Continuous Infusion Toxicity Studies in Rats; General Considerations

Fourth conference of Society of Toxicologic Pathology- India

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The equipment behind the science.

Rat Infusion Model

Rat Infusion Model

- Jugular vein
- Femoral vein

Infusion Equipment

- Catheter
- Animal connection (tethered model)
- Infusion setup

Rat Infusion Model

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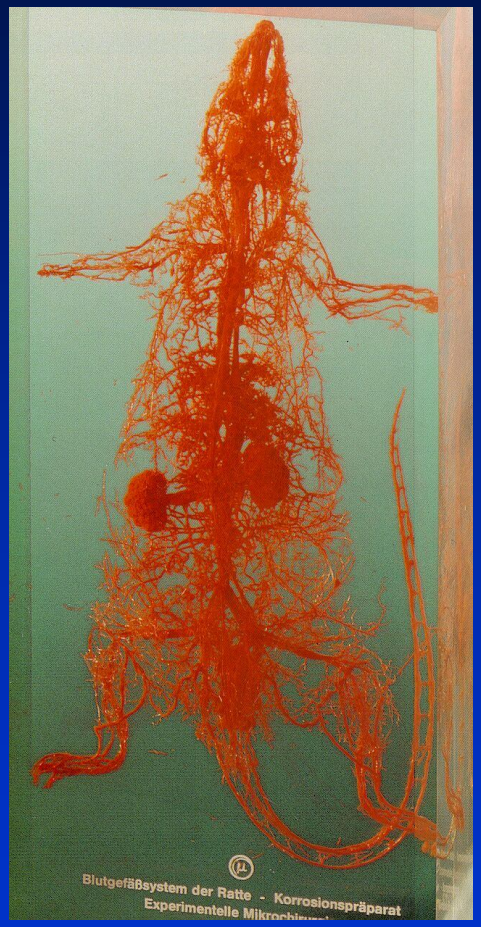
Catheterize or not?

Sampling method	Anesthetic	Age/sex	NE	E	NE+E	Reference
Decapitation	ND	20/m,f	–	–	46.1±4.8	[12]
Decapitation	ND	ND/ND	59.7±7.1	79.7±6.6		[17]
Cardiac puncture	Ether	2/ND	10.3±1.4	3.1±0.7		[2]
Cardiac puncture	Asphyxia	16–32/ND	124.1±20			[14]
Cardiac puncture	Tribromoethanol	ND/ND	21.5±2.8			[5]
Tail vein	ND	12/ND	13±1.4	0.9±0.1		[11]
Retro-orbital	ND	12/m	17.7	21.8		[10]
Retro-orbital	ND	12–32/ND	13.5±0.7	13.4±0.8		[9]
Retro-orbital	Pentobarbital	9–14/ND	1.4±0.6	1.36±0.1		[3]
Retro-orbital	Pentobarbital	10/m	6.6±1.4	0.5±0.1		[15]
Carotid catheter	ND	16–32/ND			4.7±0.8	[13]
Carotid catheter	Tribromoethanol	ND	3.8±0.6			[7]
Decapitation	No	12–18/m,f	24.6±2.7	27.3±3.8		Present study
Retro-orbital	Halothane	12–18/m,f	5.8±0.8	0.4±0.1		Present study
Carotid catheter	No	12–18/m,f	4.1±0.5	1.1±0.3		Present study

Grouzmann E, et al. **Blood sampling methodology is crucial for precise measurement of plasma catecholamines concentrations in mice**. *Pflugers Arch* 447: 254-258, 2003.

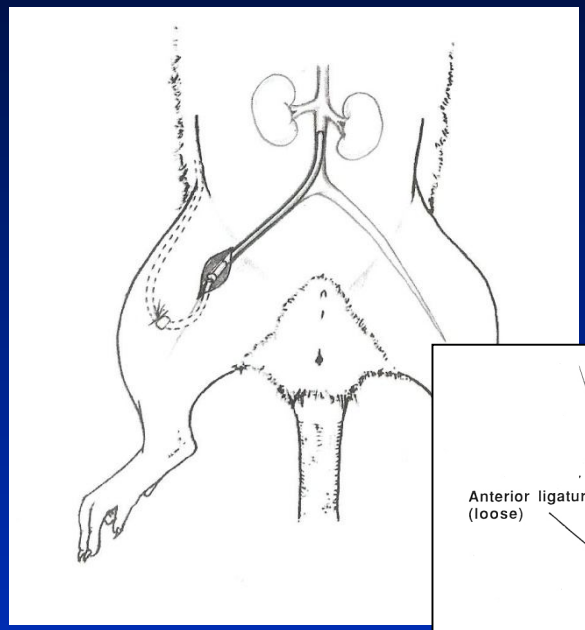
Rat Infusion Model

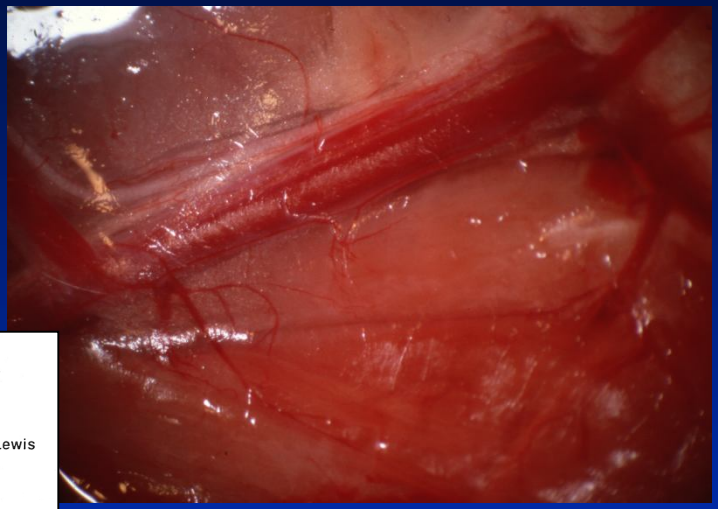


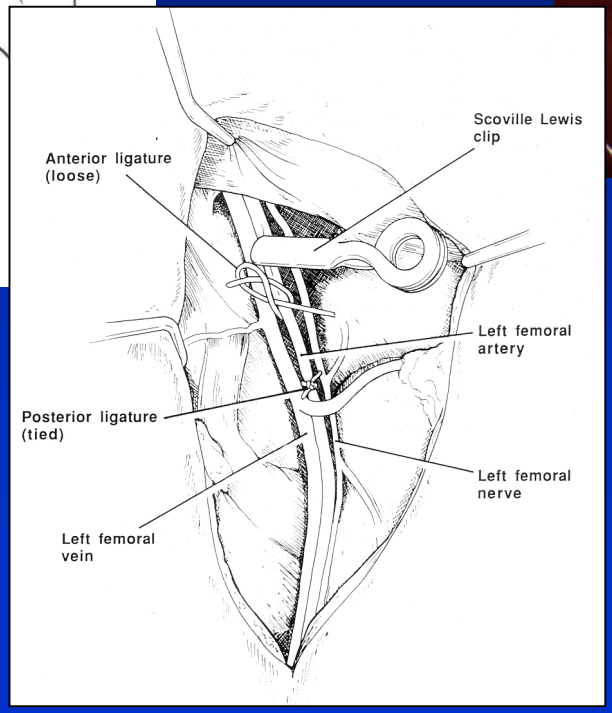
Which vessel to catheterize?

- Effect on pathology?
  - Surgery
  - Trauma
  - Reaction to materials
  - Site of drug entry
  - Stress (animal welfare)
- Practical aspects?
  - Animal dropouts (interruption of infusion)
  - Compound related e.g. absorption tubing
  - Efficiency e.g. daily weighing
  - TK blood sampling

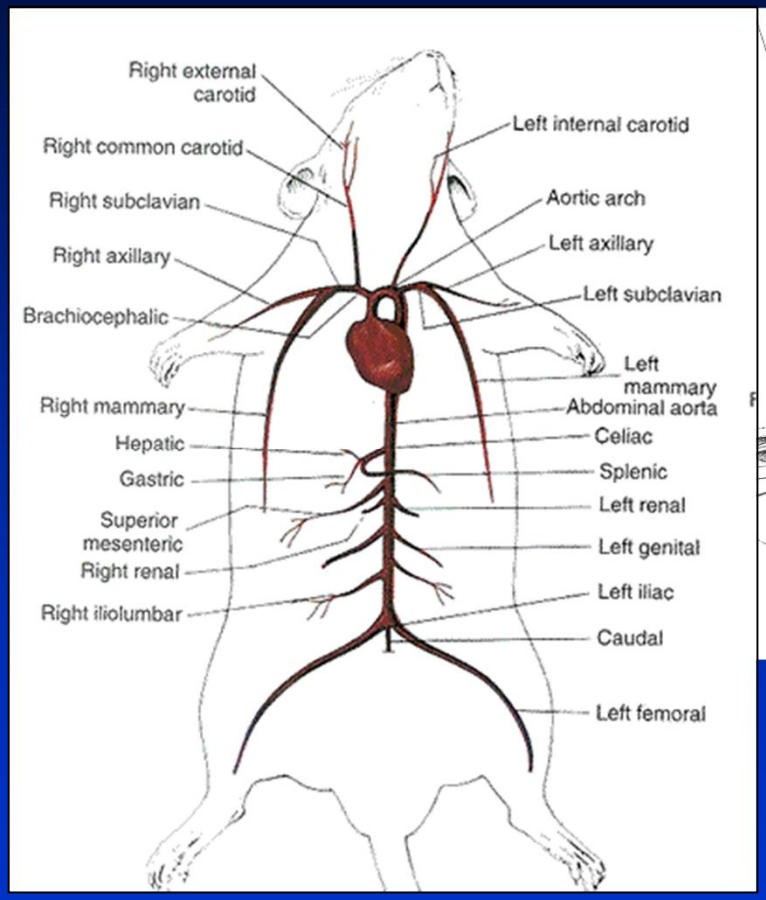
Rat Infusion Model

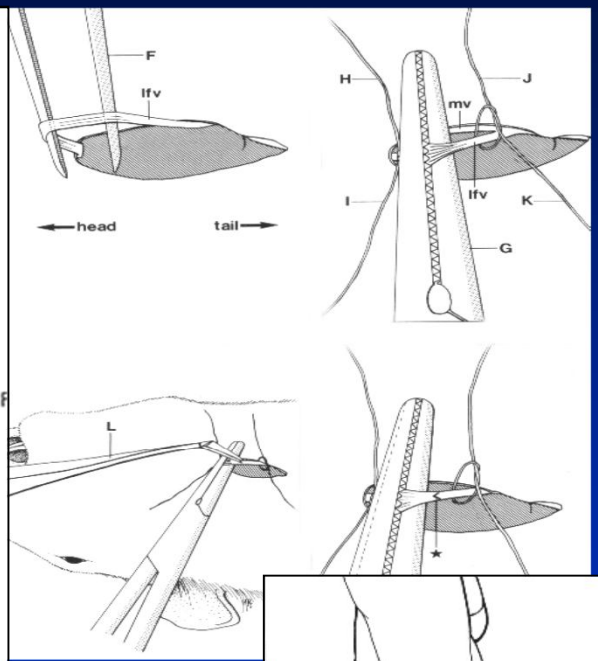


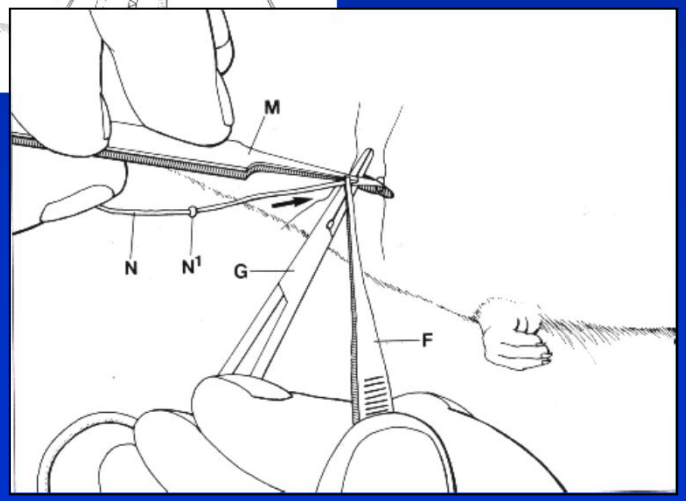




Rat Infusion Model







Rat Infusion Model

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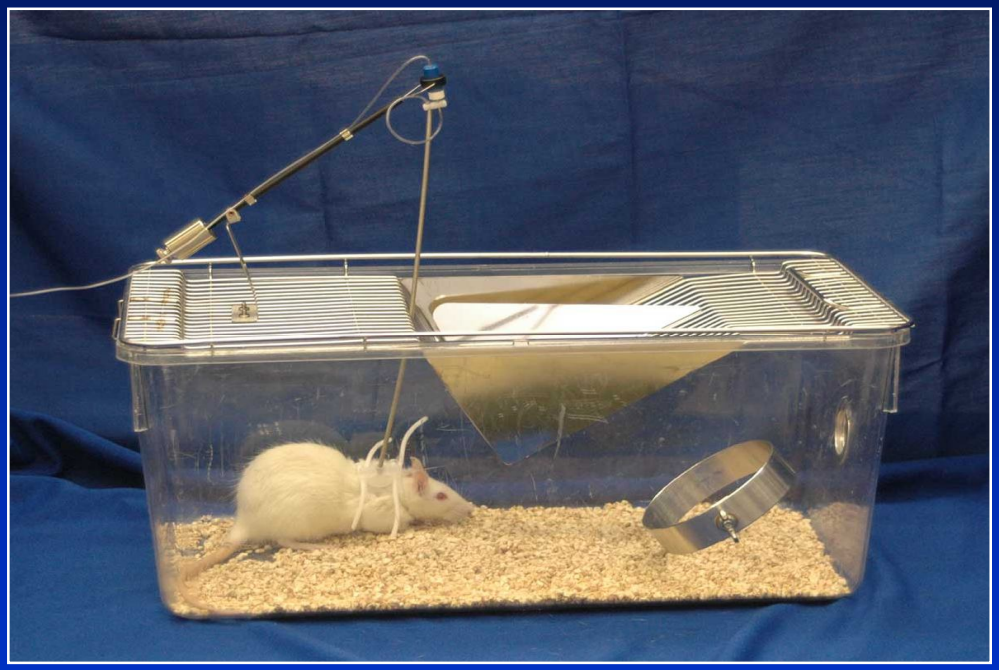
Considerations for Vascular Catheterization

- Protocol; duration and frequency
- Surgical Expertise; multi disciplinary
  - Pre operated models?
  - Learning curve
- Validation of Techniques and Materials
  - Good Laboratory Practice?
  - Good Surgical Practices; aseptic technique
  - Animal Welfare; AALAC?

Infusion Equipment (1)

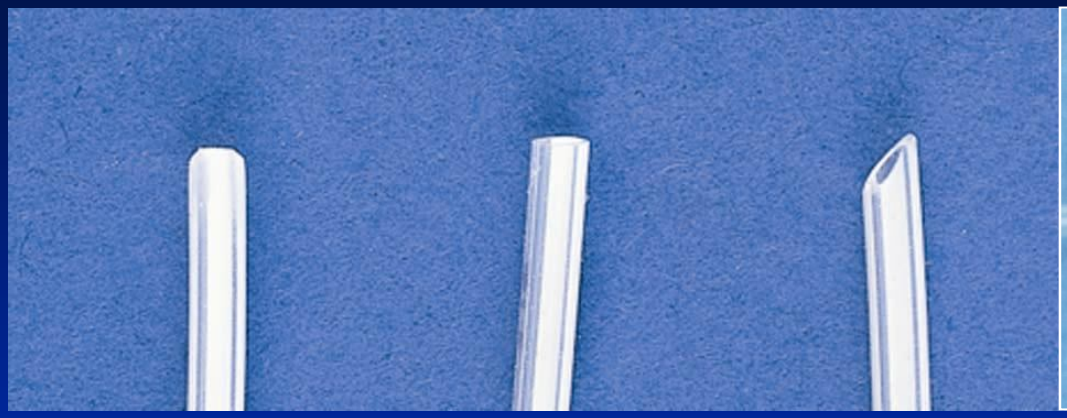


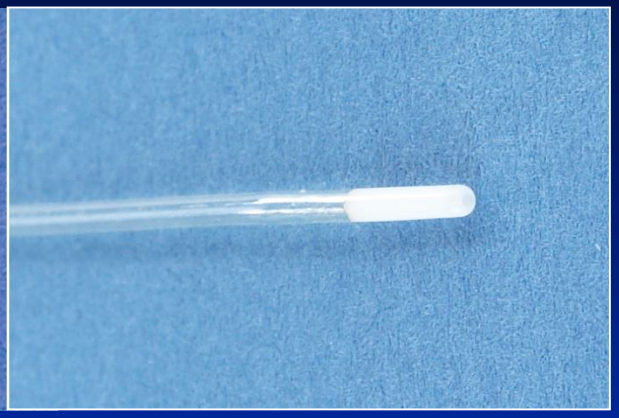
1) Catheter
2) Animal connection
3) Infusion setup

Infusion Equipment (1)

	Silicone	Polyurethane	Polyethylene	PVC
Biocompatibility	Excellent	Excellent	Fair	Fair
Compound compatibility	Possible reactivity	Possible reactivity	Inert	Possible reactivity
Stiffness	Soft	Soft	Stiff	Soft or stiff
Ease of insertion	Difficult	Moderately easy	Easy	Easy
Sizes available	Many	Many	Many	Few
Ease of bonding	Excellent	Fair	Poor	Fair
Memory	Excellent	Poor	Poor	Poor
Tear strength	Poor	Excellent	Excellent	Excellent
Sterilization	EtO, steam	EtO	EtO, steam	EtO, limited steam

Infusion Equipment (1)

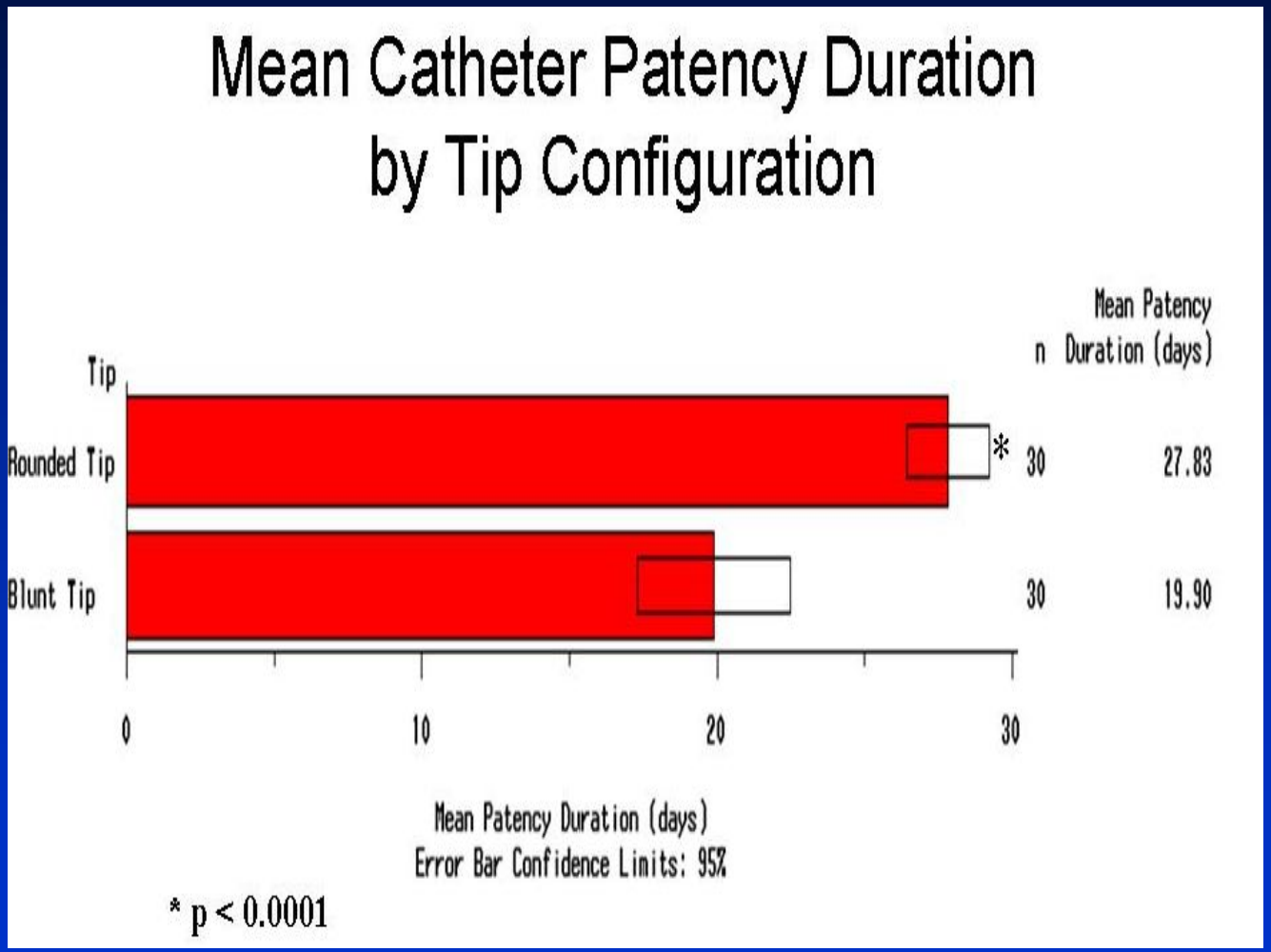




Design

- Tip Geometry
- Material
- Size
- Implantation length
- Biocompatibility (Heparin Coating, CBAS)

Infusion Equipment (1)



Infusion Equipment (1)

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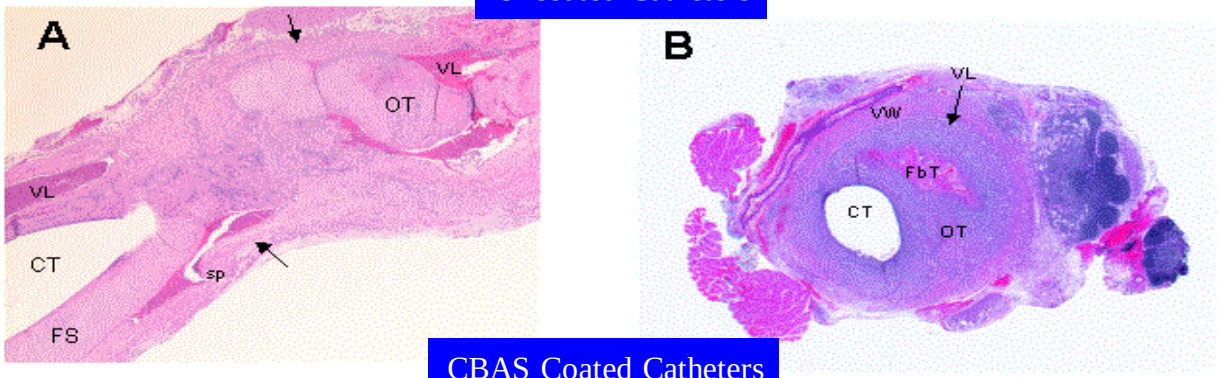
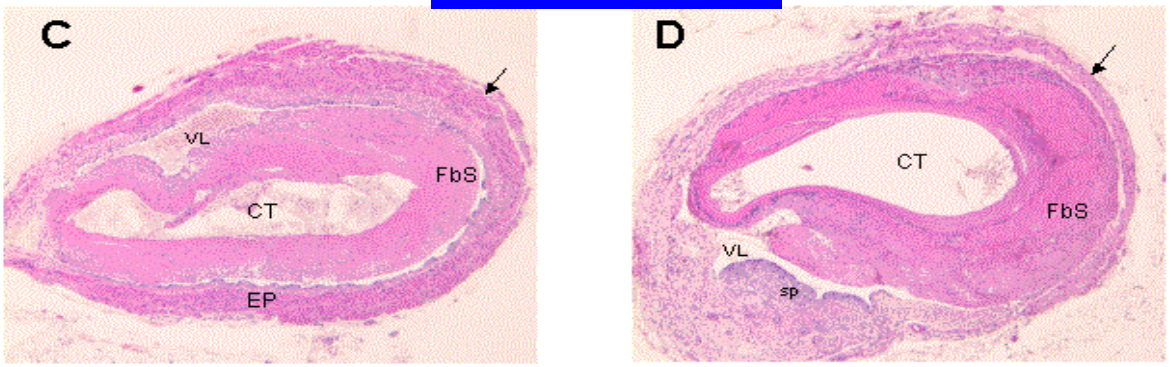
Uncoated Catheters



CBAS Coated Catheters



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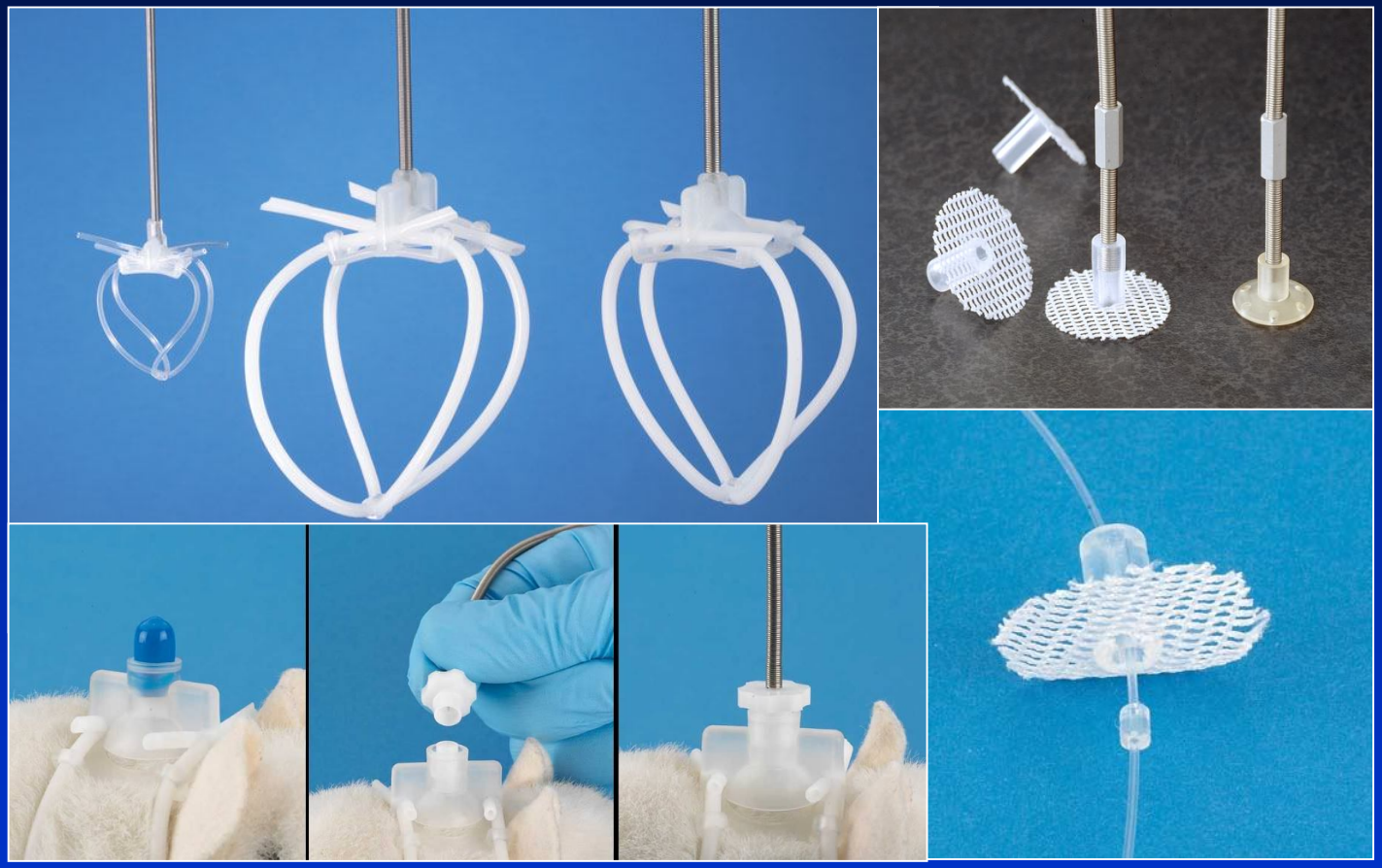
Infusion Equipment (2)

Animal Connection Device

- **Covance Harness**
- **Dacron Button**
- Subcutaneous Access Port
- Tail Cuff
- Dental Cement; head attachment

Infusion Equipment (2)



Infusion Equipment (2)

Infusion Equipment (3)

Infusion Equipment (3)

Infusion Equipment (3)

Rat Infusion Model

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Considerations for Vascular Catheterization

- Connection method
  - Efficient; e.g. weighing
  - Aseptic
- Tethering setup
  - Sterile kits; disposable
- Tubing
  - Medical grade
- Caging
  - Dedicated?

References

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Thank You

Questions?