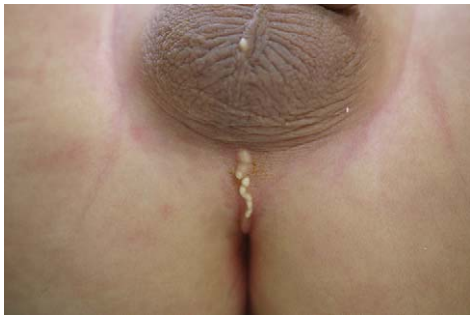

Fig 1. Linear 1- to 2-mm sized yellowish papules on scrotum and perineum.

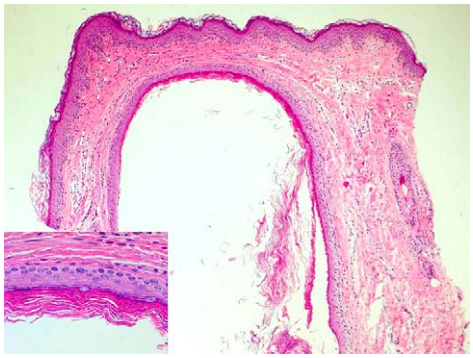

Fig 2. Cystic cavity containing eosinophilic keratin debris and cyst wall, lined by stratified squamous epithelium with well-formed granular layer. (Hematoxylin-eosin stain; original magnification: ×40, inset: ×400.)

canal is classified as either epidermoid or mucoid, depending on its lining epithelium. The epidermoid type is lined with stratified squamous epithelium and arises from rests containing ectodermal epithelium. The mucoid type is lined with a single layer of cuboidal or columnar epithelium as a result of the persistence in the skin of entodermal embryonic urethral rests.[2] The mucoid type is derived from the urethral folds and is not as commonly encountered as the epidermoid variety. The mucoid type has been erroneously reported as an apocrine cystadenoma and the epidermoid type as a perineal epidermal cyst.[3,4]

Median raphe cyst is thought to be caused by defects in the embryologic development of the male genitalia during fetal life. Two proposed explanations as to its origin are as follows: (1) they arise from epithelial rests incidental to incomplete closure of the urethral or genital folds; or (2) they develop from split-off outgrowths of embryologic epithelium after primary closure of the folds.[5] Previously reported cases demonstrated perineal nodules without involvement of the scrotum and perineum. Our case had distinct clinical features of papules on the scrotum and perineum. This location favors that it arises from split-off outgrowths of embryologic epithelium rather than from epithelial rests.

Although usually asymptomatic until adulthood, they may become traumatized and secondarily infected by *Neisseria gonorrhoeae* or *Staphylococcus aureus* producing swelling, tenderness, and purulent discharge.[6,7] The differential diagnosis includes molluscum contagiosum, syringoma, steatocystoma, glomus tumor, urethral diverticulum, and pilonidal cyst, which can all be excluded by their characteristic clinical and histologic features.[2,8]

The treatment of choice is simple excision followed by primary closure.[1] Some canals have been successfully treated by marsupialization or by surgical incision followed by electrosurgical destruction of the epithelial lining.[1,5] In our case, the parents refused any treatment because of his age.

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Botulinum toxin type A by iontophoresis for primary palmar hyperhidrosis

To the Editor: Botulinum toxin type A (BTX-A) is known to inhibit acetylcholine release in eccrine sweat glands, and is an effective therapy for primary

palmar hyperhidrosis (PPH). Intradermal palmar injections are painful, however, and require regional anesthesia. We show here, in a small, double-blind, randomized, placebo-controlled study, that BTX-A can be delivered painlessly and effectively to the palms through iontophoresis. This should be regarded as a pilot study.

PPH is one of the most debilitating types of hyperhidrosis.[1] Most conventional treatments, which include tap water or glycopyrrolate iontophoresis, systemic anticholinergics, and selective endoscopic sympathectomy, are of limited effectiveness or may be associated with major side effects. BTX-A injections, the latest addition to the arsenal of treatments, are effective but are limited by the need for regional anesthetic. This small, double-blind, randomized, placebo-controlled study shows that BTX-A can be delivered painlessly to the palms by iontophoresis.

We recruited 8 patients with PPH (6 females, 2 males; age range, 21-35 years; mean ± SD, 29 ± 6 years) into our trial. They were refractory to conventional therapy and adversely affected both socially and professionally by their condition.

BTX-A (Allergan Ltd; High Wycombe, Bucks, UK; 100 mouse units [MU] per vial) was reconstituted in 2.7 ml of preservative-free saline, and the same amount of saline acted as placebo. The hand to be treated with BTX-A was randomly selected and the other hand acted as placebo-treated control. Neither patient nor assessor (K.S.) was aware of which hand was treated with BTX-A or placebo, and all data remained computer-coded until the completion of data analysis.

Results are given as mean ± SEM. The paired Student *t* test was used for continuous variables, and statistical significance was regarded as $P < .05$. All analyses were performed using GraphPad Prism (v 3.02; GraphPad Software Inc, San Diego, Calif).

We used the Phoresor II PM700 (Iomed Inc, Salt Lake City, Utah), which has a circular drug-delivery reservoir (Moor Instruments Ltd, Devon, UK) covering 0.64 cm^2, acting as the drug-delivery cathode. Nine sites on each hand were treated with a maximum of 2.5 mA, or else with the highest comfortable current, with the total dosage extending to 15.0 mA per minute at each site.

Palmar sweating was assessed by gravimetry and by Minor's starch iodine test at baseline and at 14 days posttreatment.[2] Patients were also asked to quantify the effect of treatment at baseline and 14 days posttreatment using a 100-point visual analogue scale.[3] On follow-up, the assessor and patient were both blinded to the response given at baseline.

All 8 patients completed the study. At baseline the difference in mean sweat production between the treated hands (215 ± 40 mg/5 min) and control hands (166 ± 34 mg/5 min) was not statistically significant.

Palmar sweating in the BTX-A–iontophorezed hands was significantly reduced at 14 days posttreatment (215 ± 113 to 119 ± 34 mg/5 min; $P < .05$). Sweating in the saline-iontophorezed control hand showed an increase at 14 days following treatment (166 ± 34 to 249 ± 66 mg/5 min), although that change was not statistically significant (Fig 1). With data normalized for inter-day variability using the saline-treated control hand, sweat rate decreased significantly in the BTX-A–treated hand, from 215 ± 40 to 71 ± 23 mg/5 minutes ($P < .01$). This correlates to a mean improvement of 66%. The fold-change (1 = no change) in the saline-treated control hand and BTX-A–treated hand was 1.94 ± 0.42 and 0.34 ± 0.07, respectively. The difference was statistically significant ($P < .01$).

The changes in sweating as assessed by Minor's starch-iodine test, though patchy and difficult to quantify accurately, largely paralleled the gravimetric results. Relative anhidrosis took a roughly circular shape in some patients' palms, with a radius measuring between 0.3 cm and 1.5 cm (Fig 2).

Patients' subjective reporting, not statistically significant between the hands at baseline, showed no significant change in the untreated hands from baseline to 14 days posttreatment (65 ± 8 to 55 ± 19). The BTX-A–treated hand, however, showed a significant improvement (68 ± 5 to 45 ± 9; $P < .01$), corresponding to a 34% improvement from baseline. No side effects were reported.

It is intuitively reasonable that iontophoresis should be of use in delivering BTX-A. It might drive compounds into the skin by ion-electric field interaction, by increasing skin permeability, or by increasing bulk flow.[4] Its mechanism is not yet fully understood, but iontophoresis can deliver small molecules like lidocaine into the skin reliably.[5] In vitro studies suggest that larger molecules and polypeptides like calcitonin and insulin can also be delivered transdermally.[6] Iontophoresis is reported to transport compounds through the skin by increased current-induced water/solvent flux and increased pore size,[7] and eccrine glands should be accessible through the ducts, so even BTX-A, which is quite large (900 kDa),[8] should penetrate the skin. For these reasons we undertook a preliminary study before this one, which suggested that BTX-A iontophoresis reduces palmar sweating by up to 81%, and that this effect lasts some 3 months.[9]

Our gravimetric results correlate well with the findings of previous studies of intradermal BTX-A injections in the treatment of PPH. Using the same

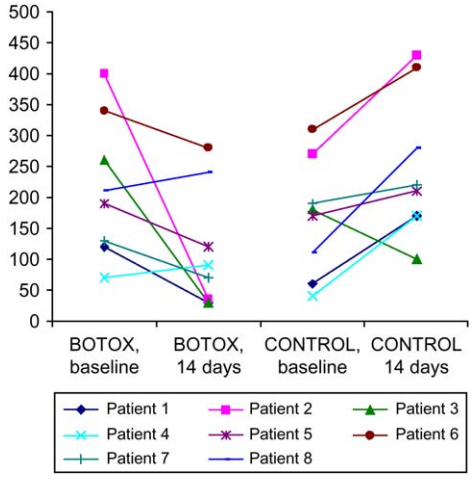

Fig 1. Individual gravimetry results, comparing the BTX-A–treated hand with the saline-treated control at baseline and 14 days posttreatment.

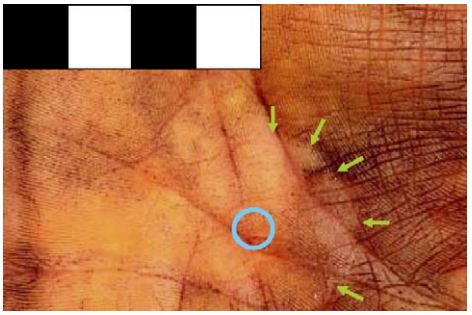

Fig 2. Detail of the BTX-A–treated palm of a female patient after Minor's starch-iodine test. Sweating areas turn blue-black. The *light blue circle* indicates the site and surface area of iontophoresis (0.64 cm^2). The *green arrows* highlight the roughly semi-circular outline of the relatively anhidrotic area surrounding the treatment site. The *black and white squares* indicate 1 cm per side of square.

amount of BTX-A, these studies show a gravimetric improvement in sweat rate of between 57% and 71%.[3,10] Our iontophoresis of BTX-A yields a similar result, at least in the short term. Interestingly, our starch-iodine results suggest that the relatively anhidrotic areas surrounding the treatment sites were typically larger than the 0.64 cm^2 covered by our drug-delivery electrode. Our mean reduction of sweating was also larger than would be anticipated from the total treated area. This would be in keeping with a diffusion area of 1 cm, as reported after the intramuscular injection of BTX-A.[11] Sweating actually increased slightly in the control palms, perhaps by a compensatory mechanism which is also observed in a small proportion of patients treated with BTX-A for hyperhidrosis.

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Increase in anticoagulant effect of warfarin in a patient using econazole cream

To the Editor: A 79-year-old male physician on chronic warfarin therapy for paroxysmal atrial fibrillation presented to our office with a chief complaint of inflammation of the groin. Examination revealed erythema of the scrotum and inner thighs with satellite lesions consistent with a Candida infection. He was given a prescription for econazole cream with instructions to apply the cream to the affected areas twice a day for at least one week beyond clearing or a minimum of two weeks. Within the first week of starting topical econazole therapy, the patient noted a marked increase in bruising. He