Virus Shedding

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What is shedding?

Excretion of virus from the infected host by any route

TABLE 45-2 Pathogenesis of Selected Virus Infections: Disseminated Infections

Disease	Common Site of Implantation	Route of Spread	Target Organ(s)	Site of Shedding
Poliomyelitis	Alimentary tract	Blood (nerves)	Central nervous system	Alimentary tract
Hepatitis A	Alimentary tract	Blood	Liver	Alimentary tract
AIDS	Injection, trauma, intestine	Blood	Immune system, brain	Blood, semen
Kuru	Alimentary tract	Blood	Brain	
Rubella	Respiratory tract	Blood	Skin, lymph nodes, fetus	Respiratory tract, excreta in newborn
Measles	Respiratory tract	Blood	Skin, lungs, brain	Respiratory tract
Chickenpox	Respiratory tract	Blood, nerves (to site of latency)	Skin, lungs	
Herpes simplex type 1 Acute	Respiratory tract	Nerves, leukocytes	Many (e.g., brain, liver, skin)	Respiratory tract, epithelial surfaces
Recurrent	Ganglion	Nerves (to site of latency)	Skin, eye	
Rabies	Subcutaneously (bite)	Nerves	Brain	
Arbovirus infection	Subcutaneously (bite)	Blood	Brain and others	Lymph and blood (via insect bite)
Hepatitis B	Penetration of skin	Blood	Liver	Blood
Herpes simplex type 2	Genital tract	Nerves (to site of latency)	Genital tract	Genital tract

Medical Microbiology, S. Baron, U of Texas

- **Do we consider every conceivable route of shedding?**

- **No, only those likely to result in potential infection**

- **Are we equally worried about every vector?**

- **No – Adenovirus vs Lentivirus vs AAV vs Baculovirus**

What are the major factors that should inform how much shedding work we undertake?

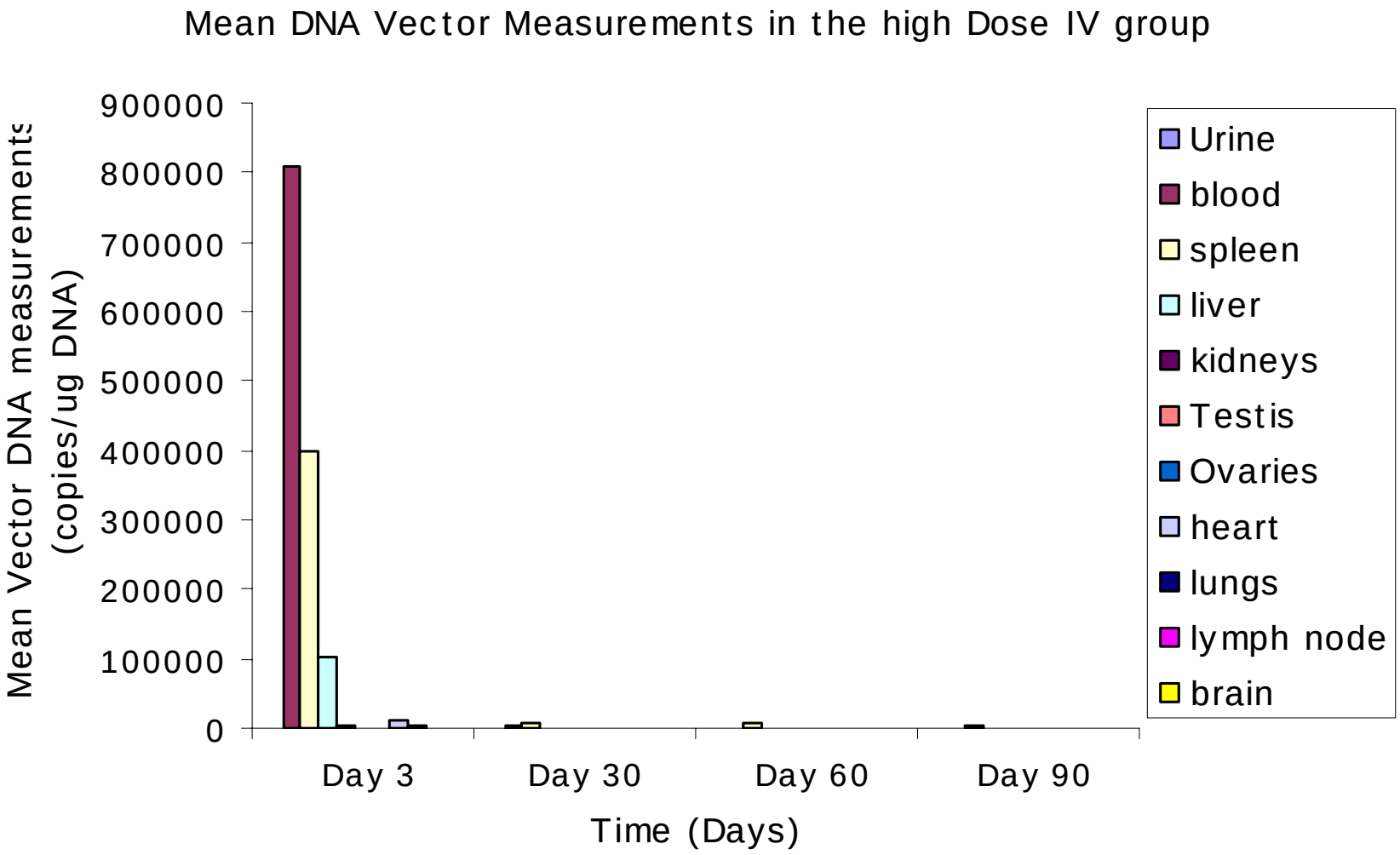
- What is the likelihood that it could be transmitted to other people? If important then,

- What is the likelihood that it constitutes a hazard?

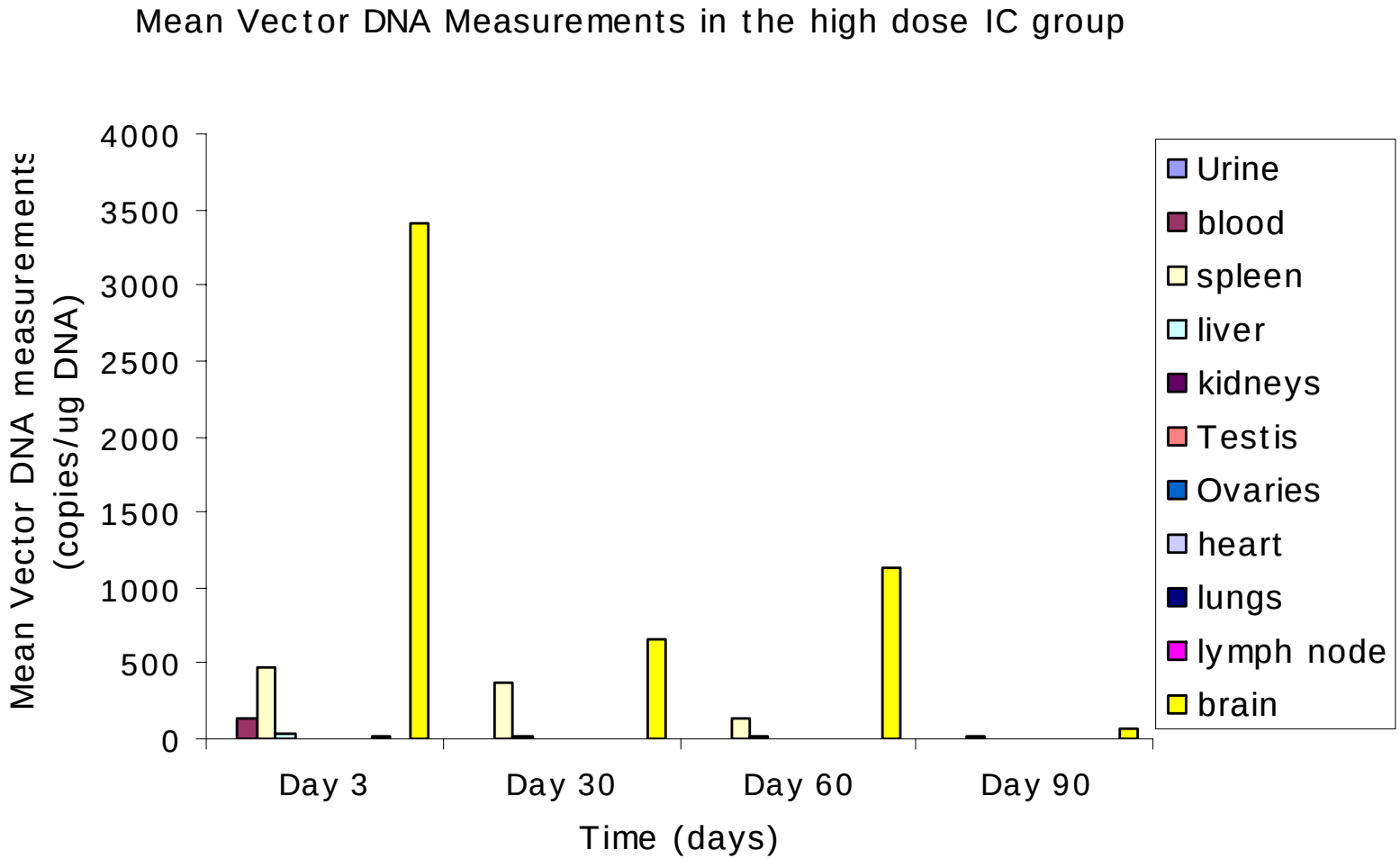
Factors to take into account

- Pathogenicity of virus
- Nature of virus (integrating, replication competent)
- Nature of construct
- Mode of administration
- Potential for, and consequence of recombination.

Biodistribution of Cerepro after IV administration



Biodistribution of Cerepro after IC administration



Human biodistribution after IC administration

Barely detected in blood or throat swabs

However, requirements for shedding information in clinical trials varies by country.

- Throat swabs/no swabs
- Isolation of patient until shedding negative

Consistent approach across Europe would be beneficial

Translation of findings from animal to man

- Knowledge of the vector
- Potential toxicity of the construct
- Route of administration
- Route of excretion/shedding
- Impact on the potentially exposed

Risk assessment is the appropriate approach to assessing shedding in man

Analogy

- The vector is present to deliver a therapeutic gene to a desired target
- It encapsulates the relevant gene
- In many respects it is analogous to an oral capsule delivering a small molecule
- At least adenoviral vectors could be considered safe from a pharmacopoeia perspective, as long as the structural proteins are unchanged