

S29 Needle-Free Parenteral Jet Injection: Past, Present, and Future

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Parenteral injection without needles dates back to the mid-1800s and has undergone several periods of profound change during its evolution. Modern jet injection methods began when doctors noted the neat, almost blood-free puncture wounds created when mechanics were accidentally injected by oil and fuel injection lines in the 1930s. Design of jet injectors used primarily for delivery of vaccines did not change much between 1940s and 1980s. However, new designs are being produced that more closely match specific drug and patient requirements, and promise greater safety, convenience, and control of injections.

Liquid jet injection works by the acceleration of a fine stream (0.004" to 0.012" diameter) of fluid to relatively high velocities and pressures so that the medicament penetrates and deposits into the tissue without the use of a needle. A typical 0.5ml shot lasts less than 1/3 of a second. Advantages include lower pain in many cases, reduction in the fear of needles, better pediatric acceptance and compliance, elimination of accidental intravenous injection, elimination of needle-stick injury, and elimination of one source of hazardous sharps waste.

Currently available jet injectors fall generally into two categories: personal use devices for self-administration of insulin, human growth hormone, etc., and multiple use devices for large-scale immunization programs. In 1985, a hepatitis B outbreak in a California weight loss clinic pointed to the potential for cross-contamination and infection between patients who were injected by jet injectors that reuse the fluid path and nozzle. While mass campaign injectors such as the PedoJet have been used for billions of injections without reported problems, the risks are grave enough to cause concern about current reusable designs.

Future developments in jet injection will include specialized devices dedicated to delivery of new drugs, prefilled unit dose packages, and safe auto-destruct cartridges. Devices as small as a marking pen and devices that can inject dried powders will change the way we deliver parenteral drugs forever.

S31 Antigenic Mimicry in Foot-and-Mouth Disease

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The possibility of developing synthetic peptide vaccines is attractive because they would constitute stable and chemically defined products obtainable at low cost and devoid of any biological risk (Nicholson, B. H., 1994 *Synthetic Vaccines*, Oxford). Considerable research efforts have gone into the development of a synthetic peptide vaccine against foot-and-mouth disease virus (FMDV) (Taboga et al., 1997, *J. of Virology*, 71, 2606).

Recently, retro-inverso (RI) peptides corresponding to the region 141-160 of the VP1 protein of FMDV (known as antigenic site A) have been shown to be excellent immunogens for eliciting neutralizing antibodies against FMDV (Briand et al., 1997, *Proc. Natl. Acad. Sci. USA* 94, 12545). RI peptides, also known as all-D-retro peptides, are composed of D-amino acids assembled in the reverse order from that of the parent L-sequence and have the same side-chain orientation as the original structure. RI peptides are much more resistant to proteolysis and elicit a higher and more durable neutralizing response against FMDV than the classical L-peptides. NMR studies have shown that the structural mimicry achieved with the RI peptide does not extend to the right-handedness of the helical region of the L-peptide that is observed in the solvent trifluoroethanol. Functional antigenic mimicry between L- and RI-peptides actually occurs because the helix is absent in the peptide under the conditions used for assessing its immunogenicity and antigenicity. These findings illustrate the limitations of structural analysis for defining the requisite properties of synthetic vaccine preparations and underscore the importance of biological assays also in the development of chemical vaccines.

S30 Analysis of the Protective Immunity Against FIV Infection Induced by DNA Vaccination

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Whole inactivated virus (WIV) vaccines based on the FL4 cell line, a cell line that is persistently infected with the Petaluma isolate of feline immunodeficiency virus (FIV-PET), have proved effective against homologous challenge with FIV-PET. However, protection did not extend to challenge with the heterologous FIV-Glasgow-8 (FIV-GL8) isolate. Using the alternative strategy of DNA vaccination, significant protection was achieved against the homologous virus when cats were inoculated with DNA from a replication-defective proviral clone of FIV based on the F14 molecular clone of FIV-PET, designated F14ΔRT. Whereas the protected WIV vaccinates developed high titers of virus neutralising antibodies (VNA), no serological responses were detectable following DNA immunisation. To determine the extent of the protection induced by DNA immunisation, cats immunised with the F14ΔRT were challenged with virus prepared from the GL8 molecular clone of FIV, but no protection was evident. Furthermore, a construct based on the GL8 molecular clone containing a similar deletion to the F14ΔRT, designated GL8ΔRT, did not protect cats from challenge with the homologous virus. In contrast, GL8ΔRT inoculation did afford protection against challenge with FIV-PET. Since the viral load that is established following infection with FIV-PET is significantly lower than that established following infection with a matched dose of FIV-GL8, it is possible that protection against FIV infection may be restricted to relatively apathogenic isolates.

S32 Nutritional Effects of Vaccination

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Enhancement of the immunological response to vaccination by "pharmacological" nutrient supplementation has been increasingly suggested in the popular press. However, such practices are rarely used with domesticated animals. The immune response to an antigen has added cost related to losses in growth, productivity, and efficiency. Cytokines (i.e., interleukin-1, tumor necrosis factor) released during the immune response not only stimulate the vaccine response, but also induce significant changes in nutrient metabolism. Interleukin-1 and tumor necrosis factor cause a marked increase in skeletal muscle catabolism. We have estimated that losses in animal performance due to vaccination alone increases the cost of animal production over \$0.5 billion per year. Is the cachectic response to immune stimulation an evolutionary conserved benefit, or is there a change in modern day nutritive patterns that increases the susceptibility of nonlymphoid tissue to the immune-induced catabolism? One major change in dietary nutrient consumption both in animals and humans is the consumption of linoleic acid. Linoleic acid is the precursor for lipid metabolites involved in the inflammatory process, immune-induced muscle wasting, and immune regulation. Dietary recommendations to reduce the consumption of animal fats has resulted in a dramatic increase in the consumption of linoleic acid, which is rich in vegetable oils. This dietary shift has also dramatically decreased the consumption of conjugated linoleic acid (CLA). Immune-induced catabolism of self is dramatically reduced in CLA fed animals. Surprisingly, CLA enhances immunological response while at the same time protecting nonlymphoid tissue from cytokine-induced wasting. It is hypothesized that improved immunological responsiveness to a vaccine is best realized if nonlymphoid tissues are protected from cytokine-induced wasting. Nutrition offers a potential method of protecting against such immune-induced wasting.