EMODIAL

The Value of Silver in Fistula Access Management

Hemodialysis Access

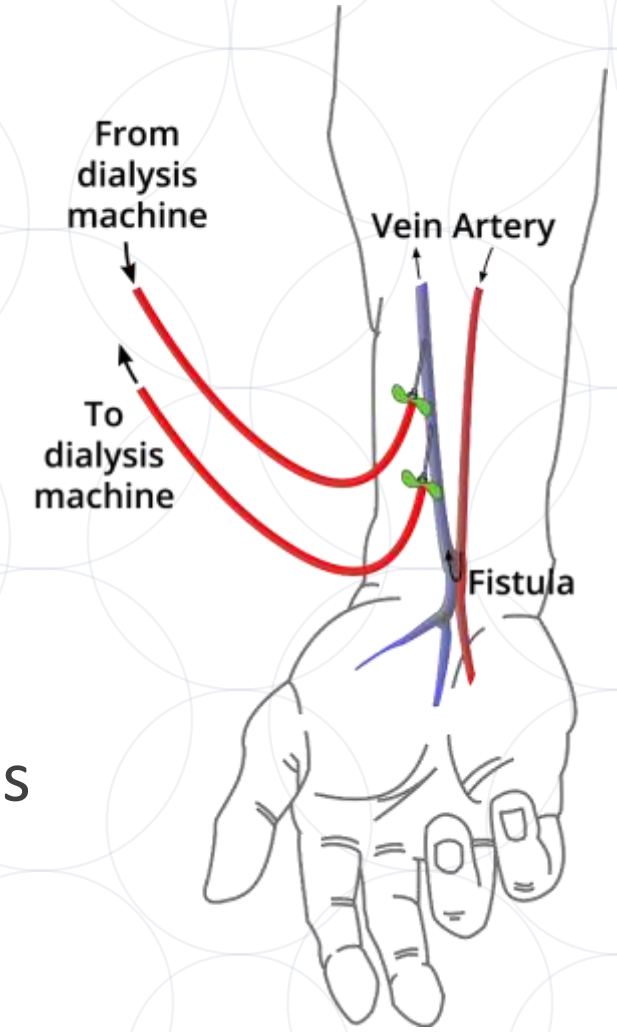
Dialysis access refers to the creation of
an entranceway into the bloodstream
so that the blood can be cleansed by the dialysis procedure

This entrance way is commonly located
in the arm, leg or neck

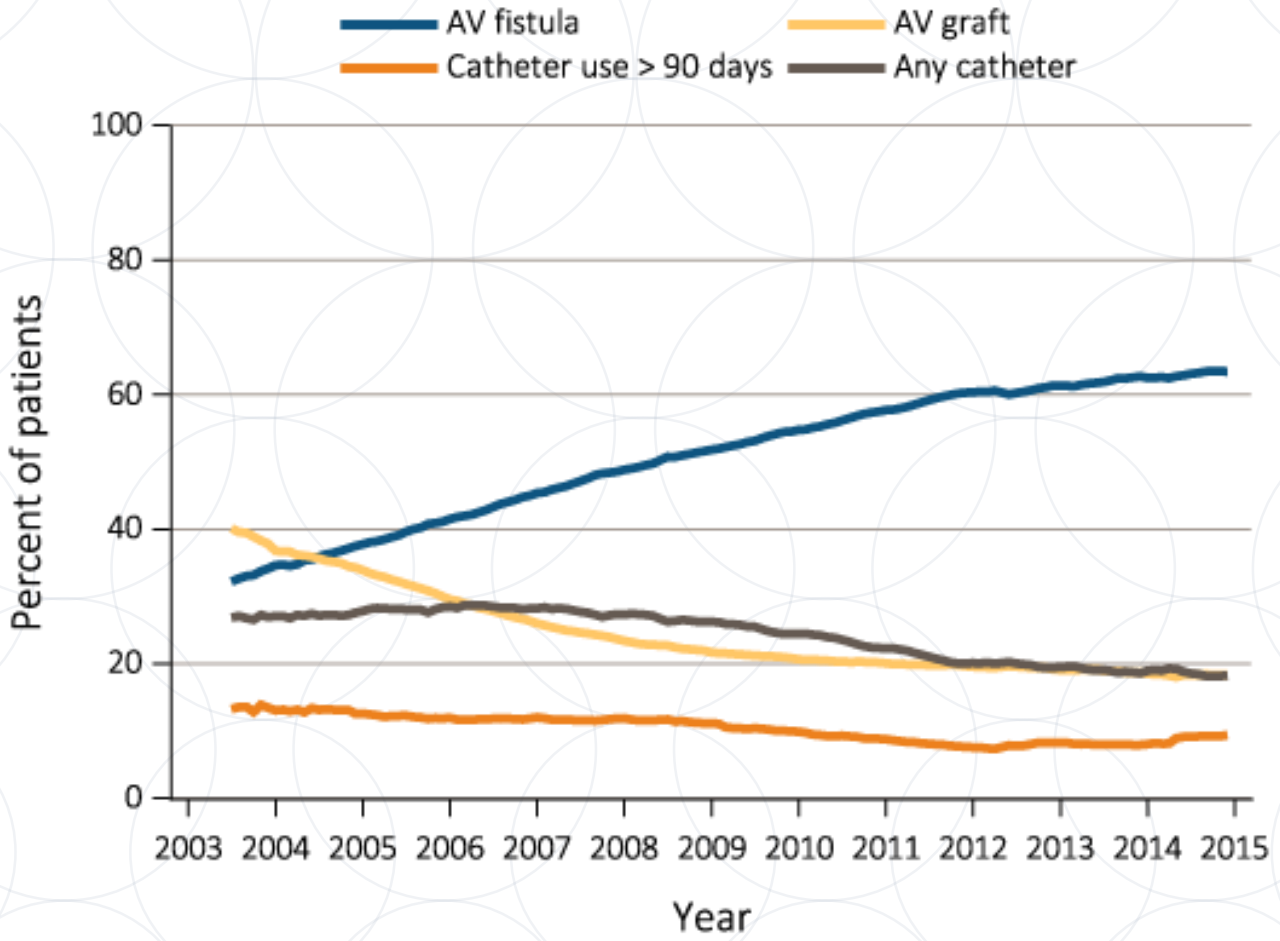
The best type of dialysis access is provided by a fistula

What is a fistula or AVF?

- AVF is created by directly connecting an artery to a vein
- The vein grows larger and stronger for easy access
- Fistula can be placed in the forearm or in the upper arm
- Consists in a minor outpatient surgery
- Usually take 6 to 12 weeks to develop
- AVF is considered the best long-term vascular access because it provides adequate blood flow, lasts for a long time and has a lower complication rate than other access



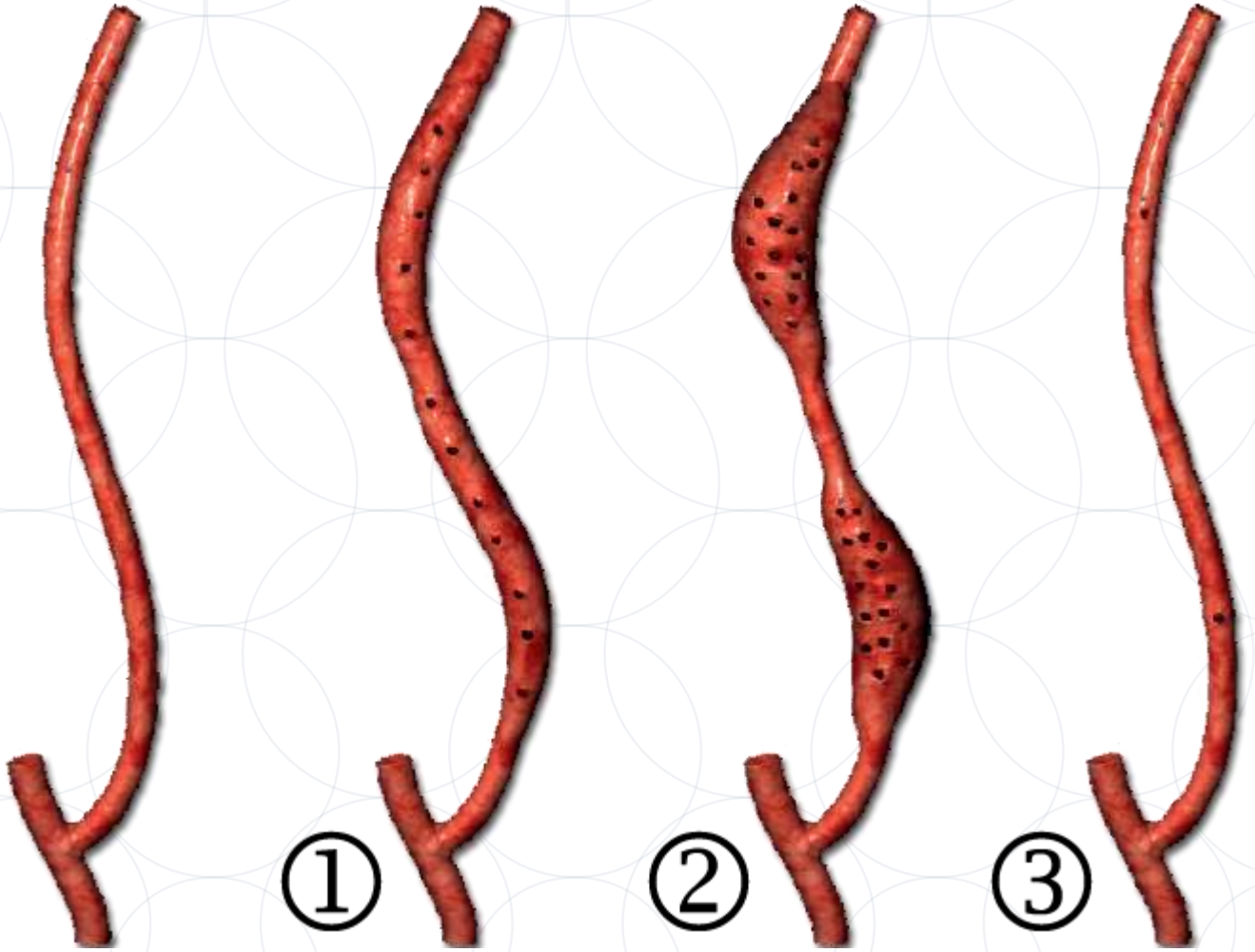
Trends in vascular access type use among ESRD prevalent patients, 2003-2014



Data Source: *Special analyses, USRDS ESRD Database, and Fistula First data. Fistula First data reported from July 2003 through April 2012, CROWNWeb data are reported from June 2012 through December 2014. Abbreviations: AV, arteriovenous; ESRD, end-stage renal disease.*
2016 Annual Data Report, Vol 2, ESRD, Ch 4 (Figure 4.6)

AVF Puncture Techniques

1. ROPE LADDER
2. REGIONAL (AREA)
3. BUTTON HOLE



1. ROPE LADDER

Site is new at to every puncture, at a distance of a few mm from the previous, for all the length of the vase. Rope ladder needs well-developed, long and linear vessels and requires expertise to make "new holes" every time.

- High puncture stress for patients and nurses
- High risk of extravasation and hematomas
- Exclusive use of sharp needles with "intense" pain at every access
- Not applicable in case of proximal or deep AVF

2. AREA PUNCTURE

Site is new at every treatment, inserting the needle in the same limited area, without an AVF project. Punction is made in the region according to the feeling of the patient. Area puncture seems easier and less stressful for patients and nurses

- Skin damages and bad look of the arm
- The vessel wall increases abnormally in limited areas, leading to aneurysm
- Aneurysms, in most cases, are correlate to the stenosis, increasing the possibility of thrombosis and vortex flow inside the vessel
- Hemostasis can be longer that usual

3. BUTTON HOLE

Site is maintained at every dialysis, were the operator punctures the same access with a blunt needle, reducing needling/cannulation pain.

- High risk of infection
- Long training of the nurses and difficult turnover
- High skill and manual competence requested

Problems connected with AVF

High pressure and prolonged bleeding

Poor development

Low flow rates

Difficulty needling / cannulation

Recurrent stenosis

Inadequate efficacy of dialysis

Recirculation

Thrombosis

Aneurysms

Superficial and deep damages

The concentration of punctures in a single restricted area produces **skin traumas** and creates the **accumulation of scar tissue**

The **destruction of the basal membrane** alters the growth of epithelial cells and makes it **very difficult to restore** the original architecture of the tissue.

Each venipuncture involves a scar producing microzones of fibrosis and the skin assumes the appearance of a pearly and fragile lamina

The **wall's dilatation** caused by the aneurysm may lead to the rupture of the vessel or to a parietal thrombus

The Value of dressings for AVF survival

DRESSING

to promote and maintain
the best conditions for the complex tissue repair process

to start and continue
until wound healing

ACTIVE DRESSING

to promote
rapid healing

to prevent
contamination or infection

SILVER ION DRESSING

to reduce
inflammation

to stimulate
skin regeneration

Silver dressings
Value of Ag

Silver is one of the best and safest **active compound** for wound care, with wide applications. Clinically, metallic silver is inert but its interaction with the moisture of the skin surface and with the fluid of the lesion, leads to the release of ions with several **properties and advantages**

- Treats and prevents infections with its **antibacterial properties**
- Has **low toxicity**, absorbtion and elimination is easy, there is no accumulation
- **Readuces Inflammation**
- **Stimulates skin regeneration**

Silver ions Reduce Inflammation & Stimulate Skin Regeneration

- Incude Vascularization ⇨ **lead** to the angiogenesys by stimulating VEGF - vascular endothelial growth factor - **creating** new vessels and **expanding** the existing bed (+)
- **Stimulate** the replication of the immune cells ⇨ lymphocytes, granulocytes, etc..(-)
- **Reduce** Inflammation ⇨ **trigger** the release of cytokines involved in the inflammatory process. Thanks to a complex regulation pathway, silver ions **downregulate** proinflammatory cytokines and **upregulate** antinflammatory cytokines (*)
- **Stimulate** Skin Regeneration ⇨ upregulate cytokines which stimulate fibroblasts growth and **tissues regeneration (*-)**

Cytokines regulation mechanism

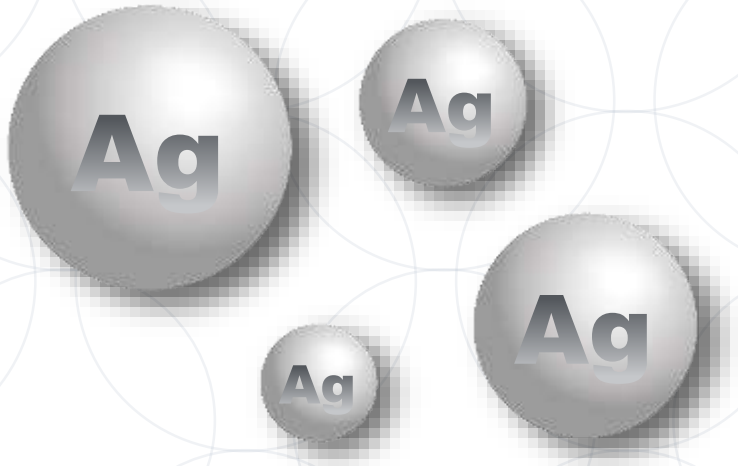
Decrease IL-6 proinflammatory cytokine	rapid resolution of the inflammatory process
Increase IL-10 anti-inflammatory cytokine (**)	rapid resolution of the inflammatory process
Increase TGF-β transforming growth factor	decreases the amount of IFN-γ
Decrease IFN-γ, interferon gamma	stimulates fibroblasts
Increase VEGF, endothelial growth factor(***)	promotes the regenerative and healing process

Journal of the American College of Clinical Wound Specialists (2012) 3, 82–96., Silver Nanoparticles as Real Topical Bullets for Wound Healing, Thirumurugan Gunasekaran, MPharm, PhDa,, Tadele Nigusse, MScb, Magharla Dasaratha Dhanaraju, MPharm, PhDa*

Ag for chronic patients

(subjected to repeated punctures)

Rapid stimulation of epidermis repairing process



Functional improvement of the skin barrier

Trigger the healing process

Solutions

To prevent the subcutaneous tissue from flattening

To avoid formation of aneurysms and stenosis

To improve the aesthetic aspect

To guarantee long fistula survival

NOVA SOVAN® AG

Antiseptic breathable adhesive dressing provided with non-adherent ionic silver based pad.

NOVA BETAFIX® AG

Elastic fistula bandage provided with non-adherent ionic silver based pad and fixing plaster.

- (+) Silver Nanoparticles as Real Topical Bullets for Wound Healing Thirumurugan Gunasekaran, MPharm, PhDa,*, Tadele Nigusse, MScb, Magharla Dasaratha Dhanaraju, MPharm, PhD. Journal of the American College of Clinical Wound Specialists (2012) 3, 82–96
- (-) Lee PY, Ho CM, Lui VCH, et al: Silver nanoparticles mediate differential responses in keratinocytes and fibroblasts during skin wound healing. Chem Med Chem. 2010;5:468–475.
- (*) Boucher W, Stern JM, Kotsinyan V, et al: Intravesical nanocrystalline silver decreases experimental bladder inflammation. J Urol. 2008; 179:1598–1602
- **(*-)** Tian J, Wong KK, Ho CM, et al: Topical delivery of silver nanoparticles promotes wound healing. Chem Med Chem. 2007;2(1): 129–136
- (**) Active Silver Nanoparticles for Wound Healing Chiara Rigo 1, Letizia Ferroni 2, Ilaria Tocco 3, Marco Roman 4, Ivan Munivrana 3, Chiara Gardin 2, Warren R. L. Cairns 4, Vincenzo Vindigni 3, Bruno Azzena 3, Carlo Barbante 4 and Barbara Zavan 2,* Int. J. Mol. Sci. 2013, 14, 4817-4840; doi:10.3390/ijms14034817
- (***) Topical Delivery of Silver Nanoparticles Promotes Wound Healing Jun Tian,[a] Kenneth K. Y. Wong,*[a] Chi-Ming Ho,[b] Chun-Nam Lok,[c] Wing-Yiu Yu,[b] Chi-Ming Che,[b] Jen-Fu Chiu,[c] and Paul K. H. Tam[a] ChemMedChem 2007, 2, 129 – 136

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Thanks for your attention