Astudy on Needle free injection systems

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Abstract—
Needle free injection systems are innovative ways to introduce a variety of medicines in patients without piercing the skin with a traditional needle. These systems work by the mechanism in which liquid medication is forced at an elevated speed through a small orifice that is held against the skin. Due to this an ultrafine stream of high pressure fluid is created, that penetrates the skin devoid of the use of a needle, thus faster administration of drug occurs as compared to conventional needles. Needle free systems are designed to solve the problems created due to conventional needles making them safer, less expensive, and more suitable. It is expected that these systems will augment the rate of vaccination and reduce the amount of antibiotics prescribed. Moreover, they should decrease the occurrence of needle stick accidents that have been seen in some health care workers contracting diseases. Today, they are an increasingly rising technology that promises the administration of medicine efficient with reduction of pain. Companies are not only working on developing technologies that are safer and easier to use, but also on alternatives which can deliver more types of medicines.
Keywords: Needle Free, Injection, Drug delivery, Technology.

I. INTRODUCTION

The first hypodermic syringes were firstdeveloped by French surgeon, Charles Gabrielpravaz, in 1853, although there is a minordevelopment in syringes since then, thetechnology has been remained unchanged for last150 years. Needle-free systems was firstdescribed by marshall lockhart in 1936 in hispatent jet injection. Then in the early 1940'shigson and others developed high pressure "guns"using a fine jet of liquid to pierce the skin anddeposit the drug in underlying tissue. Thesedevices were used extensively to inoculateagainst infectious diseases and were later applied more generally in large scale vaccinationprogram. Today, they are a steadily developingtechnology that promises to make theadministration of medicine more efficient andless painful.

The term needle free is used to describe an extensive range of drug delivery technologies, which consists of technologies that do not have a needle but make use of electrophoresis to drive drugs through the skin, technologies that use one or more very small needles, but needles nevertheless (Micro needle drug delivery system). Needle free devices can take the form of power sprays, edible products, inhalers, and skin patches. Devices are available in reusable and disposable forms, for home or physicians office use, and also in versions for multiple patients and institutional uses . This technology avoids various disadvantages that are associated with needle use:

- Therisk of cross contamination from needle stick injury
- Under or overdosing which results in poor injection technique in patients
- Needle phobia
- Injection site pain
- Poor compliance resulting in long term worsening of conditions
- Increased costs due to patients visiting the hospitals for injections

II. STRUCTURE OF HUMAN SKIN

Human skin is generally made of two layers i.e., the epidermis and dermis.

Epidermis

It is the external layer of the skin which is mainly composed of various layers of keratinocytes, melanocytes, Langerhans cells and Merkel cells. It acts as a physical and chemical barrier between the body and external environment. The epidermis is stratified squamous epithelium in nature . It has four layers:

1. Stratum basale
2. Stratum spinosum
3. Stratum granulosum
4. Stratum corneum

Dermis It is the area of supportive connective tissue between the epidermis and subcutis. The dermis mainly consists of sweat glands, hair roots, nerve cells and fibers, blood and lymph vessels. It is mainly composed of a thin papillary and thicker reticular layer. Its main function is to protect the body from stress and strain. A sense of touch and heat is provided by the mechanoreceptors harbored by the dermis .

Hypodermis
It is the layer of loose connective tissue and fat that lies beneath the dermis. Its role is to put together the skin and underlying bone and muscle and supply it with blood vessels and nerves .

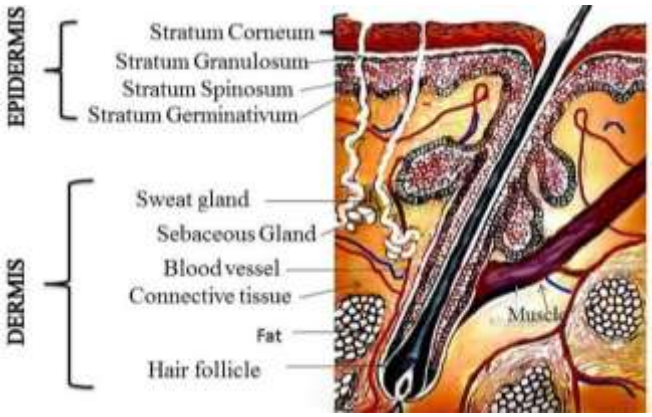

Fig. 1: Structure Of Human Skin

III. APPLICATIONS OF NEEDLE FREE INJECTION TECHNOLOGY

1. Mass immunizations such as measles, smallpox.
2. Intraject (Weston medical) technology is used to deliver drugs which consist of proteins, peptides, monoclonal antibodies, small molecules and vaccines.
3. Powderject (Powderject pharmaceuticals) technology is used to deliver inulin to hairless guinea pigs, delivery of large macromolecules across the skin, for intradermal DNA immunization against influenza virus in mice.
4. Jet injectors technology delivers proteins such as β-interferon as well as small organic conventional therapeutic agents such as lidocaine (lignocaine) for local anaesthesia.
5. The Disposable Syringe Jet Injector (DSJI) Project is supporting clinical research on the delivery of vaccines with jet injectors. Current research work includes following applications

IV. COMPONENTS OF THE NEEDLE FREE INJECTION SYSTEMS

1. Nozzle

The nozzle has two significant functions; it acts as the passage for the drug and as the surface which contacts the skin. The nozzle contains a flat surface and an orifice. The nozzle provides the surface which comes in contact with the skin and the orifice which the drug passes through when injected. The orifice controls the drug stream diameter and speed. A stream diameter of approximately 100 μm and traveling at 100 m/s can achieve the desired injection depth of 2 mm .

2. Drug reservoir

The drug volume holds the injection fluid inside the device .

3. Pressure source

The energy source provides the essential driving energy to the drug for injection. Many of the devices in the market use either mechanical or stored pressure as energy storage elements. The mechanical method stores energy in a spring which is released by pushing a plunger to provide the necessary pressure. The pressure storage method uses compressed gas in a vessel which is released at the time of injection .

V. TYPES OF NEEDLE FREE INJECTION DEVICES

Needle-free injection devices can be divided into 2 types based on the source of power:
1. Spring-Powered: Compact and lower cost, but suffer from limited range of force and reduced versatility. Spring-powered devices have been primarily used for subcutaneous administration of drugs .
2. Compressed Gas-Powered: Sustained force of generation, greater flexibility, and the ability to deliver larger volumes

VI. NEEDLE VS. NEEDLE-FREE INJECTIONSYSTEMS

To review needle vs. needle-free injectionsystems and describe the different types ofneedle-free injection systems.

a) Needle vs. Needle-free Injection
Cost Efficiency Needle-free injection systems can potentially reduce medical costs for the pork producer because the chance of injury to an employee from inadvertent needle sticks is eliminated. Needle-free systems also eliminate the purchase of needles. Needle breaks, which can damage tissue and cause a decrease in overall yield and profitability, are also therefore eliminated. However, the start-up costs associated with needle-free injection systems can be large. Pork producers should weigh the costs and benefits to these systems before adapting new technology.

b) Worker Safety:
Safety is a key ingredient to any pork operation.Employees must be properly trained on the useand maintenance of all equipment. Needleinjection can be dangerous due to inadvertentneedle sticks or cuts. However, needle-freeinjection is not 100% safe. Needle-free systemsare designed for a high force dose to beadministered very quickly and should only beused with proper training. These systems do offera limited amount of risk to the operator, ifproperly trained, and exclude the possibility ofneedle sticks and cuts.

c) Sterility

Sterility is a key factor to proper vaccination anddrug delivery. Sterility can be affected by humanerror. For example, the same needle may be usedon multiple animals. Workers may forget tochange needles when drawing vaccine from abottle. Needle-free injection takes the needle outof the equation, and due to the high powereddosing mechanism, there is a little to no chance ofcross contamination.

d) Pork Safety

The use of needles, along with human error, mayalso cause pork carcass defects. If needles aredisposed of correctly or dropped after use there isalways of a possibility of an animal ingesting theneedle or being stuck in an unassuming place.Needle-free injection systems eliminate residualneedles and needle fragments from porkcarcasses1. The Pork Quality Assurance (PQA)Plus program recommends that all producers havea broken needle policy in place2.

e) Proper Dosage

Injection site is a crucial element in making surethat a proper dosage is received by the animal. Aneedle injection provides many unknownvariables that can prevent proper dosing and inturn create havoc in your vaccination program.

Proper dosing is highly dependent on manyfactors. Among these factors are the size and ageof the pig and the recommended route ofadministration. Different methods of administration such as subcutaneous (SQ) orintramuscular (IM) are very important inguaranteeing quality vaccination. If a vaccine ordrug is not administered accordingly theeffectiveness of the drug and the withdrawal timeare altered. Incorrect injection sites in both needleand needle-free injection can impair pork safety.

f) Injection Methods

Subcutaneous injections in small pigs should begiven by pulling loose skin in the elbow or flankarea. This technique is called tenting. In sows, thearea just behind the ear is an acceptable sight forSQ injection. Intramuscular injection is conventionally administered in the neck justbehind the ear. IM injection anywhere else is notacceptable because it will compromise porksafety and it should never be injected in the loinor ham muscles.

VII. THE MANUFACTURING PROCESS

There are numerous methods of producing eachneedle-free injection system. The followingprocess focuses on the production of an air-forcedsystem. These systems are made through a stepby step procedure which involves molding the pieces, assembling them, and decorating andlabeling the final product. The individual piecesare typically produced off-site and assembled bythe needle free injection system manufacturer. Allof the manufacturing is done under sterile conditions to prevent the spread of disease.

1. Making the pieces

a) The first step requires the production ofthe component plastic pieces from plasticpellets. This is done by a process calledinjection molding. Pellets of plastic areput into a large holding bin on an injectionmolding machine. They are heated tomake them flowable.

b) The material is then passed through ahydraulically controlled screw. As thescrew rotates, the plastic is directed through a nozzle which then injects it intoa mold. The mold is made up of two metalhalves that form the shape of the partwhen brought together. When the plasticis in the mold, it is held under pressure fora specified amount of time and thenallowed to cool. As it cools, the plasticinside hardens.

c) The mold pieces are separated and theplastic part falls out onto a conveyor. Themold then closes again and the process isrepeated. After the plastic parts areejected from the mold, they are manuallyinspected to ensure that no significantlydamaged parts are used.

2. Assembling and labelling

The parts are next transported to an assemblyline. In this production phase various eventsoccur. Machines apply markings that show doselevels and force measurements. These machinesare specially calibrated so each printing is madeprecisely. Depending on the complexity of thedevice, human workers or machines mayassemble the devices. This involves inserting thevarious pieces into the main housing andattaching any buttons.

3. Packaging

After the assembly step, the injection devices areput into packaging. They are first wrapped insterile films and then put into cardboard or plasticboxes. Each part is packaged so movement isminimal to prevent damage. For consumerproducts, an instruction manual is included alongwith safety information. These boxes are thenstacked on pallets and shipped via truck todistributors.

4. Quality Control

Quality control checks are done throughout themanufacturing process. Line inspectors check theplastic components to assure they conform topredetermined specifications. Visual inspectionsare the first test method, but measuringequipment is also used to check the dimensionsincluding size and thickness. Instruments that canbe used include laser micrometers, calipers andmicroscopes. Inspectors also check to make surethe printing and labeling is correct and that all theparts are included in the final packages.

Since these devices can have various safetyissues, their production is strictly controlled bythe Food and Drug Administration (FDA). Eachmanufacturer must conform to various productionstandards and specifications. Announced andunannounced inspections may occur to ensurethat these companies are following goodmanufacturing practices. For

this reason detailedrecords must be kept related to production anddesign.

VIII. MECHANISM OF WORKING

Needle-free injection technology works byforcing liquid medication at high speed through atiny orifice that is held against the skin. Thediameter of the orifice is smaller than thediameter of a human hair. This creates an ultrafinestream of high-pressure fluid that penetrates the skin without using a needle.The design of the device has a major influence onthe accuracy of subcutaneous delivery and the stresses imposed on the product to be delivered.The design must ensure that a sufficiently highpressure is generated to puncture the skin, whilethe subsequent pressure is reduced to ensure thatthe molecule is deposited comfortably at a levelthat does not reach the muscle tissue.

High-pressure delivery could potentially damagefragile molecules, such as monoclonal antibodies.Successful delivery of such molecules, therefore,requires a device with carefully controlled powernuances. Several companies are involved indevelopment of this technology, which includes, Antares Pharma Inc, Aradigm Corporation,Bioject Medical Technolo-gies Inc and BiovalveTechnologies Inc.

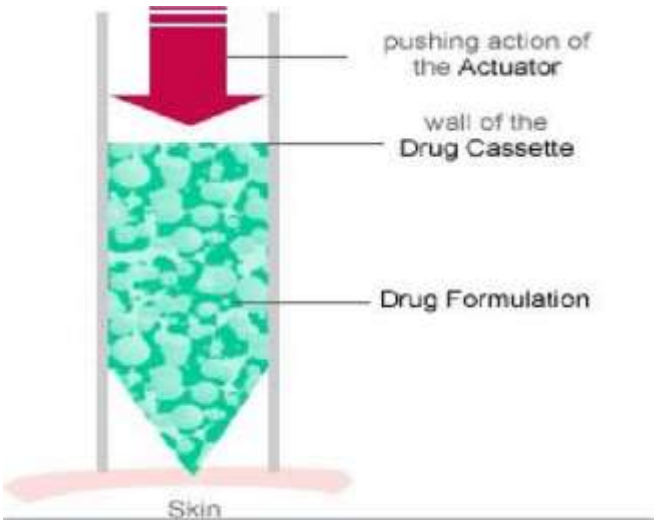

Figure 2: Mechanism of Working

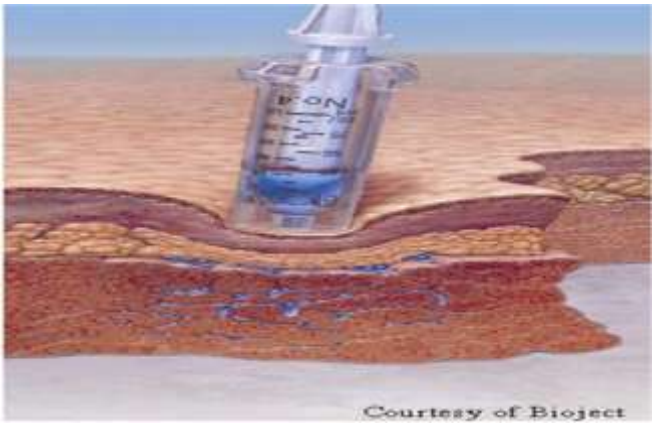

Figure 3: Injecting Medicament through Skin by Needle Free Injection

IX. THE FUTURE

Many of these needle-free alternativetechnologies are in the development stage.Companies are still working on producingdevices that are safer and easier to use. They arealso working on alternatives which can delivereven more types of medicines. Inhalers are beingimproved as are nasal sprays, forced air injectorsand patches. In the future, other foods may begenetically enhanced to deliver vaccines andother drugs. These include foods like bananas andtomatoes. In fact, bananas are being looked at ascarriers for a vaccine to protect against theNorwalk virus.

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