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## BOTOX A for CHRONIC SIALORRHOEA

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### Objective

To reduce the severity and frequency of drooling (dribbling/ sialorrhoea)

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### Background

#### Introduction

Hypersalivation (sialorrhoea, drooling) is an important social, clinical and emotional issue for people with severe neurological disease such as cerebral palsy. Salivation is controlled via the autonomic nervous system. The salivary glands function is under a complex parasympathetic and sympathetic neural control. Nerve endings within the parasympathetic postganglionic system secrete acetylcholine, and blocking these receptor sites inhibits nervous stimulation to the salivary glands. Botulinum toxin type A (BTX), diminishes salivary flow rate by blocking this release of acetylcholine.<sup>1</sup>

Clostridium Botulinum, an anaerobic bacterium, yields seven antigenically distinct toxins: A,B,D,E,F and G. These are potent neuroparalytic agents, which inhibit the release of acetylcholine at the neuromuscular junction. The effects of BTX are however temporary. The toxin penetrates the endosomal membrane where the secretion of acetylcholine is blocked. The different toxins are structurally similar but have slightly varying effects. To date only preparations of Botox-A have been available for clinical use. There has been some evidence that BTX has a longer lasting effect at the neuroglandular junction compared to the neuromuscular junction<sup>3</sup> (12 months as opposed to 3 months). Re-innervation at the neuromuscular junction is due to re-sprouting of nerve branches. It is noted that authors report a variation in the length of the effect from 2 weeks to 6 months.

Present treatments (Table -1) for drooling have had limited success. Anticholinergic drugs taken orally or transdermally can have significant side effects. Common adverse effects include constipation and irritability or urinary retention. Surgery involving salivary gland removal or duct redirection is the most popular and accepted management but is also associated with complications. Apart from the usual possible anaesthetic and peri-operative complications, increased dental caries, salivary gland calculi and excessive oral dryness can occur. Most patients require combination of treatment options.

Injection of salivary glands with BTX has emerged as a new treatment since year 2000. This results in a reduction in saliva production and improvement in drooling.

BTX is an effective treatment for a variety disorders with different aetiologies and has been said to have very few side effects. There are several studies in the literature which have reported the use in children<sup>2,3,4,8,10</sup> but the numbers used in these studies are relatively small. The efficacy of this treatment option varies from patient to patient and therefore should be used with caution in children.

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### Treatment options for sialorrhoea

- Medications - anticholinergics such as atropine and glycopyrolate
- Behavioural modifications and physical therapy
- Oromotor rehabilitation / therapy by Speech Therapist
- Orthodontic treatment
- Improvement of nasal and oral airway patency - Otolaryngology (ENT)
- Catellio moreles prosthesis
- Surgery to the salivary glands
- Botox injection to submandibular / parotid glands
- No treatment

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### Patient selection

All patients who are considering Botox injection should undergo a multidisciplinary assessment at the Saliva Clinic prior to being placed on the waiting list. Children under the age of 5 and adults over 18 should not be considered at the Starship Children's Hospital. They should be fully informed of all treatment options available and suitability of each of these options prior to selecting Botox injection. The clinic pamphlet should be sent to the family to read prior to their clinic appointment so that they are then able to clarify details of the treatment. Consent for the procedure will be obtained at the clinic appointment.

**Caution: Patients with pre-existing swallowing difficulties are not automatically excluded but should be considered only after consideration of all other options.**

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### Consent

Written consent for the procedure will have been gained on the day of the clinic appointment. The consent should specify which gland/s are being injected and proposed dose and volume should be discussed and documented. The potential complication of paralysis of adjacent musculature and swallowing difficulties should specifically mentioned. The surgeon will visit the patient and family on the day of the procedure and ensure that the family understand the procedure to be carried out. Consent for anaesthesia will be gained on the day of the procedure.

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### Dose / Volume / Dilution

**Dose – These doses relate to the Allergan Botox preparation.**

These recommendations for dose, volume and dilution are conservative. They are a rough guidelines based on the limited case series described in the literature. The dose should be titrated to the individual patient depending on the ultrasound appearance of the salivary glands.

But as a general rule:

**Maximum dose per submandibular gland should not exceed 15 units.**

**Maximum dose for both submandibular glands is 30 units.**

**Maximum dose per parotid gland should not exceed 10units.**

**Maximum dose for both Parotid glands is 20 units.**

**Total maximum dose per patient should not exceed 50Units.**

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Botox given for the first time should only be given to submandibular glands. Second and subsequent doses can be given to both glands if there is no response to the first injection. Dose per submandibular gland should be dictated by the size of the gland however in children under the age of 10, a smaller dose should be considered. Example 8-10 units per submandibular gland in children under 20 kg weight, rather than the 15 units/per gland. A similar rule applies to when considering injection in the parotid glands. Injections can be repeated up to a maximum of 2 injections 4 months apart.

### Volume

The volume of injection will depend on the dose and dilution used. Adhering to the dosing schedule shown above the total injected volume should be less the 0.5 ml (total to all glands).

### Dilution

Botulinum toxin-A (Allergan) should be diluted with normal saline 0.9%. 100U vial should be diluted with 1ml of normal saline 0.9%. No other dilution methods should be used. Standard Thermo syringe or 1ml syringe should be used.

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## Administration/Monitoring/Precautions

### Administration

Botox should be administered under ultrasound guidance at all times. If ultrasound is not available then the procedure should be postponed. An experienced sonographer is essential. A small 1 ml Thermo syringe and 3cm length 25 gauge / or 27 gauge needle should be used for accurate placement. It is useful to place injections within the capsule and multiple intraglandular sites x3, three sites maximum per gland. Placement of the injection well within the glandular tissue reduces the risk of extravasation outside the capsule. Up to 2 sites may be injected within a gland.

At the end of the procedure record the dose given to each gland and the discarded units of Botox.

Surgeon or a member of the team should talk to the parents after the procedure and discuss dose and volume if necessary.

### Monitoring

Post injection the children should be monitored in the Daystay Unit for 4-6 hours prior to discharge. The post operative instruction sheet should be given and explained to parent and caregiver prior to discharge. A phone call check on the patient in 3-4 days to check the efficacy of the Botox by a member of the team is also useful. All patients should be followed up in clinic at 6 weeks to check progress. Patient's database must be maintained to document dose and outcome using the standard drooling questionnaire.

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## Safety Precautions

Ensure that the medication is drawn up by the practitioner who is to administer the Botox – this is to avoid any misunderstanding on diluent volumes.

Do not shake the vial vigorously as the medication can become inert.

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### References

Please note that the doses below could refer to any number of a variety of preparations available and the reader is advised to check the references for the preparation used.

Ref	Author	Title (Brief)	Type	Read	Journal	Number and age	Dose	Volume	Comment
1	Jongaricus PH	US guided botox to salivary gland	Article	Full	Laryngoscope 113; 107-11; 2003	44 adults	30-50u total to SMG	1-1.5 ml per gland	1.5ml spread throughout the gland. Larger volumes not tried. No side effects
2	Bothwell JE	Botox for drooling in children	Article	Full	Ped Neurol 27; 18-22; 2002	9 children with CP	5 u to each parotid	1ml syringe	No side effects. volume not discussed.
3	Suskind DL	Botox children CP	Article	Full	Laryngoscope 112; 73-81; 2002	22 Rx on 17 children	up to 30/40 u SM/Parotid	not mentioned despite long discussion of technique	dose probably for both glands but not that clear. Said it 'does not appear to cause dysphagia' high dose more effective
4	Jongerius PH	Botox, new option for drooling children	Article	Full	Eur J Pediat 160; 509-12; 2001	3 children with CP	up to 50u total	1.5ml for each gland	no side effects. Dilution ref to their work (ref 1) but not discussed
5	Ellies M	botox and salivary flow	Article	Full	Laryngoscope 112; 82-86; 2002	4 adults	22.5u to each parotid and 10 to each SMG	not mentioned	no side effects. Volume not mentioned
6	Lipp A	RCT of Botox for drooling	Article	Full	Neurology 61; 1279-81; 2003	32 adults	Up to 75u for each parotid	0.5ml per gland	High dose more effective. No side effects. No discussion of volume.
7	Ellies M	Botox for drooling of different aetiologies	Article	Full	J Oral Max Surg 61; 454-7; 2003	13 adults and children	50-65u total to SM and parotid	not mentioned	No side effects. volume not discussed.
8	Ellies M	Successful botox in children	Article	Abstract	Neuropediatrics 33; 327-30; 2002	5 children	50-65 u total	Not in abstract	No side effects.
10	Savarese R	Botox in children with CP	Article	Abstract	Am J Phy Med Rehab 83; 304-11; 2004	21 children with CP	Not in abstract	Not in abstract	
11	Dogu O	Botox to parotid: US vs blind	Article	Full	Clin Neurol Neurosurg 106; 93-6; 2004	15 adults	30 U total	1 ml syringe'	no side effects. US inj mor effective. Volume not discussed
12	Berweck S	Management of drooling	Letter	Full	Dev Med Child Neurol 45; 845; 2003	no details	no details	no details	no details
14	Monnier G	Botos drooling (French)	Article	Abstract	Ann Readapt Med Phy 46; 338-45; 2003	review only	no patients	no patients	review only. No details in abstract
15	Mancini F	RCT on efficacy and safety of botox in drooling in parkinsons	Article	Full	Movement Disorders 18; 685-8; 2003	20 adults	450u into parotids and submandibular	0.35ml to SMG, 0.65ml to Parotid	No side effects . Shorter duration of effect
16	Carod Artal FJ	Sialorrhoea and botox	Article (Spani)	Abstract	Neurologia 18; 280-4; 2003	3 adults	20-40u per gland	Not in abstract	No side effects

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		into parotids	sh)						
17	Tscheng DZ	Sialorrhea – therapeutic drug options	Article	Abstract	Annals of Pharmacotherapeutics 36; 1785-90; 2002	no details	not mentioned		botox not mentioned in abstract
18	Friedman A	Botox in PD (Polish)	Article	Abstract	Neurologia Neuroch Polska 35 Supp 3; 23-7; 2001	11 adult	5u to each parotid	Not in abstract	no side effects
19	Guntinas-Lichius O	Salivation in pharyngectomy pts with botox	Article	Abstract	Laryngoscope 112; 187-89; 2002	3 adults	100u to parotid and 30u to SMG	100u/ml	speculate high does more effective. Volume not mentioned in discussion
20	Glickman S	Sialorrhoea and botox into parotids	Article	Full	Eur J Neurol 8; 567-71; 2001	1 adult	150 u to each parotid	not mentioned	no side effects
21	Ellies M	Blocking secretion with botox (german)	Article	Abstract	HNO 49; 807-13; 2001	4 adults	Not in abstract	Not in abstract	no side effects
22	Friedman A	Botox sialorrhea and PD	Article	Abstract	Parkinsonism Related Disorders 7; 329-32; 2001	11 adults	Not in abstract	Not in abstract	no side effects
23	Porta M	Sialorrhoea Botox neurologic disorders	Article	Full	J Neurol Neurosurg Psych 70; 538-40; 2001	10 adults	15-40u per parotid, 10-15 per SMG. Total 50-100u	not mentioned	no side effects. Volume not discussed
24	O'Sullivan JD	Botox as Rx of drooling in PD	Letter	Full	Neurology 55; 606-7 2000	no details	Not given	Not given	Discusses report of Pal
25	Giess R	Botox in salivary glands improves sialorrhoea in AML	Short report	Full	J Neurol Neurosurg Psych 69; 121-3 2000	5 adults	20 into each parotid, 5 u submand	50u/ml 0.4ml	No major side effects. No dysphagia. May be risk if dose increased. Volume not discussed
26	Pal PK	Botulinum toxin A in drooling in PD	Brief communication	Full	Neurology 54; 244-9, 2000	9 adults	7.5-15 u	50-100u/ml 0.15ml	Volume not clear. No side effects. No discussion on volume or dose
28	Bushara KO	Sialorrhea in ALS	Article	Abstract	Med Hypothesis 48 337-9, 1997	no details	Not in abstract	Not in abstract	No details in abstract
29	Bhatia KP	Botox for drooling	Letter	Full	J Neurol Neurosurg Psych 67; 697; 1999	4 adults	20 u to SMG	not mentioned	1 patient had mild worsening of existing dysphagia