

Immunoglobulins: administration routes and settings

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B cells produce proteins called antibodies

- *IgG- this provides the most long lasting protection
- IgA
- IgM
- IgE

*When Immunoglobulin is replaced, only tiny amounts of IgA and IgM are present in Immunoglobulin replacement products.

- Immune system, even in healthy individuals is imperfect; infections still may occur

A (brief) history of Ig therapy

- **1944** - The purification of serum globulins from human plasma by Cohn et al. provided material that could be safely injected into patients
 - Cohn et al. developed a series of cold ethanol precipitation steps that fractionated human plasma into classes of proteins, including the gamma globulin fraction commonly known as Cohn fraction II.
 - Stokes et al. (1944) injected intramuscularly ISG (Immune serum globulin)
- **1952**- Bruton treated a child with undetectable serum gamma globulin levels who suffered from recurring pneumococcal infections
- **1962** -The desire to deliver larger doses of ISG led to a series of manufacturing changes intended to produce an intravenously injectable immunoglobulin (Barandun et al.)
- The initial route of administration for IG was I.M.
 - very painful and limited in volume
 - Sterile abscesses developed at the site of injection and occasionally became infected
- Most recently' SCIg and fSCIg

Indications for Immunoglobulin therapy

Replacement

- Immunodeficiency diseases
- Utilises the infectious memory of the donor population
- **Primary immunodeficiency (PID)**
 - Secondary immunodeficiency states (e.g. post-solid organ transplant)

Inflammatory/ autoimmune diseases

- Vasculitis e.g. Kawasaki
- Neuro-inflammatory e.g. CIDP (Chronic inflammatory demyelinating polyneuropathy)
- Autoimmune (e.g. lupus/ juvenile dermatomyositis)

SCIg vs IVIg:- **SCIg**

- Overcomes adherence issues/ increases tolerability to treatment/ better disease specific knowledge 1 Gardulf et al
- Mobility/ flexibility increased e.g. holidays, sleepovers, adolescent activities
- QOL of both child and parents and other family members improves on SCIg 2 Gardulf et al
- Hospital admissions avoided
- Higher trough levels with same doses 3 Abolhassani et al 2012

1. Quality of Life and Health-Care Resource Utilization Among Children with Primary Immunodeficiency Receiving Home Treatment with Subcutaneous Human Immunoglobulin Clin Immunol (2008) 28:370–378 DOI 10.1007/s10875-008-9180-9

2. Replacement IgG therapy and self-therapy at home improve the health-related quality of life in patients with primary antibody deficiencies
Current Opinion in Allergy and Clinical Immunology 2006, 6:434–442nn Gardulf and Uwe Nicolay

3 Abolhassani et al Home based Sub- Cutaneous immunoglobulin Versus Hospital based intravenous immunoglobulin in treatment of Primary Antibody deficiencies: systematic review and meta analysis J Clin Immunology (2012) 32 1189-1192

SCIg vs IVIg:- **SCIg**

- More consistent / stable serum IgG levels throughout month: no peak and trough
- Reduced adverse events; mild local reactions only
- Less invasive: Useful if IV access proves difficult
- Remote families avoid travel
- Empowers patients and promotes responsibility

2012

3 Abolhassani et al

SCIg vs IVIg:- **IVIg**

- Hospitalisation with associated risks and costs to family and hospital
- Wide variation in serum IgG concentrations with lower trough levels
 - Trough symptoms (e.g. fatigue/ sinonasal discharge/ cough)
- Requires IV access; may be problematic long term
- May not be suitable for individuals with renal or cardiovascular disease (risk of hyperosmolarity& fluid overload)
- Time consuming and disruptive to school and work as well as family activities
 - Some patients perceive SCIg to be inconvenient and prefer IVIg

Monitoring while on Ig replacement

- 6-12 monthly clinic visits (may vary)
- Trough levels measured (prior to dose)
- Only interpretable in absolute deficiency, not Specific Antibody Deficiency
- Targets for IgG:
 - >6.5g/L in absolute antibody deficiency patient
 - > 9g/L with bronchiectasis
 - Absence of trough symptoms
- If Ig given at home, families must record the batch number at each infusion



Administration methods SCIg using syringe driver

Site: Usually the abdomen or front upper leg

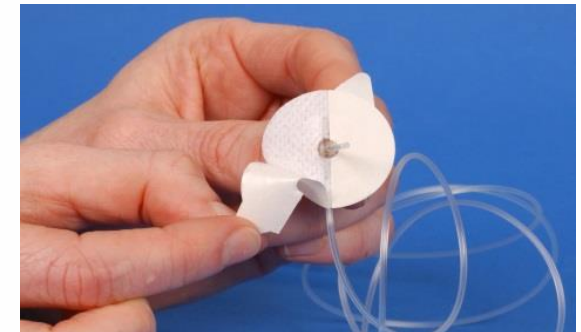
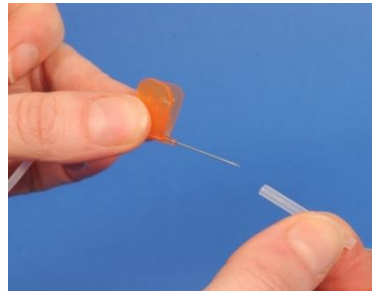
Stick with same site: allow reservoir to occur

Infused slowly initially then rate increased as tolerated

Infuse slowly initially then rate may be increased as tolerated

25 mls per site, 5 cm apart

Requires patient education



SCIg Administration methods

Rapid push

- Best candidates are infants, adolescents, adults
- No pump or syringe driver used
- Push rate as quickly as tolerated (1 ml/ minute maximum)
- Winged infusion set required: larger gauge e.g. 23g (blue) or 21g (green)
- Upsides: Rapid/ inexpensive/ no driver required
- Downsides: uncomfortable for some/ difficult as viscose /requires dexterity



Various pumps/ syringe drivers available

SCIg 60 EMED

Requires Sub Q needles + flow
control tubing
Versatile infusion duration
Inexpensive



Nikki T 34

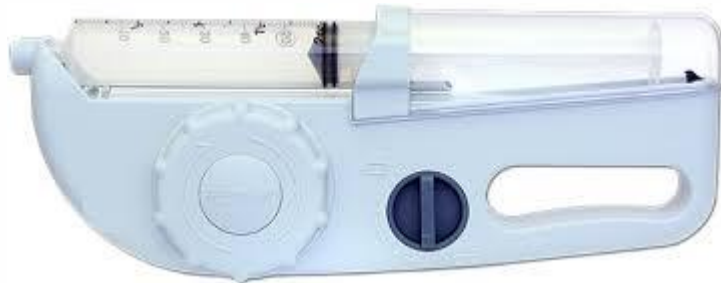
Can use any giving sets
Versatile infusion duration
Expensive



Various pumps/ syringe drivers available

Freedom 60

Low risk of occluding but requires flow control tubing: may result in slow infusions



Springfusor

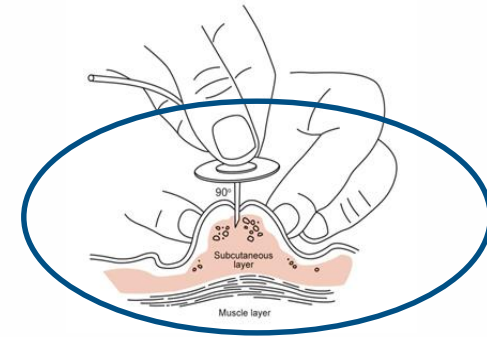
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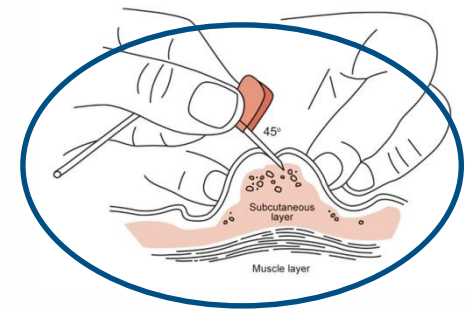
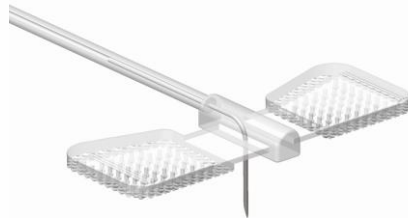
Some of the Needles and giving sets available

Neria



90 degree angle
insertion

Soft Glide



45 degree angle insertion

Winged Infusion set (Butterfly)



Overcoming common barriers

To promote comfort and adherence

- Possibly a cool pack prior to and during infusion
- Warm or cool pack following infusion

Ensure correct technique

- Consider needle/ giving device change
- Consider fortnightly rather than weekly



Overcoming barriers

Busybodies:
Weekly home
therapy

Overcoming Dexterity Issues



'Steadyject'



'Mini Spike'



Other options (in some countries)

Hyaluraonidase Facilitated SCIg ;- fSCIg

- Recombinant human hyaluronidase (rHuPH20) increases the absorption and dispersion of infused fluids and drugs.
- fSCIg allows for the administration of larger volumes at a single site

Home IV treatment;

Home delivery of Ig and consumables available

Questions

