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Transmission of Diseases by Syringe and Needle: Risks and Solutions

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Literature study

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Abstract

The use of needle and syringe shared among different patients is a common practice in veterinary science. Although there have been speculations about the possible dangers of this phenomenon, very little research has been done to asses the actual risk. In this literature study all available veterinary data on this topic are supplemented with information gathered in human medicine in an attempt to give a clear, realistic view on the scale of this potential threat in veterinary practice.

Solutions to prevent possible transmission of diseases are described in this study. Special focus is placed on alternative ways of vaccination as this is one of the major purposes for which the same needle and syringe are used for multiple patients. Brief descriptions of known topical and mucosal vaccination techniques, including their mechanism and any results relevant for our research are stated.

Keywords: transmission, needle, syringe, risks, solutions

1. Introduction

In common veterinary practice it is not unusual to treat an entire herd with only one needle and syringe. This practice is even stimulated by commercially available injection guns. The possible risk of this reuse has been neglected by many veterinarians even though information from human medicine reports that there is a significant risk for the transmission of pathogens. Direct financial reasons, convenience and a lack of evidence are possibly the largest contributing factors endorsing this practice. The scarce research on this subject reveals disturbing results making it likely that the economic loss because the use of needle and syringe reuse will outweigh the higher cost of safe injection methods.

Several commercial replacements for needle and syringe have been brought on the market and even though many of these techniques are promising, all still require more research and perfecting.[30] This implies that needle and syringe remain the most used medical equipment, thus not only posing the threat of the transmission of pathogens, but also causing patient discomfort, dangerous disposals and the risk of infection on the injection site.[44]

Since vaccination is often preformed on larger groups of animals by injection done with the same needle and syringe, alternative ways of vaccination will be discussed extensively. Much information is also found in human medicine, especially since vaccination in third world countries, where needle and syringe misuse is common practice and vaccination schedules are often neglected, has received extensive attention.

2. Risks of Needle and Syringe

The most important risk, described this study, is the possible transmission of pathogens, both between animals and from animal to humans in veterinary practice. [40,82] Already in 1945 a memorandum of the British Ministry of Health concluded that the transmission of viral hepatitis seemed to be linked to traces of blood carried over by needle and syringe from patient to patient.[55,73] Injections are one of the most common medical procedures,[40] which suggests that reusable needles cause millions of blood born infections.[37] One of the main contributing factors to the risk of disease transmission by needle and syringe is the easy misuse and unsafe use of these instruments,[8] often seen in veterinary practice, mainly in the production-animal sector.[86] In human medicine this problem is mostly seen in the developing countries and with injectable drug users, mainly due to a lack of money.[25,41] For these reasons UNICEF, amongst others, does not use disposable needles and syringes anymore in their vaccination campaigns, but advices autodestruct needles.[8,85] Even stronger is the warning from the World Health Organisation stating that governments and donor agencies cause a high risk of disease and death in the population by supplying standard disposable needles and syringes.[37,85] Sterilizable needles and syringes probably pose an even bigger threat as they require a extensive protocol to prepare them for reuse.[8] The WHO therefore calls for major initiatives to improve injection safety by fighting the overuse of needles.[37]

An occupational risk for accidental needle sticks has been described for anaesthesia personnel,[5] veterinarians[86] and healthcare workers.[45] Substances most often injected include vaccines, antibiotics, anaesthetics and animal blood. The estimated overall needle stick injury rate for veterinarians is 9.3 per 100 person-years among young female graduates of all US veterinary colleges. 4% of sticks causing severe or systemic side-effects, which can go as far as inducing a spontaneous abortus. Possibly veterinarians are exposed to a higher risk of accidental needle sticks than other healthcare workers, because they often work with unpredictable and uncooperative patients.[82] Reports were found on 60 cases of pathogen transmission: 26 viruses, 18 bacteria, 13 parasites and 3 yeasts,[78] among which hemorrhagic fever viruses, malaria, human immunodeficiency virus, hepatitis B and C, Ebola and plasmodium falciparum.[73] Therefore the development of needle-free ways of immunization and drug delivery is vital.[61]

In general, the risk of the transmission of a blood disease is determined by the used injection protocol, the number of injections and injection volume which an individual receives and the prevalence and transmissibility of the pathogen organism in the blood.[8,73] This is because not every disease is transmitted with the same ease. Reports show that the Hepatitis B virus, which can be carried over by just 10 picoliters of blood, is transmitted ten times easier than the Hepatitis C virus and even more than twenty times easier than HIV (still half of all new HIV infections in major metropolitan areas are caused by needle-transmission).[34,71,73] The transmission is supported if a pathogen ends up in a suitable environment. Intramuscular injections for instance can create a new niche which pathogens can inhabit.[60,70] Few data can be found concerning this risk in veterinary practice, but one of the scarce, older reports on this subject show disturbing numbers about the transmission of the LDH virus caused by simple subcutaneous pricking with a 26 G needle (22 out of 23 mice got infected).[14]

The eminent danger present in blood transfusion procedures has been the subject of more research.[21] It is likely that every patient with a viremia, parasitemia, bacteremia or fungemia could deliver a pathogen by accidental needle-stick injuries, but viral infections seem to be the majority.[71,78] However, blood is not a necessity to carry over pathogens as some can also be present in other body fluids, for instance HIV is mostly found in spermal and cerebrospinal fluids and hepatic viruses can be present in ascitic fluid. This must be kept in mind when assessing the risk of disease transmission.[78]

Because of this occupational risk sharp object management is a part of infection control in veterinary practice. Measures that can be taken in this respect are; not recapping the needle, the disposal of used needles in a special deposit container and the prohibition of reuse and sterilisation of needles and syringes.[86] Despite such guidelines a certain risk will remain as needle stick injuries happen during preparation, use and disposal.[8] If the costs of these occupational sticks are taken into account needle and syringe are deemed to be more expensive methods of injecting than jet-injectors or autodestruct needles.[24] Especially because needle and syringe have to undergo destructive incineration to eliminate all risks mechanically or as a vector,[8] whereas autodestruct needles are blocked after use, which happens automatically or manually, in which case an extra step has to be taken by the user.[8,24]These autodestruct needles prove to be faster, quicker and easier to work with than the conventional needle and syringe. But the higher cost, a similar number of clinical accidents and the difficulty to work at high speed make this solution one of little value in a standard veterinary clinic.[75]

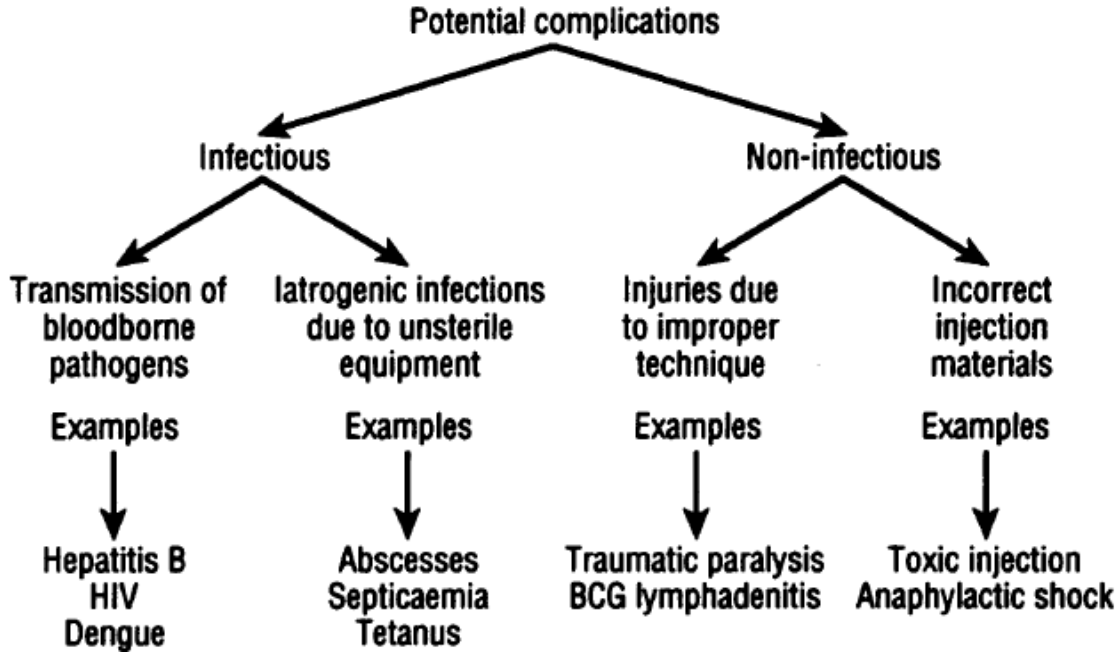

Figure 1. A schematic risk assessment by the World Health Organization, showing risks of injections with needle and syringe.[8]

3. Alternatives for Needle and Syringe

The use of injection needles will probably never be completely replaced by other techniques, because there are procedures which require penetration such as the aspiration of fluids in the body. However, these procedures are mainly performed on one individual and therefore the same needle will not be used between several individuals in contrary to procedures like vaccination.
Needle free vaccination has the potential to improve immunization processes with regard to safety for both vaccinator, vaccinee and community, better compliance with vaccination schedules, reduced or even no injection pain, faster and easier application and lower cost.[29] As application of most vaccines without needles has proven to be challenging, especially for inactivated vaccines. Needle-free vaccination still happens less, because even though it was introduced in humane medicine fifty years ago with the oral polio vaccine, it is still necessary to find a new method for every new vaccine which proves to be working sufficiently.[25,68] Current options regarding needle free vaccination can be divided into cutaneous and mucosal immunization.[58]

Cutaneous methods are: liquid jet injectors, which inject a high velocity vaccine; Epidermal powder immunization, which consists of accelerated dry powder shot into the epidermis; and topical application, which is based on passive or facilitated transport through the skin barrier.[58] The skin is an interesting organ for vaccine application as it is an integral part of the immunesystem.[63,9] The epidermis contains Langerhans' cells creating a network, making it possible to efficiently take up foreign antigens forming some sort of immunosurveillance. This network forms the second line of defense after the mechanical one of keratinized skin cells. Langerhans' cells initiate a specific immune response by processing and presenting antigen fragments to naive T-cells in de lymphatic nodes.[76] This generates both systemic (IgG and IgM) and mucosal (IgA) humoral responses. Vaccine doses, used in this system, can be smaller than the amount necessary for intramuscular vaccination.[65]

As mucosal routes, especially oral and nasal ways have been used for the application of medicines for thousands of years, thus much longer than needle and syringe.[58] Mucosal immune responses can be complementary to systemic responses protecting the host from pathogens at their port of entry. Antigen application on mucosal surfaces normally generates a mucosal response, which is strongest at the mucosa used for the administration of the vaccine.[30]

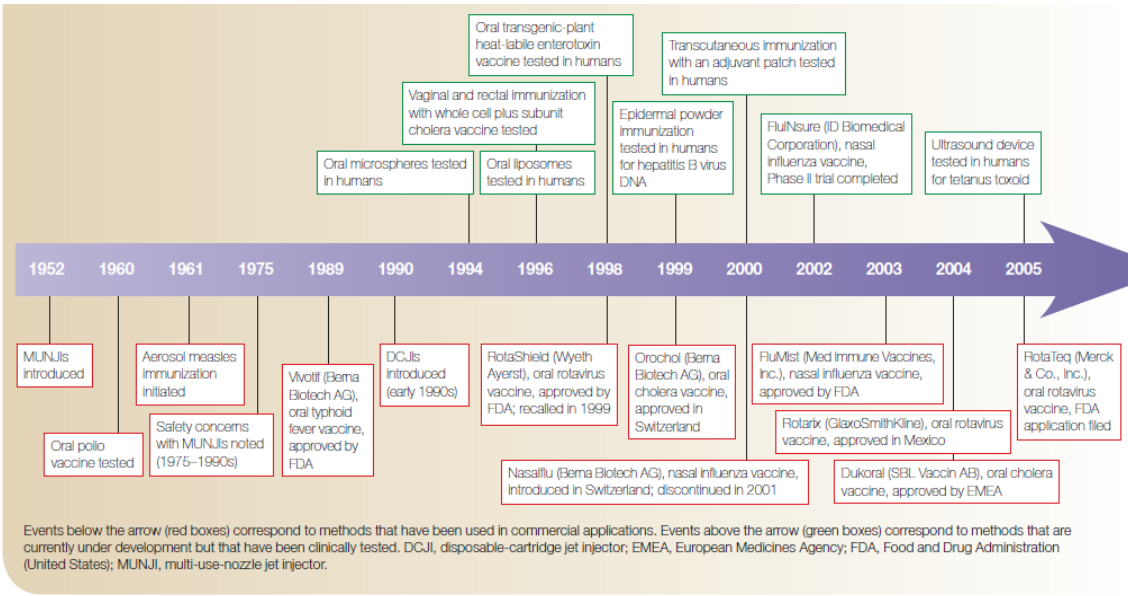

Figure 2. Important events in the development of needle free immunization.[58]

3.1 Jet injectors

The basic design of commercial jet injectors consists of a power source (such as gas under pressure or a spring), a plunger, a compartment in which the drug is loaded and a nozzle with a diameter between 150 - 300µm. If the trigger is pulled the power source forces the plunger down, pushing out the drug through the nozzle with great speed, varying from 100 - 200 m/s.[7] Some jet injectors are manually operated, where others are primarily motorized and get their energy from a rechargeable battery.[30,36,58] The current jet injectors have very few adjustable settings, which makes it hard to anticipate individual differences between the mechanical properties of the skin of patients having a direct effect on the drug delivery. Equipment used in human medicine, because of this, needs modification before it can be used in veterinary practice.[7,71] A new type of jet injection is the so called pulsated micro jets, meant for the application of protein drugs into the skin without deep penetration. This is possible because of high speed (V>100m/s), which facilitates the penetration, being compensated by small volumes (2-15 nanoliter) and a small diameter (50-100 µm), limiting penetration depth. After shaving the skin depths from 200 to 400µm are reached with this technique.[6]

The use of jet injectors is very attractive as it makes sharp needles redundant, is cheaper per vaccination than needle and syringe and can be used to give several vaccinations per hour.[24,34,81] For this reasons the use of jet injectors already started in the early nineteenfifties as a method for needle free application of drugs and vaccines.[33,58] For a few decades, needle free vaccination was the preferred method in mass immunization campaigns in the third world because of the ease in application and the presumed sterility.[25] Unfortunately, like every reusable instrument, there is a potential danger of spreading pathogens.[15] This causes the Centres of Disease Control to state in 1994 that there could be a potential risk of transmitting pathogens if the jet injector's nozzle would get contaminated with blood during injection and would not be properly cleaned for sequential injections.[45] Later research shows the transmission of hepatitis B virus and other agents via jetinjectors,[15,39] after which a new guideline is published stating that the use of MUNJI's (Multi-use Nozzle Jet Injectors) should be limited to mass immunization when there is too little manpower or vaccination with needle and syringe is dangerous to the healthcare workers.[81]

Systematic studies have reported that MUNJI's can carry over significant amounts of blood from one patient to the next (more than 10 picoliter), even if the nozzle is being separated from the skin by a plastic device. The jet injector will get contaminated the moment the pressure of the tissue exceeds the pressure in the jet injector, causing a reflow through the entry hole which was created by the jet injector. This reflow will contain blood because of the destruction of small blood vessels during the initial injection (Figure 3).[34] This is why a second main class of jet injectors was invented based on the use of a disposable nozzle piece which reduces the risk of transmission to zero,[7,23,34,45] as the used nozzle is being disconnected after the application, instantly blocking it for further use by a sequence of events.[39] A third small class of jet injectors typically contain disposable syringes to counteract cross-contamination.[32] Despite these new developments the WHO still gives the general advice not to use jet injectors for immunization.[85]

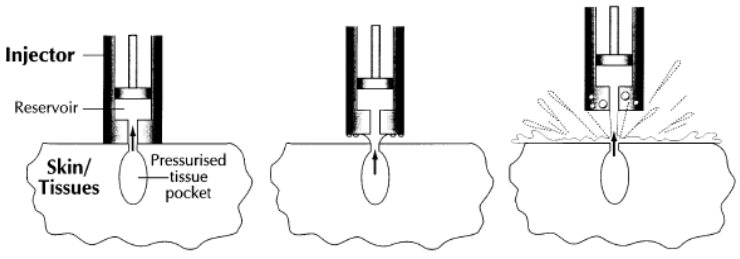

Figure 3. Proposed mechanism of contamination of the jet injector by the reflow when tissue pressure exceeds the pressure inside the jetinjector.[34]

Whether jet injectors would cause more local tissue reaction than needle and syringe is still a matter of discussion. The majority of authors agree there are more adverse reactions and bleeding with the use of jetinjectors,[25,36,49,50,83] but some authors report less reactions.[69,81] This is attributed to the deep penetration and that bruising can be minimized by penetrating less deep.[6] Exit velocity, nozzle diameter and jet volume are the variables that effect this. [10]

The importance of this discussion changes if the local reaction is thought to be a good thing as it stimulates vaccine uptake by the immunesystem.[83] This uptake is already better with the jet injector, thans with needle and syringe, as administered drugs spreads over a larger ratio of tissue. Both will lead to a more intense contact with antigen presenting cells before degradation of the antigen.[58] This is probably the reason why immunity raised with jet injectors is as good, or even better than intramuscular vaccination with needle and syringe.[62,69]

3.2 Topical immunization

For thousands of years the skin has been used to apply medication for both local and systemic problems, like the immunization against smallpox in India more than a thousand years ago by scarification of the skin of healthy individuals with wart tissue. Benefits of the skin as a place for application of drugs and vaccines are its easey reachability, its immunosurveillance function and no degradation of macromolecules like in the gastrointestinal tract.[7,58] However simply applying a vaccine on the skin does not give a satisfying immune response, with the exception of some rare cases.[58] A solution can be found in a simultaneous administered adjuvant, with which both systemic and mucosal immune responses can be observed.[30,32] Animal studies show that antibodies induced by transcutaneous immunization in the presence of an adjuvant is functional and can offer protection, even without disrupting the skin.[31,32] Still there are some obstacles of which one of the most prominent is the lack of absorption of most drugs through a intact skin or the dependence on intact functional hair follicles.[19,85]

Increasing the permeability of the stratum corneum without damaging the underlying keratinocytes is a great challenge. Mechanical methods like microneedles, tape, ultrasound, microporation and electroporation are being used and investigated, both for the application of drugs and for immunization.[58] But administering molecules with a weight above 500 Da to the depth of the dermal blood vessels has not been possible so far. Fortunately transcutaneous vaccine antigens and adjuvants are meant for the more superficial epidermis. So even with a minimal stratum corneum disruption it is possible to raise a strong immune response with molecules up to 1 million Da.[30]

Penetration of the stratum corneum can be enhanced with techniques like hydration, mechanical disruption or a combination of both.[30] These techniques can be divided into passive and active methods, depending on whether an external energy source is used.[7]

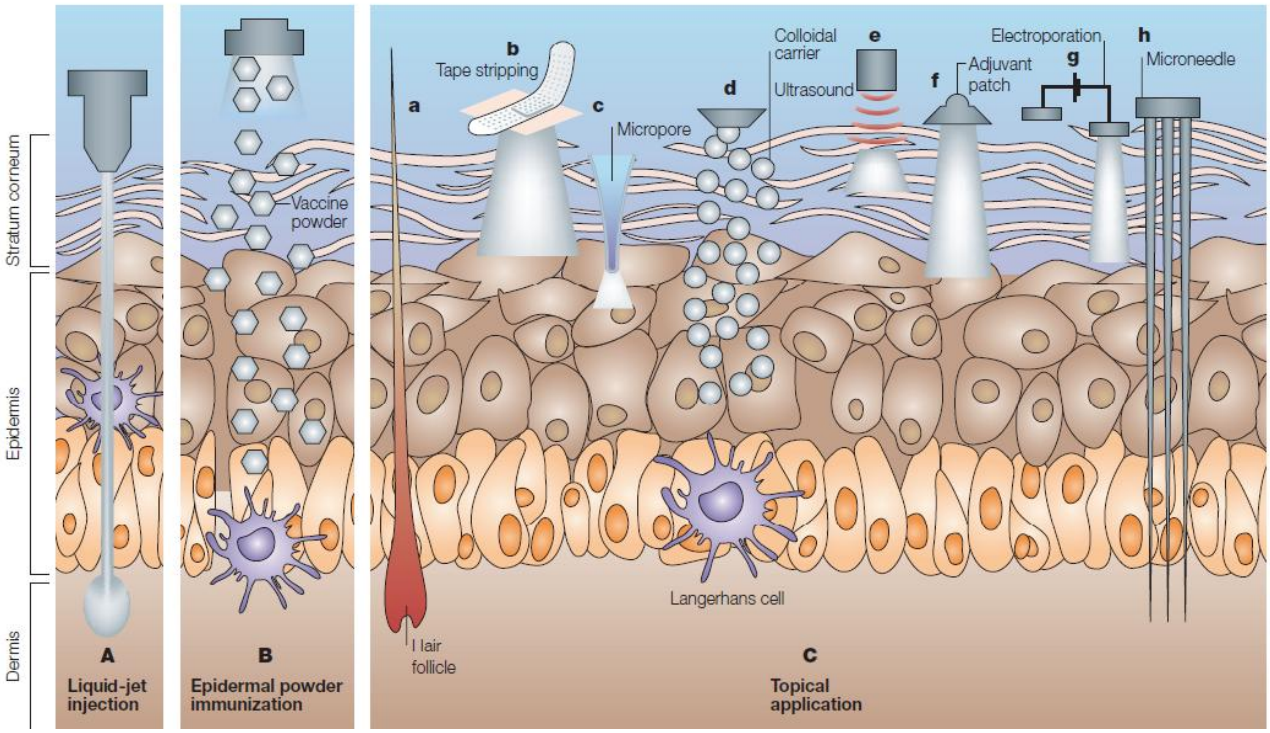

Figure 5. Cutaneous ways of Immunization.[58]

Microneedles

Microneedle patches are made in fields of hundreds of microneedles standing on a silicon plate.[7,20] The microneedles are between 10 - 15µm long and therefore able to penetrate the stratum corneum, without touching the nerves present in deeper layers. The length of the microneedles logically has great influence on the pain sensation of the patient.[7] Experimental clinical studies affirm this as volunteers report no pain and minimal sensation with microneedles shorter than 15µm.[51,52] Residual holes after taking out the needles are only a few micron in diameter and exist 24 hours if kept covered, but are already gone after two hours if left uncovered. Results show that microneedles are capable of establishing a stronger and less variable immune response than topical administration and that less applications are needed for a full seroconversion. In these studies microneedles generate immune responses that are at least equal to those elicited by subcutaneous or intramuscular injections with a lower dose. An alternative form are the micron-scale silicon projections called micro enhancer arrays (MEA's), these fully silicon based spikes are up to 200 µm long and display results similar to the microneedles.[53]

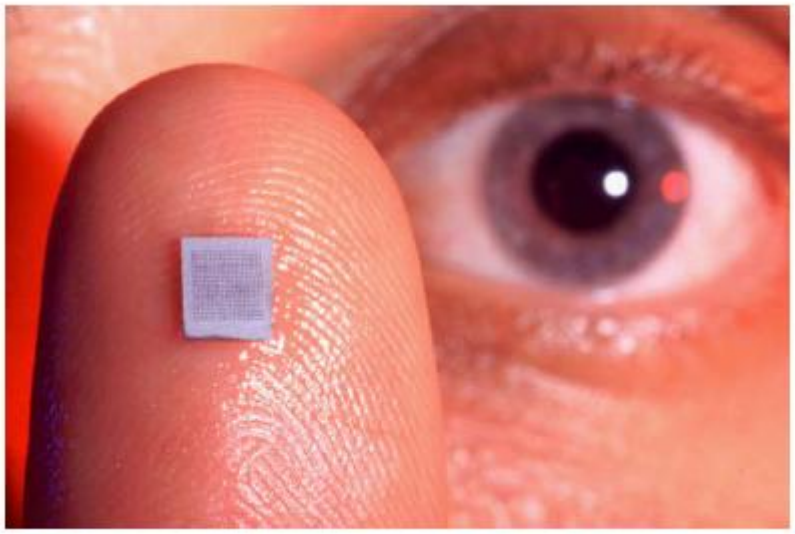

Figure 6. An array of 20 x 20 microneedles.[30]

Microseeding

This is a technique in which a tattoo gun is used to spread drugs or DNA into a larger surface of skin, as this will affect more cells and potentially have more contact with the immunesystem.[63]

Tape

The stratum corneum can be efficiently removed by taping the skin several times, just like the use of a razor or toothbrush.[80]

Ultrasound

Topical application of a vaccine gave a tenfold stronger immune response than subcutaneous injection after the skin was treated with a low frequency (20 kHz) ultrasound, as the lipid layer of the stratum corneum gets disrupted by the collapses of cavitation bubbles.[58]

Electroporation

The permeability of the stratum corneum can also be increased by electroporation, a mechanism also used for in vitro gene transfer in cells.[16,64] Electroporation is also known to elicit a strong immune response after transdermal application of peptide vaccines.[58]

Hydration

Hydration of the stratum corneum, possible through occlusion and making the skin wet, causes keratinocytes to swell and fluid to accumulate in the intercellular spaces.[30] This enables drugs and vaccines to diffuse more easily across the skin barrier.

Thermal ablation

Recently, instruments have been developed for micro-ablation of the stratum corneum, which results in a strongly increased permeability of this layer. The stratum corneum is selectively burned away, without damaging the deeper tissue. This is possible because of full control over the temperature on the surface of the skin and the short time span in which the high temperature is maintained. The microscopic mechanism is still unclear. One hypothesis is that the water bound in the stratum corneum vaporises so that the sudden enlargement of volume makes holes in the skin layer. Another theory is that temperature has to be much higher than the boiling point of water and that the mere incineration of the skin is responsible for the increase in permeability. The holes created with this technique are small enough to limit undesired responses like pain, irritation and infection. Other benefits are a better control over physical and psychological impact on the skin compared to needle and syringe.[7]

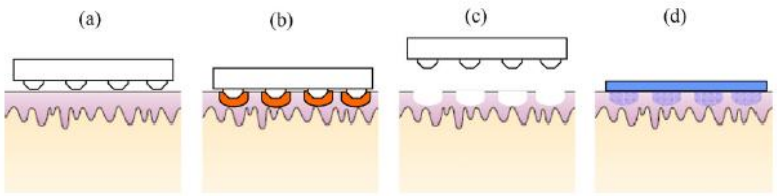

Figure 7. A schematic overview of the thermal ablation method. Electrodes are pressed against the skin (a) and heated (b), which creates small holes in the skin (c) after which a drug patch can be placed (d).[7]

Biological vectors

The efficiency of epicutaneous administration might be enlarged if the live vectors being used would have an affinity for a specific type of cells present in the skin, like keratinocytes, APC's or other skin barrier cells. Such a 'skin binding' vector might be more effective because of overexpression of antigens in specific cells which are potent immunostimulators.[72]

Powder immunization

Certain methods, called ballistic methods, accelerate drug powders so they can penetrate the outer layer of skin (stratum corneum) to be deposited in the epidermis or the outer layers of the dermis. This is also called epidermal powder immunization (EPI).[7,58] This technique would also ban the risk of disease transmission by needle[25] and still make direct contact with Langerhans' cells. Storage and use of powder would be considerably easier than liquid solutions.[58] Higher titres of antibodies than after intramuscular injection can be reached, but an adjuvant is needed to get such results.[18] Again the thickness of skin in cattle could be a problem hard to overcome. Despite promising results in clinical studies, it seems that the commercial development of EPI has stopped.[58]

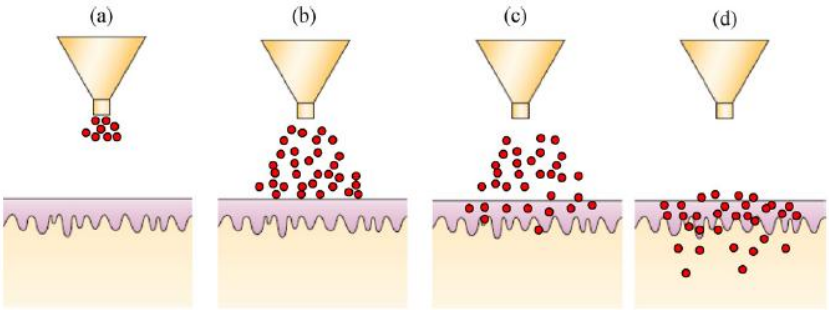

Figure 4. Powder immunization in four steps, after which most of the drug is accumulated in stratum corneum and viable epidermis.[7]

A variation is the technique of mini projectiles. These hollow, bullet-like objects into which drug formulations can be loaded are shot into the skin of the animal using compressed air. The administration device can remain a distance of 3 to 10 mm, thus minimizing the chance of pathogen transmission. Tissue damage by these projectiles is comparable to the tissue damage caused by conventional needle and syringe and animals, indeed, did not show an adverse reactions stronger than those to needle and syringe. Positive results with this technique used on pigs are reported. The main limitation of these mini projectiles is the small volume they can carry (maximum 500 µl).[79]

3.3 Mucosal vaccination

In healthy individuals up to 80% of all immunocytes are gathered in the mucosa.[35] Therefore, the mucosa are important immunological organs, which function as a permanent surveillance system against external antigens.[46] Antigens provided by bacteria in a fagosome or in cytoplasm will be presented as Major Histocompatibility Complex (MHC) I molecules by Antigen Presenting Cells which will trigger a CD_8+ response. Once the content of a fagosome is degraded the dead bacteria and their contents will be presented as MHC II molecules triggering a CD_4+ response.[19] Mucosal immunization is the only way of needle free vaccination that is often used successfully in current immunization programs. All mucosal routes and surfaces, like oral, nasal, pulmonary, rectal, conjunctival and vaginal mucosa could be possible vaccination sites. Because of practical reasons and the issue of social acceptation most research in this field is aimed at oral, nasal and aerosol administration.[46]

Mucosal immunization is seen by some as the best way of vaccination against local infections of the mucosa or against pathogens which use the mucosa as their portal of entry.[22] But apart from triggering a mucosal response these vaccines also trigger parts of the systemic immune system, leading to the production of serum antibodies, lymphocyte proliferation, cytokine production and cytotoxic T-cell activation. Thus eliciting protection against some systemic infections.[56] Although it was initially thought that mucosal vaccines only initiated short term protection, it has been proven that they are also capable of giving long term protection,[47] making it possible to use the many benefits that mucosal immunization has to offer.[30]

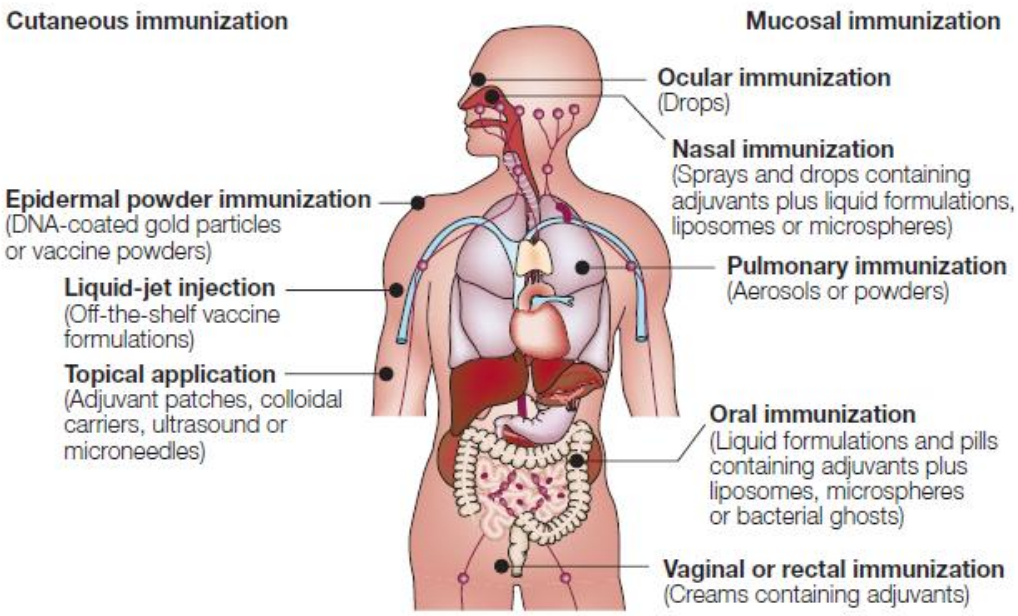

Figure 8. A schematic representation of various methods of needle free immunization.[58]

Oral vaccination

After the success of oral vaccination for the global eradication of poliomyelitis the development of other oral vaccines was strongly stimulated.[84] The efficacy of oral immunization has been proven in several animal studies, clinical field studies however present variable results.[38,43,57] Oral vaccines are mostly based on attenuated, living vaccines,[37] which are recognized by M-cells in the Peyer's patches and dendritic cells in the same region to be presented to the underlying lymphoid aggregates.[36,65] Gastric immunization is also possible but induces a short-lasting response.[17]

Oral administration of protein antigens poses great challenges, because of the strong natural barriers in the gastrointestinal tract, like stomach acid and proteases that degrade these molecules. Next to that, the absorption of proteins from the gastrointestinal tract is often low.[19] Several solutions have been developed for these problems such as: nanoscale fat particles known as immunostimulating complexes or ISCOMs, consisting of fatty acids, adjuvants and antigens, both membrane associated and water soluble;[17,42,44] or bacterial ghost cells, which are bacteria without cytoplasm content used as carriers for the vaccine; biodegradable polymeric parts (mostly polylactide-co-glycolide or PLG encapsuling the antigen) have been developed.[17,44] These microspheres do not only protect the antigens against the hostile environment in the gastrointestinal tract; they are also believed to slowly release the antigens they contain, which might make booster vaccination redundant.[58] Strong adjuvants also successfully stimulate the immune response in oral vaccination. The three most successfull adjuvants appear to be ADP-ribosylating enterotoxins, synthetic oligodeoxynucleotides containing unmethylated CpG dinucleotides and monophosphoryl lipid A.[28]

Two promising techniques that have been developed in oral vaccination are attenuated bacteria, which express foreign antigens, and transgenetic 'eatable' plant vaccines. The attenuated bacteria deliver heterogenic antigens to the immune system by bacterial expression of the antigens encoded by the plasmids or by inserted heterogenic genes.[29,30] Unfortunately plasmids are often lost during division. The most important approach to this problem is creating a mutation in the essential genes of the bacteria. The deficiency caused is solved by introducing a plasmid with a working copy of this gene. Though promising in theory, reality shows that bacteria produce way more essential protein than necessary, putting a metabolic burden on themselves, which reduces the fitness of the organism and in the meantime lowers the pressure of selection because of the excessive amount of this protein present in the direct environment.[19]

Transgenic 'eatable' vaccines are unique in their ability to both suitable for the production of antigens as well as the oral administration of it.[28,66,77] The rigid cell wall of the transgenic plants offer protection against the low pH in the stomach. Other benefits are the absence of contamination with animal antigens, low production costs and thermostability. They can also be designed in such a way that they contain more than one antigen in order to lower the cost even more.[28,66] Strong adjuvants are still needed as non-replicating antigens are usually poorly immunogenic.[28]

A possible extra benefit of oral vaccination with attenuated vaccines is the immunization of non-vaccinated individuals by vaccinated ones after excretion of live virus shed in the faeces. Although very positive for herd immunity, it may also be a possible danger in case of reversion of the virus to the wildtype.[27] A downside is that the dose for oral immunization needs to be a lot higher (up to a hundred times) than for injected vaccines, which of course raises the cost. Potential problems could be finding the balance between attenuation and efficacy and the immunity induced in an animal against the vector organism after sequential administrations.[19]

Nasal vaccination
Nasal administration is a practical way of administering, using lower doses than oral vaccination and because of less enzyme activity in the nasal lumina.[4,11,12,58,72] Nasal application can achieve high levels of antibodies after a single dose, not rising after a booster vaccination.[72] There is very little local reaction after nasal application of a vaccine, also because the use of an adjuvant is not necessary in order to create an immuneresponse.[11,58]

Antigens trigger the immune system via the nasofarynx associated lymphoid tissue, inducing an efficient and antigen-specific immune response.[58] The organogenesis of the nasal-associated lymphoid tissue is different from other lymphatic organs because of its initiation and regulation. The initiation of the organogenesis of the nasal associated lymphoid tissue starts only after birth in contrast to other secondary lymphatic tissues, starting to develop during the embryonic period. This difference could cause serious and functional consequences that should be taken into account in the development of future nasal vaccines.[67]

Pulmonary vaccination
For vaccination via the lungs, powders are used or solutions are vaporized to produce aerosols small enough to travel into the alveoli. This old technique gives a strong immune response, stronger than the one after subcutaneous administration.[74,67,30,20] Even small doses of vaccine can already elict such strong responses, though comparison is difficult as different size particles and several nebulizers are being used.[20] The possibility for retrograde contamination of the vaccine by pathogens in the vaporizer, enabling it to carry over to other patients is thought to be minimal, because of the loose fit of the mask on the head and the high pressure maintained in the vaporizer.[30] Other benefits are the non-traumatic nature and thus the possibility of application by non-medical personnel. Even vaccination by introducing aerosols into a stable might be an option as reports from the former U.S.S.R. successfully endeavoured this in classrooms filled with children.[20]

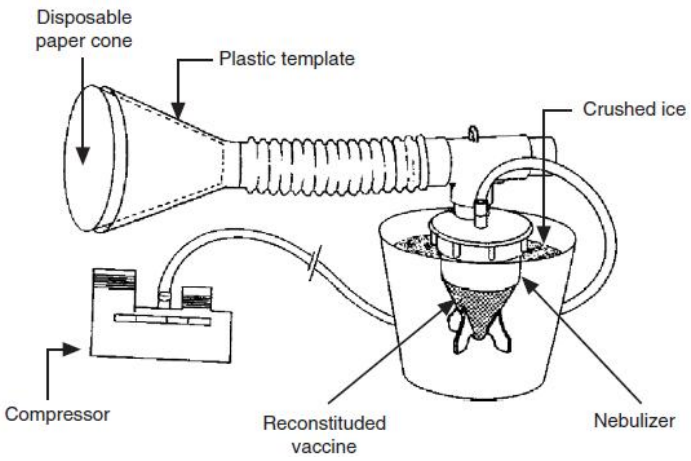

Figure 9. An example of an equipment diagram used in pulmonary immnisation.[30]

Rectal and vaginal vaccination
Though like all other mucosa's a valid possibility research on rectal and vaginal vaccination is found to minimal, mostly because of social inacceptance.[46] Naturally less resistance is to be expected for the use of these techniques in veterinary practice.

Conjunctival vaccination
Though conjuntival vaccination has been proved to be able to give strong immune responses there seems to be only a little interest, because application is not necessarily without problems.[11,59]

4. Discussion

Data from animal experiments and human clinical trials make it unequivocally clear that there is a significant risk when a needle and or syringe are used for more than one patient. Common grounds with human medicine are found in those settings where financial reasons are a limiting factor. Possible economic loss because of this iatrogenic spread of pathogens should be subjected to further investigations as should the potential threat to public health.

Alternative ways of drug delivery and vaccination have been developed but at this time no method seems to be superior to the others.[58] These solutions still need perfection as results sometimes vary between authors and equipment and techniques are not adjusted to veterinary use. Methods based on physical principles, like ultrasound, electroporation and microporation use expensive devices and require the presence of electricity.[58] Other problems are the size of some devices and the high price for one- time-use or the reuse of parts. Future designs should be focused on making these devices smaller, cheaper and with better standardization between individuals.[7]

Results now published based on experiments with mice should be interpreted with caution as their predictive merit is still uncertain.[12] For the comparison of antibody titres between different techniques it is necessary to realise that the used antigens often are very stable proteins, therefore different from natural, immunological relevant, 'real' antigens. This might also be the reason why immunization still fails to reproduce an immune response, probably caused by problems with presentation of the antigen to the immunesystem.[48] Antigen structure might be the crucial factor causing these differences.[57]

In an attempt to assess which techniques to develop, the cost of solutions should be taken into account since veterinary practice is limited in their financial possibilities. The total cost does not only consist of the initial price of the equipment, but also depends on the costs to sterilise or dispose it. Life-span of the instrument and production cost will have to be balanced in such a way that veterinarians are able to buy and maintain their materials in order to prevent misuse or falling back to needle and syringe.

This discussion could be better founded if more accurate data about the actual transmissibility of common pathogens in cattle is investigated. This information would make it possible to calculate the financial loss caused by the illness of the animals.

5. References

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