Percutaneous Ethanol Ablation in Outpatient Endocrine Practice

Advanced US Neck Ultrasound Course, AACE
objectives

1. To review the etiologies of cysts encountered in neck US endocrine practice
2. A brief over-view about the efficacy of ETOH ablation
3. To review the equipment required for ablation
4. To describe the procedure of ETOH ablation
5. Complications of ETOH ablation and risk reduction
Agents used for ablation

- Absolute alcohol
- Bleomycin
- Talc (pleurodesis)
- Tetracycline
- OK-432: penicillin-killed lyophilized Streptococcus pyogenes – lymphocele in children
Reasons to ablate...

- Outpatient procedure
- Percutaneous, under local anesthesia
- Cost effective
- Effective in select benign conditions
- Not well studied in malignant conditions

Cons:
- Risk of extravasation causing tissue injury
- Damage to RLN
- Pain and sclerosis of surrounding tissue
- Recurrence and need for repeat procedure
How does alcohol work?

Denaturation of proteins
Gradual sclerosis and fibrosis of tissue
‘Equal opportunity’ tissue destructing agent
CYST

Post inj

CAVITY
Percutaneous ethanol ablation - indications

- Thyroid cysts
- Other congenital neck cysts – Thyro-glossal and branchial cleft cysts
- Parathyroid cysts and adenomas
- Solitary toxic adenoma
- Palliation in subjects with un-resectable lymph node metastasis or advanced disease
- Isolated lateral compartment lymphadenopathy in thyroid cancer subjects
Classification of cysts

Congenital cysts
• Branchial cleft
• Thyro-glossal
• Cystic hygroma
• Lymphocele

Acquired cysts
• Thyroid
• Parathyroid
• Cystic nodules
• Thoracic duct cysts
• Post operative cysts
• Cystic metastatic lymph-nodes
True - Cysts vs Pseudo-cysts

**True cyst**
- Lined by epithelium
- Classic example is thyroglossal cyst
- Often associated with recurrence
- Therefore, may require more alcohol (or sclerosants)
- Multiple sittings

**Pseudo-cysts**
- Not lined by epithelium
- Classic example: following pancreatitis
- Spontaneous degeneration of thyroid nodules
- ? possible reduced chance of recurrence if PEI is performed early
- Some thyroid cysts eventually epithelialize
Effectiveness of PEI on cystic thyroid nodules

<table>
<thead>
<tr>
<th>Author</th>
<th>Yr of publication</th>
<th>No. of patients treated</th>
<th>Follow-up (months)</th>
<th>Study design</th>
<th>No. of treatments</th>
<th>Success rate(^a) (%)</th>
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<td>13</td>
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<td>Verde (20)</td>
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<td>10(^b)</td>
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<td>1–10</td>
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<td>Del Prete (25)</td>
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<td>98</td>
<td>115</td>
<td>Open</td>
<td>1–4</td>
<td>94</td>
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</table>

\(^a\) Near disappearance or marked (>50%) size reduction of cystic lesion.

\(^b\) Treated with simple aspiration.

\(^c\) Control group treated with saline.
Branchial cleft cyst
Parathyroid cyst
Benign nodular goiter with cyst formation
FV PCT- cystic degeneration
# Prediction of response to PEI

## TABLE 2. Treatment characteristics and response

<table>
<thead>
<tr>
<th></th>
<th>PEI</th>
<th>NaCl</th>
<th>$P$</th>
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</thead>
<tbody>
<tr>
<td>Treatment-volume (ml)</td>
<td>3.5 [2;5]</td>
<td>3.0 [2;5]</td>
<td>0.7</td>
</tr>
<tr>
<td>% Treatment-volume</td>
<td>36 [25;48]</td>
<td>36 [27;50]</td>
<td>0.4</td>
</tr>
<tr>
<td>No. of treatments</td>
<td>1 [1;2]</td>
<td>3 [2;3]</td>
<td>0.0002</td>
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<tr>
<td>Cure after</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 treatment</td>
<td>21</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>2 treatments</td>
<td>4</td>
<td>7</td>
<td>0.006</td>
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<tr>
<td>3 treatments</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Failure</td>
<td>6</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>% Cyst volume-reduction</td>
<td>100 [83;100]</td>
<td>68 [21;94]</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Values are medians (with quartiles) or number of cases.

## TABLE 3. Effect of variables on treatment response

<table>
<thead>
<tr>
<th>Variable</th>
<th>Multivariate effects on treatment success</th>
<th>Univariate OR</th>
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<tr>
<td></td>
<td>OR</td>
<td>$P$</td>
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<tr>
<td>Ethanol vs. saline</td>
<td>27.752</td>
<td>0.005</td>
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<tr>
<td>Previous aspirations</td>
<td>0.058</td>
<td>0.005</td>
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<tr>
<td>Gender</td>
<td>2.435</td>
<td>0.524</td>
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<tr>
<td>Age</td>
<td>1.026</td>
<td>0.561</td>
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<tr>
<td>Months from diagnosis</td>
<td>1.039</td>
<td>0.179</td>
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<tr>
<td>Cystic vs. complex</td>
<td>0.855</td>
<td>0.873</td>
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<tr>
<td>Additional nodules</td>
<td>7.820</td>
<td>0.127</td>
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<tr>
<td>Cyst volume</td>
<td>0.830</td>
<td>0.005</td>
</tr>
<tr>
<td>Thyroid volume</td>
<td>0.921</td>
<td>0.052</td>
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</tbody>
</table>

OR, Odds ratio; CI, confidence interval.
How to manage non-diagnostic aspirates during FNA of cysts

• This is a commonly encountered with thin walled cysts
• The entire fluid should be analyzed by cytology
• High risk patients – EBRT, strong family history, should be closely observed even after PEI
• If abnormal lymphnode(s) are seen, then FNA LN before attempting ablation of cyst
Parathyroid adenoma or gland ablation

- Surgery is the mainstay currently
- Poor surgical candidates
- Advanced age
- Failed surgery or recurrent surgeries
- MEN 1 (following failed surgery)
- Renal failure patients
Outcomes in MEN 1 in 22 subjects

![Graph showing serum calcium levels before and after ablation.](image)

Serum Calcium Level (mg/dL)

- Before Ablation
- After Ablation

ETOH ablation for PHPT

- Retrospective review MEN1 -1977 to 2013
- 37 pts underwent 80 treatments. 35 have had prior surgery
- 4 developed transient hoarseness and cough
- 1-9 episodes of injections
- 54 of the 80 treatments episodes resulted in eucalcemia

Singh Ospina et al JCEM January 2015, 100(1): E87-90
Renal failure patients

- 46 subjects – PTH dropped from 600 to 200
- Remained so for one year
- One subject developed RLN palsy
  - Prognosis of parathyroid function after successful percutaneous ethanol injection therapy guided by color Doppler flow mapping in chronic dialysis patients. 201 patient – CRF

  - Efficacy of percutaneous ethanol injection therapy (PEIT) is related to the number of parathyroid glands in haemodialysis patients with secondary hyperparathyroidism.
Toxic thyroid adenoma

• Several case reports
• Small Italian studies have tried alcohol ablation
• Some studies suggest failure with larger volume >30 ml, whilst other studies have not observed any difference between <40 ml vs >40 ml
PEI for toxic adenoma

• 70 patients treated with PEI
• Complete cure was achieved in 60 (77.9%) patients with toxic adenoma, while partial cure was observed in 7 cases (9.1%) and failure in 10 (13%).
• At the end of treatment, a significant shrinkage of nodule volume was observed in all patients (P = 0.0001).
• Toxic patients with pretreatment volume > 40 ml (n = 8) did not show a significant difference in treatment response rate as compared to those with volume < 40 ml.
• One patient developed hypothyroidism

205 patients with TMNG, TA

- 56 PEI: 29/56 remission
- 50 RAI: 43/50 remission
- 99 surgery: All were in remission

Hypothyroidism

Treatment of autonomously functioning thyroid nodules at a single institution: radioiodine therapy, surgery, and ethanol injection therapy. Yukiko Yano et al Annals of Nuclear Medicine, December 2011, Volume 25,10 pp 749-754
ETOH injection of metastatic thyroid cancer lymph nodes

14 patients injected, 10 considered poor surgical candidates. All were treated with RAI – not effective

ETOH ablation of Lymphnodes

- Surgery and RAI are mainstay of therapy
- Large number involvement
- Avoid injecting bulky lymph nodes
- Strictly palliation
- Poor surgical candidates
- No data to suggest improved outcome or reduce recurrence of progression
Materials needed for ETOH ablation or PEI
Hypodermic vs cannula for aspiration/injection

- **Hypodermic**
  - You can attach directly to the syringe or extension tube
  - Must stabilize needle with one hand
  - The sharp tip often scratches the posterior wall and can induce bleeding into the cyst
  - Risk of extravasation of alcohol
  - Can be used for solid targets and cysts
  - Better visibility on US
  - 5 cents

- **I.V soft cannulas**
  - Can be slightly harder to insert, particularly in softer cysts
  - NEVER reinsert the sharp trocar once it is pulled out
  - Risk for kinking
  - Least risk for posterior wall injury and extravasation of alcohol
  - Useful for cysts
  - Not useful for solid lesions
  - Reduced visibility compared to hypodermic needles
  - 2-3 dollars
Differences between ablation techniques

Cyst / cavity ablation
- Goal: Obliteration of cavity
- Empty cavity first
- Make sure needle does not puncture posterior wall or displaced
- Extravasation risk
- Sharp needle tip can induce bleeding as cyst is emptied
- Easy to inject most patients
- Larger volume of injection – anywhere from 30 % to 75% of the cyst cavity volume

Solid nodule/mass inj
- Goal: Destroy nodule or ‘down size’
- Reduction of functional volume
- Careful assessment of blood flow within the nodule is critical for maximal success
- Injection occurs under some pressure
- Typical volume of alcohol – 1 to 2 cc at the most into vascular regions
- PA – may require even smaller volume
ETOH

- Injection grade USP for neuronolysis
- Pharmacy / Laboratory grade alcohol USP
Degenerating thyroid cyst
Branchial cleft cyst
Chylous cyst, following thoracic duct injury
Acute chylous post op...note bloody tinge
The only way to identify a parathyroid cyst is by measuring PTH in the aspirated fluid.
Characteristics of thyroid cysts that are amenable to PEI

- Symptomatic cysts – or large, cosmetically disfiguring
- no reason to inject small or asymptomatic cysts
- Calculate volume of the cyst (APxTRANSxLONG/2)
- Fluid / mural mass analyzed cytologically and determined benign prior to injection
- 75% or greater volume of the lesion is cystic
- Collapsible cysts – floppy walls
- Thick walled, non-collapsible cysts do not respond well to ablation
- **Rule out malignancy**
How much alcohol to inject?

• Cystic thyroid lesions:
  30-50% of cyst aspirated volume

• Parathyroid and lymphnodes:
  0.25 – 1 cc – One to two rounds depending upon Doppler flow following injection

• Toxic adenomas:
  – 1-2 cc rarely two rounds, again the use of Dopper for determining reduction or disappearance of flow is key
Important technical precautions:

• Once cyst cavity is entered, either steady the needle or use an assistant to hold needle in place
• Do not puncture posterior wall
• If vascular mural mass is encountered, use soft tip catheter
• Disadvantage of i.v catheter— not echogenic
• IF the needle or catheter comes out or unsure of location, do not inject
• Unusual resistance to injection – abort procedure
Parathyroid adenoma ablation
Safety policies:

- Do not keep alcohol and lidocaine out at the same time on the table
- Do not load syringes with lidocaine and alcohol prior to procedure and leave on the table
- Always record Lot No and manufacture date
- Avoid ampoules or dispensing bottles that appear the same
- Safer to load one at a time when needed prior to use
Complications of ETOH injection

- Pain and swelling.
- More the injected volume of alcohol, more the symptoms
- Extravasation – RLN injury. Most commonly hoarseness
- Avoid injuring the walls, particularly the posterior capsule or medial wall
- Stop, if there is unusual resistance
- Hypoparathyroidism - <10%

Mauz PS, Maassen MM, Braun B, Brosch S.

Abstract

OBJECTIVE: Since 1990, percutaneous ethanol injection therapy (PEIT) has been clinically applied as a treatment for autonomous functioning nodules of the thyroid as well as for cystic lesions. Some additional indications are currently under consideration, e.g. inoperable advanced cancer of the thyroid. Since its inception, PEIT has generally been regarded as an effective, low-risk, inexpensive procedure which can be performed on an ambulatory basis.

MATERIAL AND METHODS: We report the first case of severe ethyl toxic necrosis of the larynx combined with necrotic dermatitis in a patient treated with PEIT by a radiologist.

RESULTS: The patient was admitted to hospital, where the necrosis and dermatitis were treated conservatively. A cyst which developed in the right false vocal fold was removed by microsurgery 10 months later. Voice was restored almost to normal but a significant reduction in nodular volume was not seen, probably due to the inexperience of the operator.

CONCLUSION: PEIT for functional thyroid gland autonomy is an inexpensive method of treating hyperthyroidism with focal autonomy on an ambulatory basis if surgical intervention and radiodine therapy are not feasible either for medical reasons or because of refusal by the patient. Severe complications must be taken into consideration and discussed with the patient. To avoid complications, substantial experience and a precise ultrasound-guided injection are required. In the case of complications the opinion of a specialist should be sought at an early stage.
Safety policies

- Do not keep alcohol and lidocaine out at the same time on the table
- Do not load syringes with lidocaine and alcohol prior to procedure
- Always record Lot No and manufacture date
- Safer to load one at a time when needed prior to use
Summary

• Patient selection is key
• Rule out malignancy in the case of cystic thyroid nodules by FNA
• Perform thyroid scan to confirm toxic adenoma
• Confirm by FNA PTH that the lesion is a parathyroid tumor prior to ablation
• Calculate volume of injection and keep track of injected volume of alcohol
• Avoid puncture of the walls in the case of cysts
• Avoid injection into the posterior / medial aspects of parathyroid tumors
• Lymphnode PEI is purely palliative, and it is best to wait till more data becomes available
Conclusions

• Carries risks, therefore, counsel patients
• Use first line therapies first
• Low volume injection is safer
• Confirm nature of the target being ablated by performing appropriate tests
• Monitor patient for 15 – 20 minutes prior to discharge
• Use of local anesthesia is recommended. Particularly if >23g needles are used
• If not anything, it relaxes patients