CATHETER INFECTIONS IN PARENTERAL NUTRITION
Infection Criteria for Catheter Related Blood Stream Infection (CRSBI)

CDC - Systemic evidence of infection with both catheter and peripheral blood cultures positive with same organisms

In one European study <50% of reported cases of CRSBI failed to meet this criteria
The Shifting Sands of Epidemiology

- Catheter infection rates range in PN from 0.35-4.5 BSI per 1000 catheter days some as high as 11.1 /1000 in a single study at Emory
- Hemodialysis catheter 2.2-5.5 BSI per 1000 catheter days
- CRBSI 80K annually in ICU 250K overall
- 150 M iv devices annually in US 5million CVC
Cost of CVC infection difficult to assess

Krankenhaus Infection Surveillance System
KISSL

30 K euros per infection -33-75$ in US
LOS of 7 days increased
Some Context for these numbers

2.1/1000 in RICU - 5.1/1000 in MICU/SICU 5.8/1000 in NICU 9.1/1000
In trauma ICU 18.1/1000 in burn units
30.2/1000
CRBSI third leading cause of hospital infection behind CAUTI and SSI lies just between C diff and MRSA
Catheter factors and Infection

- Central venous catheters (CVC) 64 x PIV
- PICC lines increased infections over CVC
  SC < IJ < F for CRBSI and thrombosis but higher rate of pneumothorax with insertion
Single lumen < triple lumen
Implantable port 1.2/1000 < Tunneled 1.6/1000 < Non tunneled 4.8/1000
Host factor and Infection

More infection occur in males 60-75%
Most within first 6 months of catheter insertion
Others? : Diabetes, Malignancy, Organ Transplant, Granulocytopenia, and APACHE score
Parents = Home nurse > Self
Parenteral Nutrition and Infection

No proven link to hyperglycemia in ICU

Increased risk in one study with total calories/kg infused

Associated with increased fungal infection and possibly linked to lipid infusion tho recent data suggest no diff

Epidemic outbreaks are rare S marcesens (home) E cloacae C. Albicans (NICU) attributed to solution contamination
Organisms in PN similar to all CVC infections
Gram Positive Infections

Staph epidermidis is the most prevalent infectious isolate in home PN patients ~60%
ICU data suggest a more indolent infection

Methicillin sensitive Staph aureus second most common. Incidence may be reduced by surveillance
3 month swabbing of exit sites

Methicillin resistant Staph aureus ~20% of GPC isolates-more common in prisons Less responsive to catheter salvage therapy strategies 27% vs 80%
Gram Negative Infections

Klebsiella pneumonia most frequent isolate

Followed by E. faecalis and E. coli

Sixty percent of infection associated with clinical sepsis or SIRS

E Coli EBSL and Enterococcus faecium VRE on rise
Fungal Infections

Candida albicans most common

Candida parapsilosis is increasing isolated from PN patients – PN is a suitable growth media

PN use is incorporated into the Candida score in ICU

Candida colonization of urine and skin may predict risk
Evidence of specific infection complications is rare

- Endophthalmitis described in ICU patients in 9% but clinical significance is questionable
- Endocarditis is rarely reported in recent years but suspect still seen
- Vertebral osteomyelitis has been described as increased frequency in a Montreal study
Case at UIC

- On 8/11, she developed fevers, chills, back pain. Elevated ESR and CRP
- Blood cultures grew S. epidermidis
- Most common presentation back pain and elevated CRP and ESR
- Treated with antibiotics 6 weeks
- Ultimately required 2 level discectomy

Image from Dr. Amanda Allen, UIC Department of Radiology
Malignancy and Parenteral Nutrition

- Up to 40% of home PN patients have a diagnosis of malignancy
- Inferior overall survival and lower tumor response rates
- 4x increased infection rate including non-catheter related infections
- Selected role in some indolent intestinal tumors
Anatomy of Catheter infection

- Short term location is usually skin <10 days
- Long term catheters location is hub
- Antibiotic impregnated catheters work short term
- Antibiotic and alcohol dwell have been tried in long term catheters with varying success
**Biofilms in Catheter infections**

Catheter post insertion are coated with fibrin fibronectin and collagen
Also pyruvate and glucose

These proteins are scaffolding adhesins for microbes MSCRAMMS also eDNA

Provide refuge for opsonization and phagocytosis resistance
Creates a niche of cells called persisters vs planktonic cells

Metabolically inactive and non dividing which leads to antibiotic resistance

May be polymicrobial
Biofilms as target in Catheter infections

Up to 80% of infections associated with biofilms

CVC catheters but also implantable medical devices

Inhibitors and Dispersal agents both design goals

2AI and tryptophan derivatives as potential inhibitors
Biofilms as target in Catheter infections

C-di-GMP levels regulate formation and dispersal.

- Synthesized by DGC
- Degraded by PDE
- Target in P. aeruginosa infection


Quorum Sensing (QS) The Internet of Biofilms

- QS is a bacterial specific communication system developed within biofilms based on autoinducers (AI). This system allows bacteria to communicate and share information about cell density and regulate expression of pathogenicity factors. Ultimately allows LDP to recognize crossover to HDP and behave more aggressively.
Autoinducers are species specific but have a general structural pattern in GNB and GPB analogous to a lac operon.
Auto inducers are species specific

- Gram negative bacteria use acyl homoserine lactones
- Staph aureus uses peptideAIP I-II-III

17-25 amino length with cyclic thiolactone ring
Candida albicans also form biofilms and QS regulates transition between yeast and hyphae phase

- Farnesol increases production of budding yeast cells. It also inhibits bacteria and other Candidia species.

- Tyrosol derived from tyrosine promotes hyphal phase of growth. May have anti-oxidant properties. May inhibit phagocytosis and promote virulence.
RNA III activated in Staph aureus can be inhibited by RIP and natural QSI

- RNA III polymerase induced by S aureus agr system promotes toxin production and limits adhesion
- A natural inhibitor RIP `to the RAP/TRAP receptor exists which inhibits RNAIII production
- Hammamelitannin a natural analogue of RIP is an active component in the astringent witch hazel
Typical antibiotic strategies are failing
We need new weapons and maybe- new strategy

- OODA loop was developed by Col. John Boyd USAF
- Concept of military strategy with application to business
- First effort is to move faster than the enemy – we aren’t- the bugs are smarter
- Second effort is to disrupt the OODA loop of the enemy - and disrupt his command of the battlefield – maybe we can