughts and review the literature on the topic at hand.
- Sent your paper to colleagues in your filed for an opinion before submitting it to a journal.
- It is important that you are the main author of the manuscript.
- Your initial manuscripts are most likely to be retrospective studies.

Grant Writing

- Once you have the background data and you have analyzed that data, then the conclusions of your initial study will give you the basis for the next project.
- It will be better if you have performed several studies before you start writing a grant.

What makes a “good” grant?

- Hypothesis driven
- Technically feasible and within expertise of the investigator
- Not overly ambitious
- Novel/innovative
- Challenging an existing paradigm
- Mechanistic studies

What makes a “good” grant?

- Specific aims page
  - One page only
  - Define the problem and key issues
  - Hypothesis
  - 3-5 sentences for each aim
  - Finish with a significance statement

- Preliminary data to address feasibility
- Discuss pitfalls and alternate strategies
- Productivity of the investigator
- Independence of the investigator
  - Senior author on papers
  - Publications independent of the mentor
  - Letter from mentor stating independence
- Specific aims page
In essence

- Research proposal: Hypothesis, Aims, Background and significance, Preliminary data, Relevant research experience of the applicant, Experimental design and methods, Environment and equipment, Statistical analysis, References.
- Applicant’s biosketch
- Sponsor and mentor’s letters
- Letters of support
- Research experience of the applicant
- Experimental design and methods
- Environment and equipment
- Statistical analysis
- References

Reviewers’ perspective

- Significance
  - Important problem being studied
  - Advance scientific knowledge
- Approach (75%)
  - Conceptual and integrated
  - Potential pitfalls and alternative approaches
- Innovation
  - Original and innovative
  - Does the project employ novel concepts?

Reviewers’ perspective

- Investigator
  - Qualifications
  - Experience level
  - Collaborative arrangements
- Mentor
- Environment
  - Institutional commitment
  - Protected time for young investigators
- Budget
- Human subjects and Vertebrate animals

Priority Scoring

- 1-1.5 Outstanding
  - Wow
- 1.5-2.0 Excellent
  - Exciting
- 2.0-2.5 Very good
  - Fixable
- 2.5-3.5 Good
  - Boring
- 3.5-5.0 Acceptable
  - Fundamental problems

* Different score for NIH grants

Why did I (not) get funded?

- Top five deficiencies
  - Study design (76%)
  - Statistical issues (34%)
  - Ownership of work, mentor and environment (29%)
  - Weak hypothesis (24%)
  - Lack of novelty (24%)

Facts

- Grants from non-profit and government organizations target a wide audience
  - pre- and post-doctoral trainees, residents, fellows, fellow to faculty transition, junior and established investigators.
  - Non-profit organization’s grant provide funding as an initial step to generate preliminary data for more substantial funding from NIH and other major sources.
- Give protected time (academic).

Agarwal, Chertow, Mehta. CJASN October 2005
Funding your research

- Non-profit organizations: NKF, ASN, AST, etc. (www.kidney.org/professionals/research/)
- Government funding: NIH: www.lrp.nih.gov/about/lrp-clinical.htm
- University grants
- Industry: Bard, Amgen etc.

Major non-profit organizations

- American Diabetes Association (ADA)
- American Heart Association (AHA)
- American Society of Nephrology (ASN)
- American Society of Transplant Surgeons (ASTS)
- American Society of Transplantation (AST)
- International Society for Heart and Lung transplantation
- National Kidney Foundation (NKF)

National Kidney Foundation

- Basic and clinical science
- Postdoctoral fellowships
- Young Investigator awards
- Clinical Scientist awards
- Deadline: December
- Award activation: July

National Kidney Foundation - Postdoctoral fellowships

- Relevant to kidney disease
- No >4.5 years of research training after a doctoral degree
- No >10 years from last doctoral degree
- $40,000/year for 2-3 years
- US citizens priority
- Mentor based
- 75% effort required
- Sponsor training plan very important
- 107 fellowship applications per year / 23 funded.

National Kidney Foundation - Young Investigator Award

- Mentored career development award
- Concurrent NIH K08/K23 funding permitted
- Completed fellowship in nephrology, urology or related disciplines and within 4 years of first faculty appointment
- $50,000/year for 2 years ($15K for salary support)
- 75% protected time
- Chairman and Sponsor letters required
- 17 page proposal: Aims, background and significance, preliminary data, Experimental design and methods
- 100 fellowship applications per year / 10 funded.

American Heart Association - Scientist Development Award

- National (2/year) and affiliates (1/year)
- Instructor/Assistant Professor level
- <4 years since first faculty appointment
- Current funding <$95,000/year
- No concurrent K awards allowed
- US Citizen/perm. resident/H1/O1/TN visa
- $65,000/year for 4 years
- No sponsor required
- Success rate 24% (356/85)
American Heart Association
-Fellow to Faculty transition award

- National, once a year, 5-year award
- 1-3 years as a trainee with completed clinical training or 2 years as faculty
- No more than 5 years of postdoctoral research training
- Mentor required
- US citizen/perm. Resident/H1B or TN
- 80% protected time
- No concurrent K series or AHA SDG allowed
- Budget:  
  - Training stage: $65,000/y ($50K for salary)
  - Faculty stage: $132,000/y ($90K for salary)
- Success rate: 39/9 (23%)

American Society of Nephrology
ASN-AST John Merrill Grant in Transplantation

- Full time faculty
- Project independent of mentors
- 75% protected time
- $100,000/year for 2 years (up to $70K for salary)
- One award/year
- Allowed to have previous NIH K awards but not R01 or VA merit awards
- 10 page research proposal
- March is the deadline

American Society of Nephrology
Carl W. Gottschalk research scholar grant

- Full time faculty, <7 years of initial appointment
- Project independent of mentors
- 75% protected time
- $100,000/year for 2 years (up to $70K for salary)
- 3-4 awards/year
- Allowed to have previous NIH K awards but not R01 or VA merit awards
- 10 page research proposal
- March is the deadline

Government grants

- NIH: [NIH website](https://www.lrp.nih.gov/about/lrp)
- K-23: Mentored Patient-Oriented Research Career Development Award
- K-08: Mentored Clinical Scientist Research Career Development Award
- R03: will support small research projects that can be carried out in a short period of time with limited resources.
- R01: is an award made to support a discrete, specified, circumscribed project to be performed by the named investigator in an area representing the investigator’s specific interest and competencies.