Background:

Jet injection was developed in the 1940’s, conceived by Robert Hingson and invented by Oscar Banker, to vaccinate billions of people who needed immunizations with the speed of a machine gun. The results proved convincing as, by 1990, no more smallpox epidemics were reported by the Center for Disease Control [1,2]. Jet injection became more popular afterwards among veterinarians. Despite more than 50 years of clinical use, jet injection technology has still not reached its full potential [3] as a strategic tool to deliver rapid intradermal injections painlessly in clinical dermatology. Its general acceptance in routine dermatological practice remained low due to several concerns such as: risk of cross infection [4], occasional pain [5], bruising [6], perforation [7], damage to delicate nerve and vessel structures [8], accidental injury into the operator’s finger [9] and cellulitis [10]. Technical difficulties such as “splash and splatter” after each discharge, occasional clogging up of the orifice of the device and difficulty with its sterilization also discouraged the use of some jet injectors. Consequently, many practitioners still prefer the syringe-needle method of administration over jet injection to deliver an intradermal medication.

Definition:

Jet injection can be defined as a needle-free drug delivery method in which a high-speed stream of fluid impacts the skin and delivers a drug [11]. The fluid can be a corticosteroid [10], lidocaine [12], Botulinum Toxin Type A (BTX-A) [13], bleomycin [14], a vaccine, or any other medication.

Risk of infection:

Although there was no immediate explosion of hepatitis following large-scale use of jet injection in the forties, an outbreak of hepatitis B, arose in 1990, revealing that jet injectors can become contaminated with hepatitis B virus and turn out to be vehicles for its transmission [4]. In 1997, Dimache developed an anticontaminant disposable device between the nozzle of the injector and the patient’s skin to overcome the risk of cross infection among patients [15]. Weintraub et al. ran a similar study and came to the same conclusion [16]. Both studies advocated that there is no need to sterilize the jet injector in-between patients as long as the anticontaminant disposable device is replaced. However, autoclaving the instrument at 134°C for 18 minutes at the end of the day is strongly recommended [17].

Pain at injection:

Jet injection of lidocaine, besides providing immediate anesthesia, is also a highly accepted technique by most patients, especially in instances of needle phobia [18]. Most patients willingly accept one or two needle injections during a treatment session but would hardly tolerate 30 or 40 such injections, especially on sensitive areas, such as the palms and soles. Patients get more apprehensive in such circumstances and may refuse to be injected altogether. For the needle phobic, not even a single injection is likely to be accepted. Pain at jet injection remains a controversial issue in the literature. Some studies claim that jet injection is totally painless while others claim the opposite. Pain perception is usually assessed on a scale of “0” to “10”, where “0” is absence of pain and “10” is the worst imaginable pain. Zsigmond observed that zero pain score was consistently observed in over 100,000 persons who received jet injection of lidocaine (jet-anesthesia) [19], while other investigators have stated that jet-injection is more painful than traditional needle injection [5]. An additional problem is that some patients can hardly differentiate between pain and anxiety and this may lead to inaccurate evaluation of pain perception. Goodenough et al. reported that observed facial expression is a more reliable measure of pain evaluation at injection than self-reporting techniques [20]. Inaccurate assessment of pain score may also occur due to the sudden noise released during jet injection, described by some as a sound of a blast. Patient reassurance could be attained by delivering a single injection in the air to show the patient that he is getting just a spray and no needle is involved. Pain sensitivity is also affected by age, anxiety level, and genetic traits besides being subject to a wide range of interpersonal variability as well as to the skin properties of the injected site. The average thickness of the skin is 0.1 mm but the epidermis may vary in thickness from 0.04 mm on the eyelids to 1.6 mm on the palms. Jet injection into some anatomical areas, such as the pericircular area, should be performed with great caution in order to prevent accidental eye injury [21]. Of all the skin covering the body, none is thicker and as densely innervated as the skin covering the palms and soles. Lamarche et al. reported that EMLA application is effective in easing the pain of electromyography needling in forearm skin, but is ineffective when applied to the skin of the palmar surface of the hand [22]. This may explain why needle injection on the palms and soles, contrary to other sites on the body such as the axillae, requires an effective pain management method [23].

 Controversies around pain at jet-injection probably stem from different jet injector parameters used in different studies. As the full details of these parameters are not always mentioned, it is hard to objectively compare their results. Jet injection parameters include: the volume per spurt, the
driving pressure, the orifice of the nozzle and the distance from the tip of the nozzle to the skin surface. As these parameters play a major role in pain perception and determine the penetration level of the injectate into the skin, they will be discussed with further detail.

**Jet injection parameters:**

A **Driving pressure** (Table I).

Traditional jet injectors like Dermojet® and Madajet® are spring loaded. Their driving pressure is fixed and may vary from 1400 psi (pounds per square inch) for the Dermojet® to over 1800 psi for the Madajet®. The disadvantage of fixed pressure jet injectors is that they do not work universally for different areas of the body and some manufacturers like Advanced Meditech International even warn against their use on the hands and fingers. Naumann et al. have used the Dermojet® safely to inject BTX-A directly into the skin for plantar hyperhidrosis but did not advocate its use for palmar hyperhidrosis due to the superficial location of many nerves and vessels under the palmar skin [8]. Cohen et al. observed perforation of the buccal mucosa during injection of triamcinolone acetonide with Dermojet® while treating a case of atrophic lupus erythematosus on the cheek [7]. Having said that, high-pressure injectors are particularly useful to treat hypertrophic scars and keloids [24]. Mitragorti reported that traditional jet injectors may cause pain, due to the jet’s deeper penetration level [3]. Wolf et al. reported that a driving pressure above 435 psi, has the potential of increasing skin damage [25]. In the author’s experience, pain perception at injection increases with increasing driving pressure, increased volume, wider nozzle diameter and a shorter distance between the tip of the nozzle and skin surface. Low pressure settings (130 - 160 psi) are usually associated with a pain score close to zero. This score may rise up to 2 when injections are performed on the hands and feet. With higher driving pressure settings, pain and risk of tissue damage may also increase.

B **Volume per spurt**

Depth of fluid penetration increases with larger volumes per spurt [26] which may also increase pain perception. Gaylarde et al. found that the volume of liquid entering the skin is less than the volume the injector is set to deliver. This point has been ignored in a number of reports where it was assumed that the total volume delivered is completely deposited in the skin [27]. The discrepancy between the volume set on the injector and the volume delivered into the skin is due to liquid lost during the splash back that occurs during injection. The volume of lost liquid will also vary according to the distance between the nozzle and the skin surface which is determined by a spacer. The volume that exits the injector can be accurately assessed by counting the number of shots needed to expel 1 ml from the reservoir of the injector. If 15 shots are needed to expel 1 ml, then the volume per spurt is 1:15 = 0.07 ml. It is advisable to use a volume smaller than 0.1 ml per spurt since larger volumes, such as 0.5 ml, may cause even greater pain than needle-tipped injections [28], and that is expected since the volume per spurt used in this latter study is five times larger than the standard volume of 0.1 ml, used in most traditional jet injectors.

C **Orifice (nozzle diameter)**

In 1972, Gaylarde et al. were the first to observe that the depth of fluid penetration increases with a wider nozzle diameter (0.15 – 0.2 mm) [27] which also may increase pain perception. Contrary to what one might expect, an orifice of a smaller diameter is accompanied with a shallow penetration of the injectate [29].

D **Spacer (distance from tip of the nozzle to skin surface)**

The spacer’s role is to avoid the tip of the nozzle from touching the skin by keeping a distance of 3 mm between the two. That distance is important, first, because it minimizes the risk of contamination and, second, because it restricts the injectate to the superficial layers of the dermis, third it affects the volume of splash back (lost liquid) with each injection. When the nozzle is in direct contact with the skin surface, the volume of splash back is almost nil. Removal of the spacer results in deeper penetration level of the injectate and reduces or eliminates the splash back. Deeper penetration could also be achieved with higher pressure settings or a wider nozzle diameter. The risk of contamination may theoretically occur with the removal of the spacer as the tip of the nozzle directly touches the skin [30]. In this case, multiple injections could still be performed on a same patient, but not on a subsequent patient unless the anticontaminant disposable device is changed to avoid cross contamination. The size of a spacer helps to determine the intended level of penetration [27].

**Jet injection with the Med-Jet MBX** (Fig.1)

MIT Canada has revolutionized the field of needle free parenteral administration by developing injectors that avoid most of the shortcomings of the earlier devices. This new technology relies on a variable pressure profile (Fig. 3), featuring an initial jolt of pressure set high enough (> 1000 psi) to create dermal pore opening while the actual injection of the substance is done at low pressure (130 - 160 psi). As a result, the injectable is delivered accurately and precisely into the targeted area at the desired depth of tissue and virtually pain free.
The Med-Jet MBX® is a versatile, low pressure, CO₂ powered jet injector, approved by Health Canada and the European Union, for intradermal, subcutaneous and intramuscular delivery of medication. The device features an adjustable volume per spurt (range 0.02 -0.3 ml) and an adjustable pressure (range 130 – 300 psi). It comes with 0.1 mm disposable nozzle. It is worth mentioning that the 0.1 mm nozzle orifice is 3 times smaller than the outer diameter of a 33 G needle (0.2 mm). The internal aperture of the nozzle holder (Fig.1) is 5 times wider than the internal aperture of the disposable nozzle that fits on it. This is an important feature since clogging that may sometimes occur in traditional jet injectors is avoided with the Med-Jet MBX. Splash back, is another drawback known with traditional jet injectors that necessitate the use for universal precautions such as wearing a face mask by the operator etc. The Med-Jet is equipped with a splash guard that protects against splash and splatter during jet injection and may obviate the use of a face mask. The operator can still aim the nozzle of the injector with great accuracy through the central aperture of the splash-guard to the intended area of injection. The splash guard is also a disposable spare part and comes in two models: one with an integrated spacer which keeps a 3 mm distance from the tip of the nozzle to the skin surface and another model without a spacer (see fig 2). The disposable nozzle and the splash guard are both changed in a matter of seconds.

Preparation of the Med-Jet MBX: sterile water or saline is drawn into a standard syringe of any size (usually 10 to 12 mL) which is then fit to its designated area on the injector to become its reservoir. The volume of the injector is temporarily raised to 0.3 mL per spurt in preparation to expel the air present in the device. Initially, the plunger of the syringe is slowly pushed and a few shots are fired until a distinctive sound is heard indicating that the air is totally expelled. At this time, the operator must pay attention to the jet stream ejecting from the device and make sure it is straight and strong, meaning there is no clogging. During the setting adjustment of the volume and/or pressure, the trigger should always be kept in a semi-pulled position. The syringe is then replaced with a new one filled with the desired liquid to be injected: lidocaine, triamcinolone, BTX-A etc. and put back on the device. The selection of optimal parameters depends on the intended use and the skin properties of the site to be injected. The recommended parameters cited in this article apply to the Med-Jet MBX only and should not be extrapolated to other types of jet injectors.

Jet anesthesia prior to minor surgery: for jet anesthesia the syringe is filled with 2% lidocaine (with or without epinephrine) and the author’s preference is with epinephrine) and the volume per spurt is set anywhere from 0.03 ml to 0.1 ml per spurt, the pressure set to 130 psi and one shot is fired. If a subepidermal wheal is not formed, the pressure is gradually raised by increments of 10 psi until a subepidermal wheal appears. The size of the epidermal wheal is proportional to the volume per spurt injected. If the volume used is extremely small (≤ 0.03 ml), instead of a subepidermal wheal, a tiny red (bleeding) spot indicates the site of jet injection. A volume of 0.07 ml per spurt is considered by the author to be an optimal volume to perform most tasks. If a flaccid blister occurs, this means that at least part of the injectate is located intra-epidermally and therefore, the pressure should be slightly raised until a subepidermal wheal appears. If larger areas need to be anesthetized, repeat injections at adjacent sites could be performed until the desired area becomes pain free. To reach deeper penetration levels, as the volume per spurt is already set, the author recommends a gradual increase in the pressure setting. The orifice of the injector is determined by a 0.1 mm in diameter disposable nozzle. A smaller diameter causes less pain and helps to restrict the injectate into the superficial layer of the skin. A single disposable nozzle is capable of sustaining 30 to 50 sites depending on the skin resistance. The nozzle is preferably replaced after such a number of injections and also in-between patients. When the tip of the nozzle comes in direct contact of the skin, the risk of cross-contamination may occur. This requires the replacement of the disposable nozzle with a sterile one before using the injector on a subsequent patient.

Pressure setting, volume per spurt, use of a spacer and nozzle diameter are the parameters that determine the intended targeted depth level in the skin. The pressure setting is rarely raised above 160 psi in routine dermatological procedures, but this may be needed when facing a thicker skin, such as the heel. In that case, trimming a few layers of the stratum corneum from the heel with a scalpel or soaking the foot in lukewarm water for 10 minutes can help the jet injection to penetrate deeper into the skin. Also, higher volumes per spurt (0.1 ml), as well as higher pressure settings (up to 300 psi) together with the removal of the spacer could exceptionally be used for certain indications.

Jet anesthesia is a very convenient and painless way of providing anesthesia in clinical practice prior to minor surgery: skin biopsy, removal of superficial tumors, benign or malignant, removal of multiple acrochordons, genital warts, mollusca contagiosa in children. The spacer, helps to keep a 3 mm distance between the tip of the nozzle and the skin surface.

Jet anesthesia prior to injection of BTX-A with needle: If the purpose of jet anesthesia is to inject BTX-A with a needle, keeping the volume settings low, between 0.03 and 0.07 ml will usually generate a pain score of 0 – 1. Jet anesthesia is the preferred pain management technique used by the author to inject BTX-A with a needle in the treatment of palmar and plantar hyperhidrosis. Vagal symptoms (lipothyria, sweating and nausea) occur much less frequently with this technique and when they do, they are much milder. Ideally, BTX-A should be injected in the subepidermal layer because the toxin would be in greater proximity to the sweat glands. Injecting BTX-A with needle without anesthesia or analgesia in the subepidermis would cause exacerbating pain because of the presence of a rich network of pain receptors [31]. Accordingly, some authors suggest injecting the BTX-A deeper, into the subcutaneous tissues, to overcome such unbearable pain. Nevertheless, injection of BTX-A into the subcutaneous tissues is not recommended because of their proximity to muscles which could increase the incidence of muscle weakness [32]. It is crucial to increase the driving pressure very gradually until a subepidermal wheal is formed, or until a tiny red spot appears, if the volume per spurt
is very small. This is the location at which the BTX-A needle should be introduced. A subepidermal wheal or tiny red spot, insures that the injectate is restricted to the superficial dermis, a safe way to avoid deeper penetration of the injectate that may cause pain and damage to nerve or vessel structures. Mitragorti, also believes that restricting jet penetration to superficial layers of skin, may significantly minimize pain intensity and potential damage to underlying vessel and nerve structures [8]. Jet anesthesia has been used, prior to BTX-A injection with needle, in over 250 patients within the last seven years. Details of the technique have been published elsewhere [12,33,34,35]

Jet injection of BTX-A directly into the subepidermis: Jet anesthesia is best used prior to BTX-A injection with needles, but, BTX-A was also directly injected with a jet injector in some needle phobic patients with unconvincing results. Although the procedure was painless and well accepted by patients, the author does not recommend this method for two reasons: (1) there is a waste of the expensive BTX-A through the splash back, and (2) bubbling and agitation may result in partial denaturation of BTX-A which decreases its efficacy. Needle phobia affects over 10% of the population. It can be managed by reassurance, education and avoidance of needles [36]. It is not uncommon to see patients suffering from disabling diseases such as palmar hyperhidrosis, refuse to be treated because they are needle-phobic [23]. When BTX-A has to be injected into the palms directly with a jet injector in a needle phobic patient, the removal of the spacer is recommended to avoid unnecessary waste of BTX-A. See table III for recommended parameters of BTX-A delivery through jet-injection in the needle phobic. Future studies should also consider the use of higher doses of BTX-A to compensate for possible denaturing of the delicate protein during pressurized injection. Removal of the spacer also implies the use of a lower pressure setting.

Jet injection of Intralional Triamcinolone: several conditions require multiple injection of triamcinolone, into different sites of the body: extensive alopecia areata [37], generalized granuloma annulare [38] and, nail psoriasis [39], to name a few. Typically, a 5 ml triamcinolone vial of 10 mg / ml, is filled in a 10 ml regular syringe to which 5 ml of saline is added to yield a final concentration of 5 mg / ml. Depending on the volume per spurt used, the total number of available injections may vary. For example, the total number of injections is 100 when the volume per spurt is adjusted to 0.1 ml and 142 when the volume is adjusted to 0.07 ml.

Conclusion

Infection is no more a threat with the availability of disposable anticontaminant devices, spacers, splash guards together with advanced sterilization techniques. The key issue for a successful procedure is the thorough understanding of the skin properties in order to select the optimal parameters, particularly in relation to: driving pressure, volume per spurt, small orifice and optimal distance from the tip of the nozzle to the skin surface. Like any other medical instrument, improper use of the injector can cause significant pain and injury, therefore, proper training and thorough commitment from the clinician are crucial to develop skill with the device. Jet injection looks promising in experienced hands to alleviate phobia and pain at injection. It also allows painless treatment of large areas of skin lesions. In certain anatomical areas such as the palms, deeper penetration of the injected fluid may increase the risk of pain and injury. Future research should elaborate more on measurable parameters of jet injection to insure a safe and effective outcome.

Fig (1)
Parameters enhancing safe and effective *jet injection* by restricting injectate to the subepidermis

**Fig (2)**

NEEDLE-FREE INJECTION PRESSURE PROFILE of 1 ml water, 0.15 mm nozzle

**Table I**: Needle free injectors
### Traditional Jet Injectors

**Dermojet® & Madajet®**

<table>
<thead>
<tr>
<th>Power source</th>
<th>Springloaded ➔ fixed pressure</th>
</tr>
</thead>
</table>
| Pressure          | Dermojet® = 1421 psi
                  | Madajet® = 1800 psi          |
| Nozzle Diameter   | 0.20 mm                       |
| Potential         | Risk of cross-contamination  |
| contamination     | through splash-back           |
| Volume per spurt  | Fixed : 0.1 ml                |
| Reservoir         | 4 ml                          |
| Sterilization     | Autoclave 134° Celsius        |
|                   | For 18 minutes.               |

### Innovative Jet Injectors

**Med-Jet MBX®**

<table>
<thead>
<tr>
<th>Power source</th>
<th>CO₂ ➔ versatile pressure</th>
</tr>
</thead>
</table>
| Pressure          | Med-Jet MBX
                  | 130 to 300 psi                |
| Nozzle Diameter   | 0.10 mm                       |
| Potential         | Disposable nozzle, splash     |
| contamination     | guard with or without spacer  |
| Volume per spurt  | Adjustable : 0.02 to 0.3 ml   |
| Reservoir         | 3, 5, 10, 12 ml according to syringe mounted on device |
| Sterilization     | Autoclave 134° Celsius        |
|                   | For 18 minutes.               |

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**Table II**

**A rapid guide for the use the Med-Jet for common procedures in clinical dermatology**

<table>
<thead>
<tr>
<th>Med-Jet settings</th>
<th>Volume per spurt in ml</th>
<th>Pressure in PSI</th>
<th>Diameter of disposable nozzle</th>
<th>Use of spacer* combined with splash guard or splash guard alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range</td>
<td>0.02 to 0.3 ml per spurt</td>
<td>130 - 300 psi</td>
<td>0.1 mm</td>
<td>3 mm spacers with splash guard</td>
</tr>
<tr>
<td>Jet anesthetics for minor surgery or jet injection of triamcinolone in normal epidermis</td>
<td>Recommended volume : 0.07 to 0.1 ml at first</td>
<td>Recommended pressure 130 – 150 psi</td>
<td>Recommended nozzle orifice is 0.1 mm</td>
<td>the use of a spacer is highly recommended to restrict the injectate to the subepidermis</td>
</tr>
<tr>
<td>Jet anesthetics prior to botox injection with needle in thick epidermis such as the palms and soles</td>
<td>A volume of 0.03 -0.05 ml</td>
<td>Recommended pressure 130 – 150 psi may be gradually increased by increments of 10 psi until an anesthetic wheal or a tiny red punctum into which Botox can be injected totally pain free is obtained. For the palms, the pressure is rarely increased beyond 200 psi while on the feet, particularly on the heel, a pressure of up to 300 psi may be needed.</td>
<td>An orifice of 0.1 mm is enough to treat the palms.</td>
<td>If the formation of an anesthetic wheal or red punctum is still a problem, the spacer could be removed and just a splash guard mounted on the nozzle so that the nozzle directly touches the skin. Trimming a few layers of the stratum corneum with a scalpel or soaking the area in water for 10 minutes is another option to reach the subepidermis in the thickest skin of the body.</td>
</tr>
</tbody>
</table>

*Removal of the spacer implies the use of a sterilized device in a subsequent patient*
Table III

<table>
<thead>
<tr>
<th>Recommended parameters of Jet injection of BTX-A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of BTX-A units</td>
</tr>
<tr>
<td>100</td>
</tr>
</tbody>
</table>

References: