



BREATHLESS  
(NOT COVID)

# Call by peripheral hospital ED

23F with 4<sup>th</sup> presentation of anaphylaxis to Emergency Department in 6 weeks

- Symptoms included stridor, shortness of breath, throat tightness, presyncope, pruritic erythematous rash on upper body
- Each episode was treated with IM Adrenaline, which improved symptoms
- No overt angioedema or GI symptoms
- No hypotension or desaturation recorded
- **No known trigger**
- Prescribed EpiPen by ED

*\*\*Asked to perform tryptase levels and refer to Clinic\*\**

ED	10/05/2019 13:34	10/05/2019 16:38	CSNCK / 1) Treatment Bay 02	[REDACTED] / EMERGENCY	T78.4 - Allergy
OP	07/05/2019 09:00	07/05/2019 10:00	JHNTR / JHMPFL	[REDACTED] / Respiratory	
ED	06/05/2019 14:42	06/05/2019 18:27	CSNCK / 1) Treatment Bay 06	EMERGENCY, Dr Doctor / EMERGENCY	R06.0 - Respiratory - Shortness of Breath
ED	02/05/2019 21:01	03/05/2019 03:58	MAITL / 5) Fast Track 02	MEDICAL, Triage / EMERGENCY	M79.69 - Pain - Limb Upper
ED	01/05/2019 11:29	01/05/2019 14:47	CSNCK / 1) Treatment Bay 01	[REDACTED] / EMERGENCY	
IP	01/04/2019 13:48	02/04/2019 09:35	CSNCK / COUQ202	[REDACTED] / Medical Service	anaphylaxis
ED	01/04/2019 13:33	01/04/2019 18:00	CSNCK / 1) COU Monitored Bed	[REDACTED] EMERGENCY	R06.0 - Respiratory - Shortness of Breath
OP	28/03/2019 10:20	28/03/2019 10:25	CSNCK / CHSURGPD	NURSE / General Surgery	
IP	26/03/2019 14:21	27/03/2019 16:45	CSNCK / SUCDH	[REDACTED] / Medical Service	exacerbation of Asthma
ED	26/03/2019 14:00	26/03/2019 17:15	CSNCK / 1) Treatment Bay 01	[REDACTED] EMERGENCY	T78.2 - Allergic Reaction
ED	19/03/2019 09:52	19/03/2019 12:00	CSNCK / 1) Treatment Bay 05	[REDACTED] EMERGENCY	T78.2 - Allergic Reaction
ED	13/03/2019 12:50	13/03/2019 16:20	CSNCK / 1) Treatment Bay 01	MORGAN, Ms Ruth / EMERGENCY	T78.2 - Allergic Reaction

# Review in Immunology Clinic

- Further history:
  - **Episodes began after lower respiratory tract infection 6 weeks prior**
  - Typical episode:
    - Sudden onset shortness of breath, throat tightness and stridor leading to lightheadedness
    - Often occurred at work
    - Occurred in absence of food or medication use
    - Eventually resolved after period of rest (if not taken to hospital)
  - Daily dry cough with feeling of throat irritation
  - Recent onset dysphonia
  - Sensitivity to noxious smells causing rhinorrhoea and eye irritation

# Background

- **Mild asthma since childhood**
  - No hospitalisations for asthma
  - Seretide 2 puffs bd
  - Ventolin prn (daily use more recently)
- **Mild hayfever and eczema**
  - Nasonex bd
  - Loratidine 10mg daily
  - Phenergan 10mg nocte
- Multitude of sporting injuries
- No known drug allergies

# Social History

- Works as teacher's aide
  - Many of the episodes occurred at work, causing stress and anxiety
- Volunteer firefighter
- Non smoker
- Still able to play soccer
- Psychosocial issues
  - Older brother died when she was a child
  - History of oppositional defiant disorder
- No relevant family history

# Examination

- Dysphonia
- Erythematous rash over upper torso, neck and face, not urticarial
- No dermatographism
- Chest clear on auscultation
- No facial tenderness or nasal obstruction present
- Throat exam unremarkable

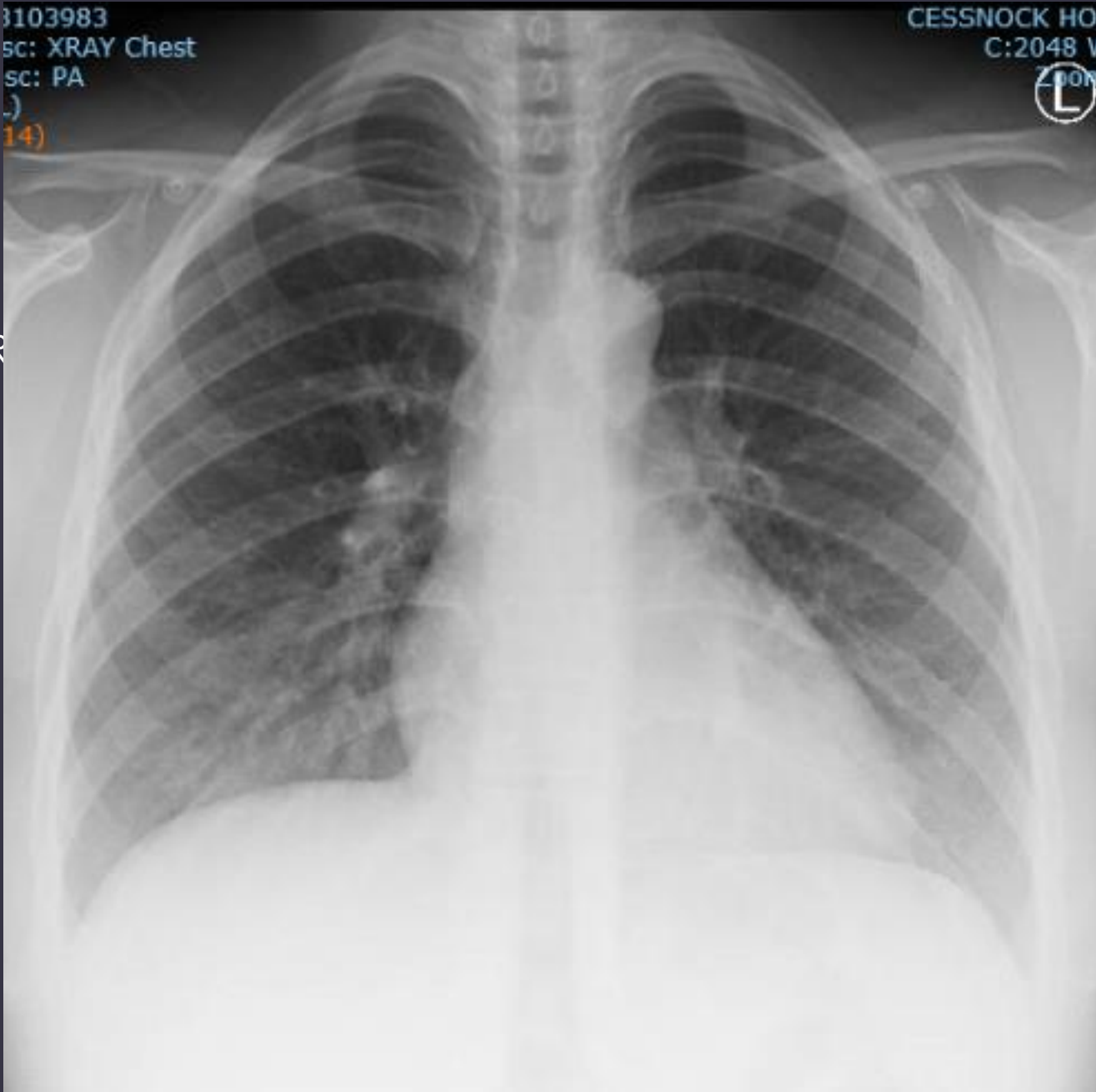
# Investigations

- Tryptase 2.8 (2 separate occasions)
- C3 1.29
- C4 0.29
- WCC 12 (post adrenaline)
- FBC and EUC otherwise unremarkable



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- CXR

# Issues

- Recurrent hospital presentations due to pre-dominantly respiratory symptoms treated as anaphylaxis
  - Atypical for anaphylaxis
  - Normal tryptase
- **Likely diagnosis of severe vocal cord dysfunction,** complicated by underlying asthma diagnosis
- Increasing stress and anxiety surrounding work environment, uncertainty of diagnosis, use/need of EpiPen

# Plan

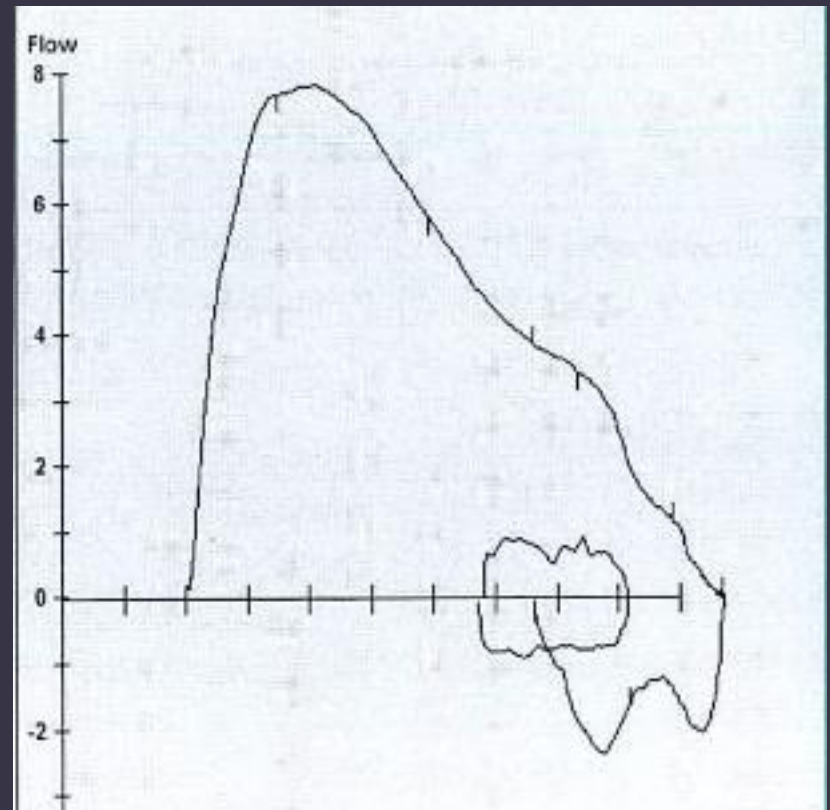
- Referred for respiratory function tests
  - Review asthma
  - Look for suggestion of vocal cord dysfunction
- Referred for urgent speech path review
- Follow up for hopeful Epipen de-prescribing

# Respiratory Function Report

- FEV1 108%
- FVC 107%
- FEV1/FVC 87%
- KCO 74% (TLCO 77%)
- FeNO 23 (normal < 41)

Comment: **Spirometry within normal limits.** Carbon monoxide transfer factor mildly reduced indicating some lung parenchymal and/or pulmonary vascular dysfunction.

The inspiratory flow loops visible on flow volume are her forced inspiratory loop and are **barely different from the flows and volume achieved on tidal respiration**, and suggest significant inspiratory flow limitation. **Overall results suggestive of vocal cord dysfunction**



# Speech Pathology Assessment

- Agreed inspiratory flow volume loops were truncated, with a W-pattern

Questionnaire	Score	Norm
Laryngeal hypersensitivity questionnaire	10.5	>17.1
JHH Symptom frequency & severity		
Breathing	10	<4.1
Cough	13	<6.2
Voice	15	<5.7
Upper airway	16	<5.8
Pittsburgh VCD Index	9	<4

© Vertigan, Bone & Gibson, 2014

## NEWCASTLE LARYNGEAL HYPERSENSITIVITY QUESTIONNAIRE

Please circle the answer that best describes you currently. Be sure to only select one response:

**EXAMPLE: I watch television**

All of of time time	Most of the time	A good bit of the time	Some of the time	A little of of the time	Hardly any of the time	None the
1	2	3	4	5	6	7

1) There is an abnormal sensation in my throat:

(O)

All of time	Most of the time	A good bit of the time	Some of the time	A little of of the time	Hardly any of the time	None of the time
1	2	3	4	5	6	7



# Speech Pathology Assessment

- **Cough:** frequent suppression of urge to cough
- **Cough triggers:** fumes, cold air, air conditioning, irritable feeling in throat, talking, eating, drinking
- **Cough characteristics:** dry, upper chest
- **Breathing pattern:** thoracic, nose breathing
- **Respiratory rate:** 20bpm
- **Voice quality:** moderately strained, rough, low pitch
- **Muscle tension:** Extrinsic laryngeal muscle tension present on palpation, painful to palpate

# Speech Pathology Review

- Education provided
- Breathing exercises taught
- Head and neck stretches to reduce extrinsic laryngeal muscle tension
- Functional transnasal laryngoscopy booked urgently



# Clinic Follow Up

- Improvement in symptoms
  - Still experienced 3 x week
  - Usually able to abort episodes with breathing exercises
- 3 further ED presentations
  - **Had nasoendoscopy performed by ENT in Emergency, paroxysmal vocal cord movements seen consistent with VCD**
  - One occasion given 2 x IM adrenaline and 8 x nebulised adrenaline
  - Has had to fight ambos NOT to give adrenaline!
  - Found O2 flow from Hudson mask helpful
- Work environment very understanding
- Follow up with Speech Path and Respiratory organised




# VOCAL CORD DYSFUNCTION

# Definition

**An inappropriate, transient, reversible narrowing of the larynx in response to external triggers** (*Halvorsen et al 2017*)

- Often due to episodic unintentional adduction of the vocal cords on inspiration

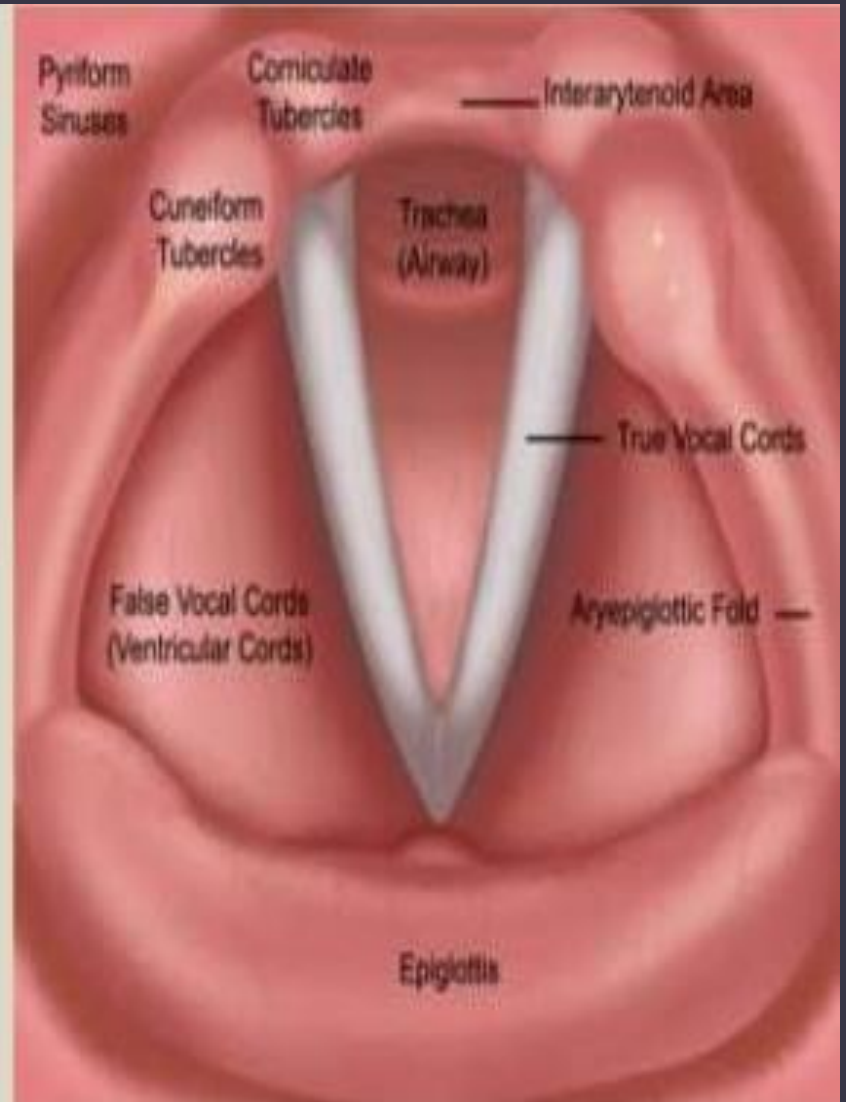
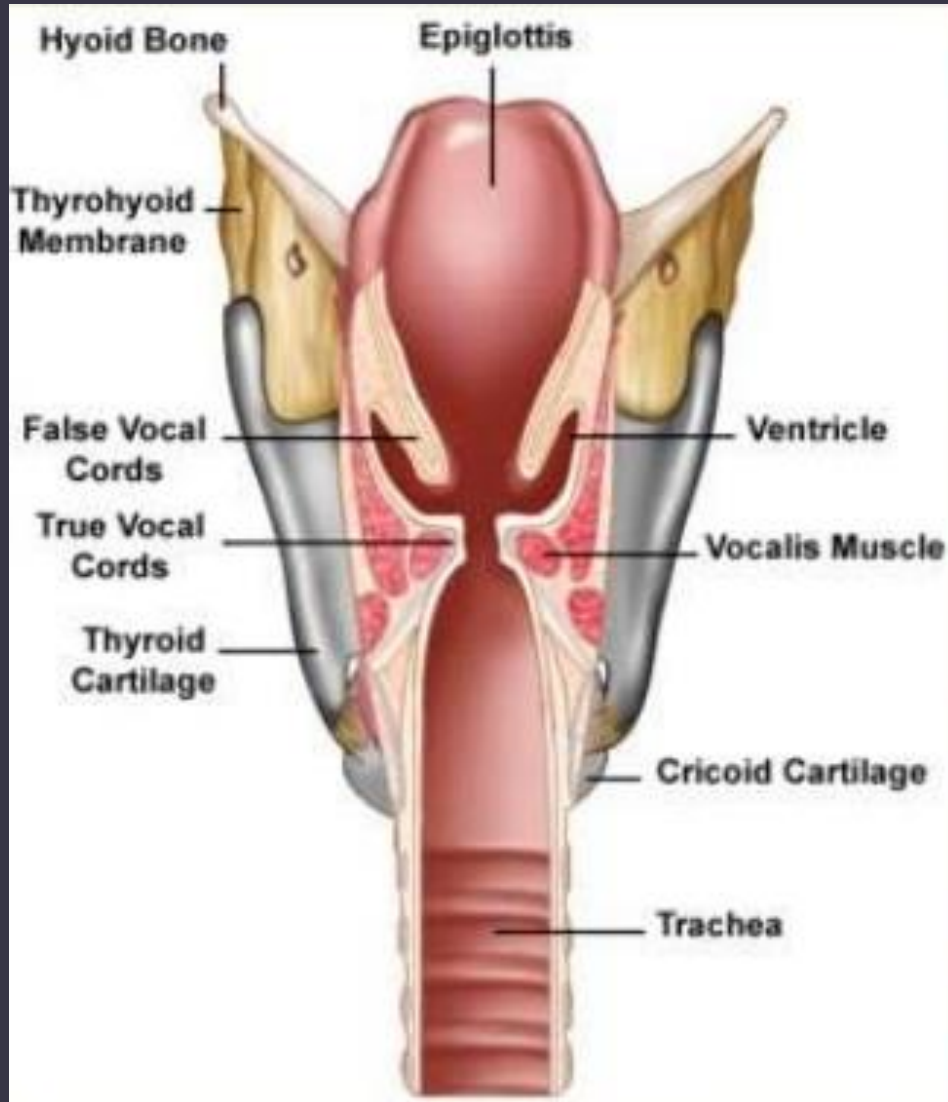
# Vocal Cord Dysfunction

- Also known as **inducible laryngeal obstruction**
  - Other names:
    - Paradoxical vocal fold motion
    - Laryngeal dyskinesia
    - Complex breathlessness
    - Complex dyspnoea
    - Munchausen's stridor
    - Factitious asthma
    - Hysterical croup
- 
- Discouraged to use these names!

# Related Disorders

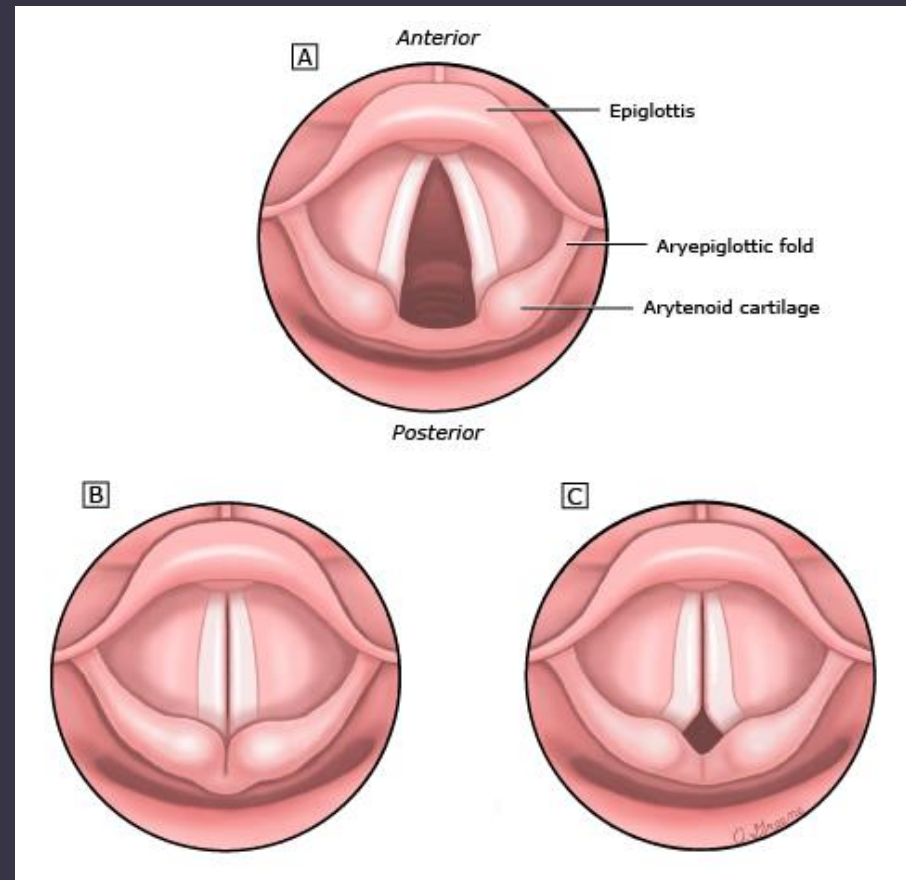
- Breathing pattern disorders
- Chronic cough
- Globus sensation

# Anatomy

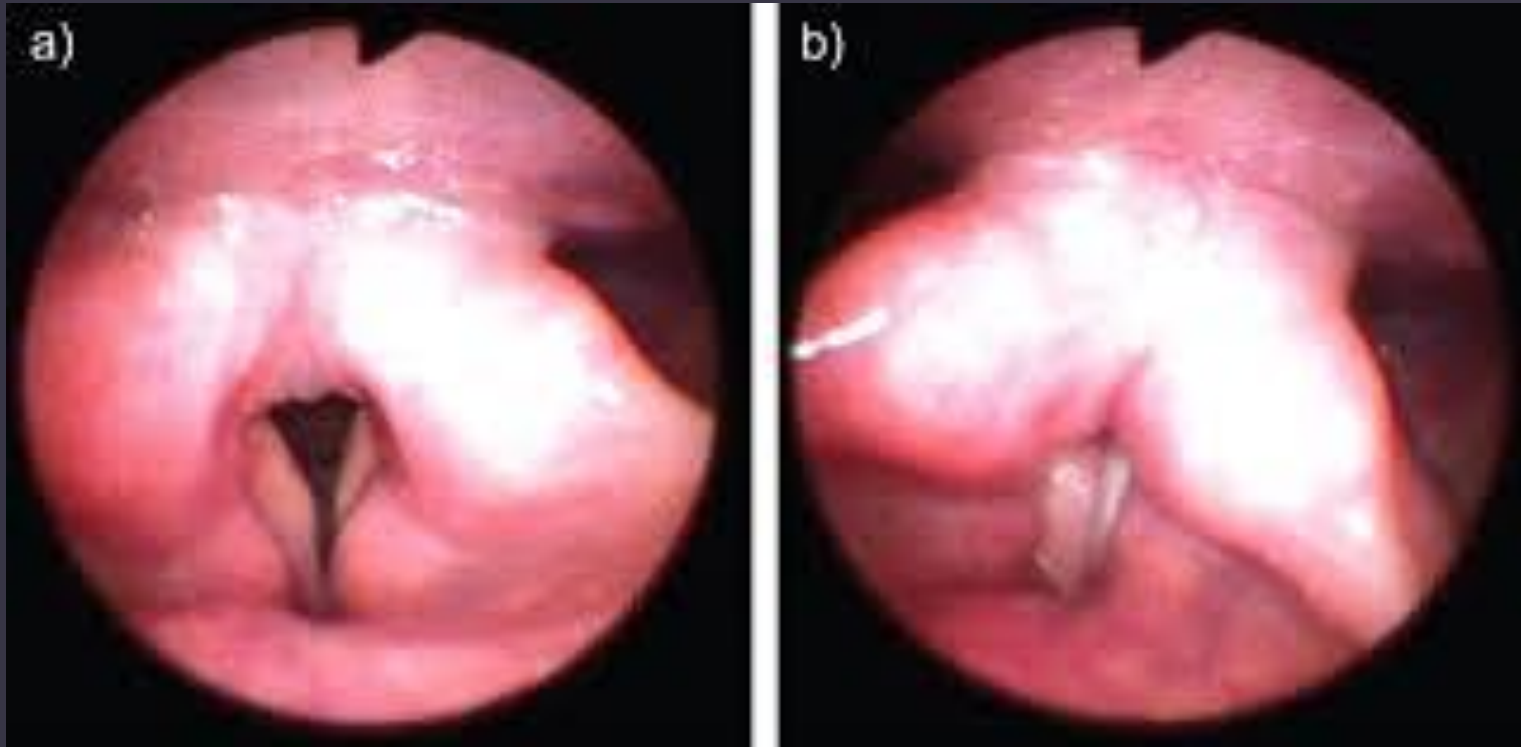


# Function

- Human larynx highly complex
  - Close to prevent aspiration
  - Open during exercise to optimise airflow
  - Perform fine movements during phonation
- Breathing: true vocal folds abduct (open) during inspiration and partially adduct (close) during expiration
  - 10-40% adduction normal in expiration
- Normal adduction of the true vocal folds occurs with phonation, coughing, throat clearing, swallowing, and during a Valsalva maneuver



*UptoDate 2019*

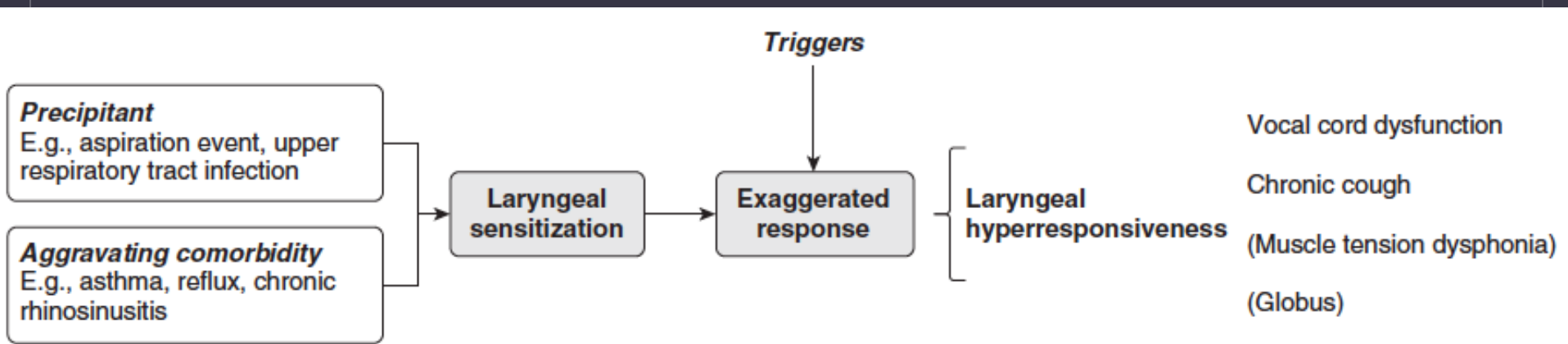


*Kenn et al 2011 European Respiratory Journal*



# Pathogenesis

- Caused by excessive closure of the laryngeal airway



## Other factors

- Chemoreceptors
- Sensory perception:
  - Cold receptors
  - Stretch receptors
  - Pulmonary C fibres
- Neuroplasticity: **anticipation of dyspnoea leads to increased fear**

# Potential Contributing Factors

- Asthma
- Upper respiratory tract infection
- Exercise
- Post-extubation
- Inhalational exposure to irritants
- Laryngopharyngeal reflux
- Psychosocial disorders and stress

# Clinical Presentation

- **Sudden onset** of breathlessness, worse on inspiration
- Feeling of fullness or tightness in the throat
  - Manifests as **inspiratory stridor** or “wheeze”
  - Choking sensation
  - Minimal improvement with salbutamol
- Dysphonia
- Non-productive cough

# Clinical Presentation

- May also have symptoms of:
  - Gastroesophageal reflux
  - Dysphagia
  - Rhinosinusitis
- Often **not affected by exercise** (although subset is exercise-induced)
- No haemodynamic instability
- Female predominance (similar to chronic cough and many voice disorders)
- Occurs at all ages

# Questions to distinguish between asthma and VCD

- Worse on inspiration (rather than expiration)
- Sudden onset (asthma takes 2-3 minutes to build up)
- Feeling in throat which cannot clear
- Minimal response to asthma treatment
  
- Duration: hours to days
  - Compared with Laryngospasm (lasts seconds to minutes)

# Differentials

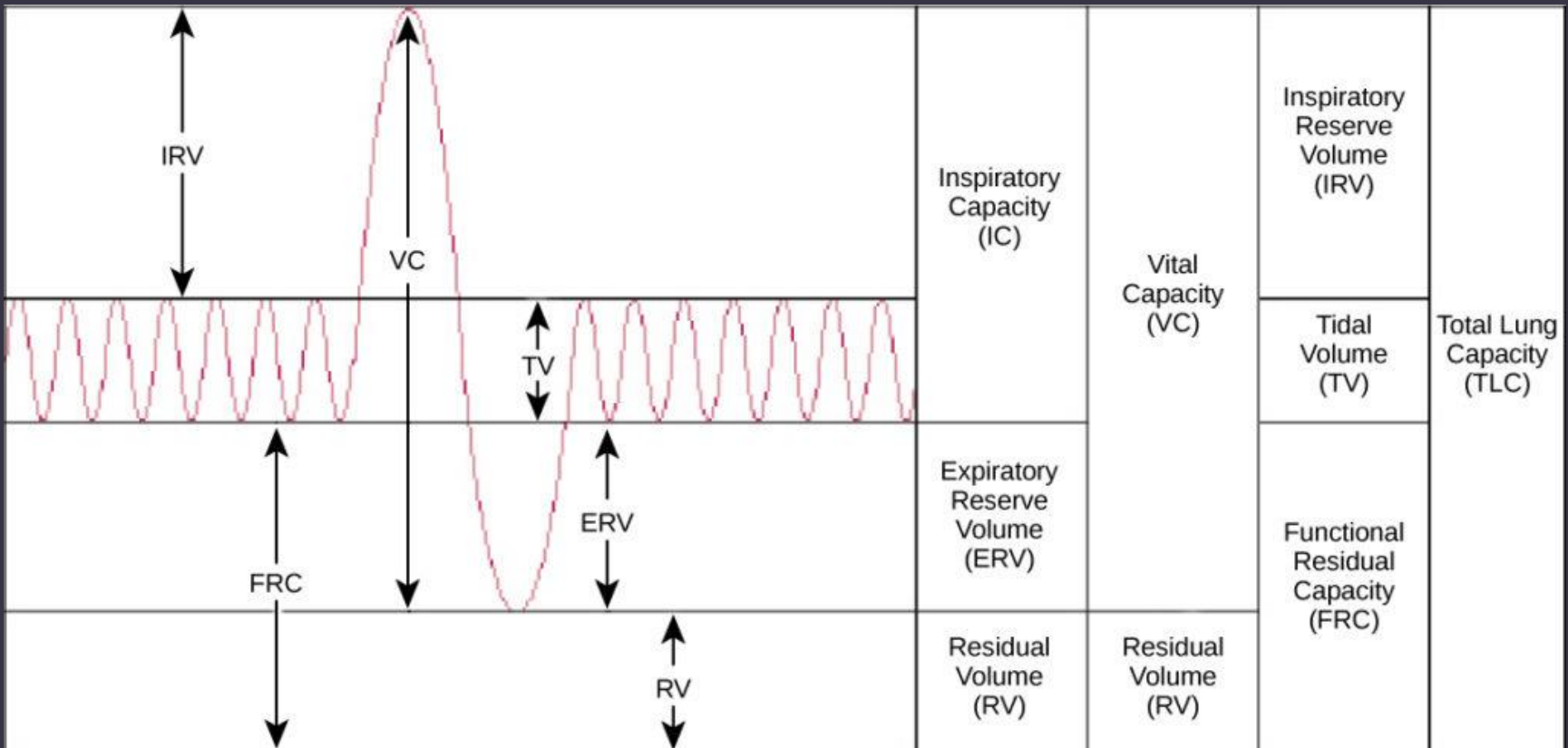
- Asthma
- Laryngospasm:
  - Older population
  - Lasts seconds to minutes
- Laryngeal oedema:
  - Anaphylaxis, ACEI, HAE
- Mass lesion causing upper airway obstruction
- Bilateral vocal fold paresis
  - Due to central or peripheral neurological cause

# Investigations

- Pulmonary function tests
- Questionnaires
- Imaging
- Flexible nasoscopy

# Spirometry

- Normal spirometry values
- Ratio of forced expiratory flow to forced inspiratory flow at 50% vital capacity (MEF50 : MIF50) > 1
- MIF

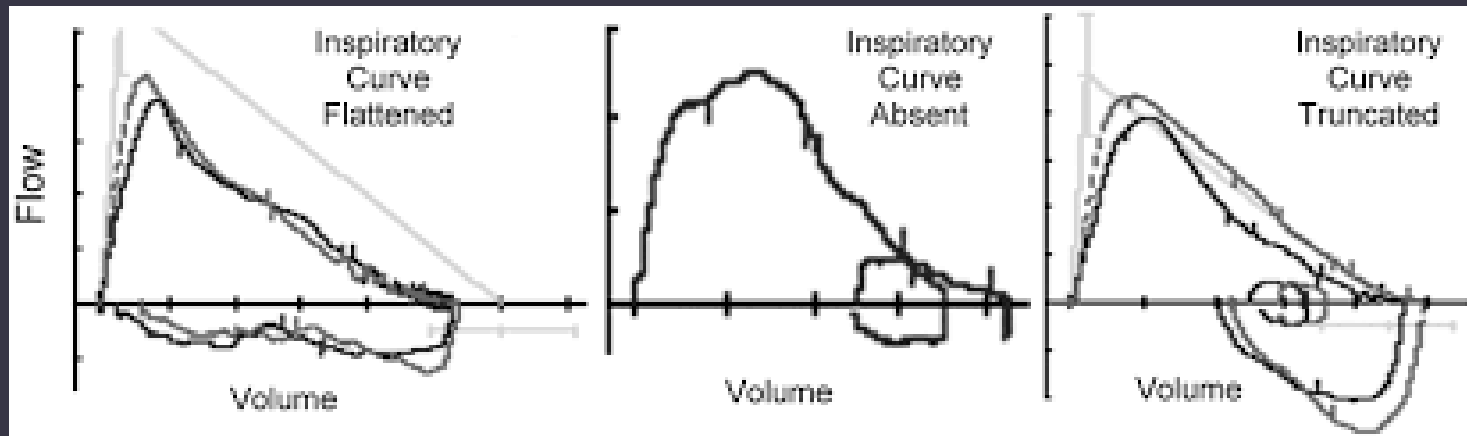




# Flow Volume Loops

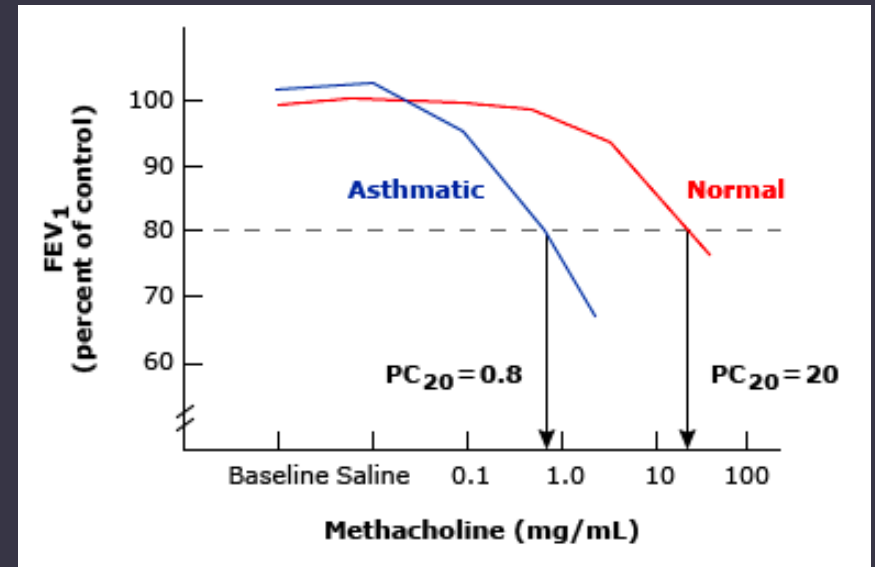
- **Flow patterns in ILO:**

- Variability in baseline flow on inspiration
- Absence / Flattening / Plateau = absent flow
- W: Reversal of flow
- Late drop off (most common) - reasonable inspiratory flow then tapers off



# Bronchial Provocation Test

- **Can sometimes induce obstruction with inhalation challenge, through irritant mechanism**
- Challenge airway with osmotic agent
- **Graph** showing FEV<sub>1</sub> vs dose of provoking agent
  - **Positive for asthma:** FEV<sub>1</sub> drop of >20% at PC<sub>20</sub> of 8mg/mL or less.
  - **Suggestive for VCD:** Reduction in FIF50 > 25% at PC<sub>20</sub> of 8mg/mL or less (Bucca et al 2011)
- **Agents:**
  - Methacholine – poor sensitivity
  - Histamine - good correlation but method criticised because induces laryngeal oedema
  - 4.5% Hypertonic saline – potentially good correlation
  - Mannitol – good correlation



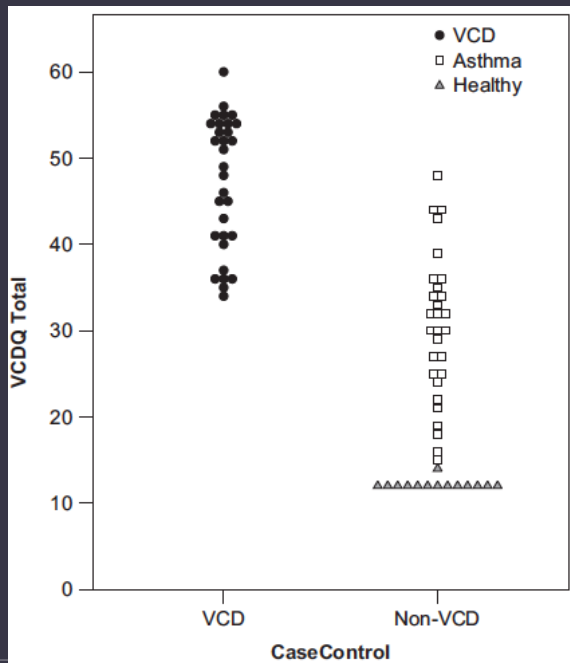
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**Table 3. Questionnaires Addressing Laryngeal Dysfunction**

<b>Questionnaire Name</b>	<b>First Author (Ref.), Year</b>	<b>Study, Validation Population, and Design</b>	<b>Reported Findings</b>	<b>Potential Usefulness</b>	<b>Limitations</b>
VCDQ	Fowler (70), 2015	Prospective two-stage study: (1) Focus groups (patients and health care professionals); then (2) prospective validation and testing of 12-item questionnaire in patients	VCDQ score different between patients with VCD, patients with asthma, and healthy control subjects, and in VCD was sensitive to change after speech therapy	Monitoring benefit of current treatments and testing novel treatments	Not yet tested as a diagnostic questionnaire; likely to require refinement in this regard as some items nonspecific
VCD screening checklist	Pinto (95), 2016	Prospective observational study in cohort (n = 80) diagnosed with severe asthma. Six questions identified to detect VCD and then compared with laryngoscopic findings	The question "Does pulmonary auscultation reveal wheezing, predominantly in the cervical region, and/or stridor?" was significantly higher for the VCD group	Simple screen to highlight VCD as a cause of symptoms and thus prompt consideration for work-up with laryngoscopy	Highly selected population. Lack of information regarding other contributory factors. Needs replicating in other centers and less selected cohort
Newcastle laryngeal hypersensitivity questionnaire	Vertigan (96), 2014	Prospective evaluation in patients with laryngeal dysfunction (n = 82) and in control subjects (n = 15). Evaluated factor analysis, discriminant analysis, responsiveness to change	Discriminant validity: Mean difference between patients and healthy control subjects was 5.5 Responsiveness: Score improves after intervention, by 2.3 units	Identify patients with laryngeal dysfunction  Measure response to intervention	Numbers tested are limited  Needs evaluation in a second validation population and in different settings to assess reproducibility

# Symptom Questionnaire

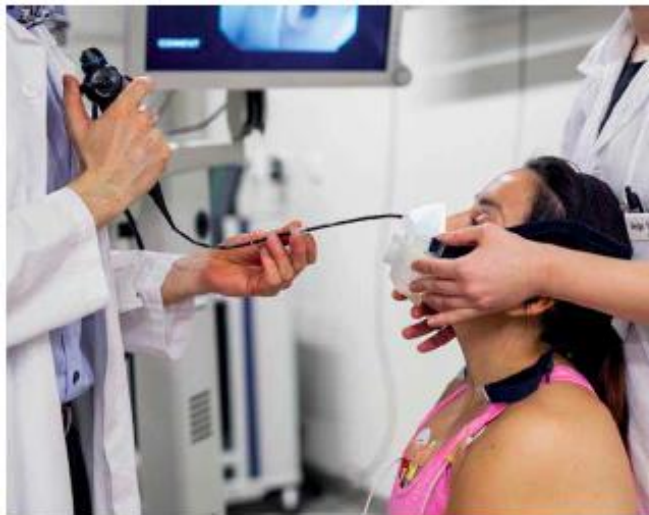
- **VCDQ – A questionnaire for symptom monitoring in vocal cord dysfunction** (Fowler et al 2015)
- Validated and reliable tool
- Used to score severity (not diagnostic)



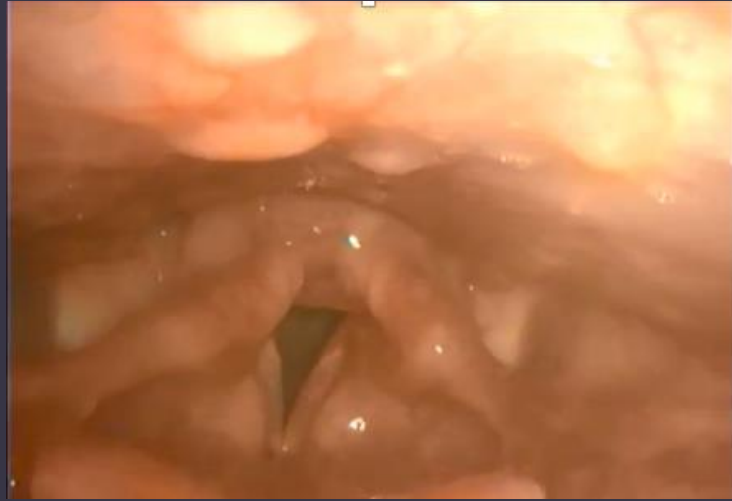
1. My symptoms are confined to my throat/upper chest
  2. I feel like I can't get breath past a certain point in my throat/upper chest because of restriction
  3. My breathlessness is usually worse when breathing in
  4. My attacks typically come on very suddenly
  5. I feel that there is something in my throat that I can't clear
  6. My attacks are associated with changes in my voice
  7. My breathing can be noisy during attacks
  8. I'm aware of other specific triggers that cause attacks
  9. My symptoms are associated with an ache or itch in my throat
  10. I am frustrated that my symptoms have not been understood correctly
  11. I am unable to tolerate any light pressure around the neck, e.g. tight clothes or bending the neck
  12. The attacks impact on my social life
- Total

# Laryngoscopy

- Gold standard
- Essential to confirm abnormal adduction of true vocal cords and to exclude other laryngeal pathology
- Can use strong scent to provoke obstruction
- Can perform continuous laryngoscopy during exercise

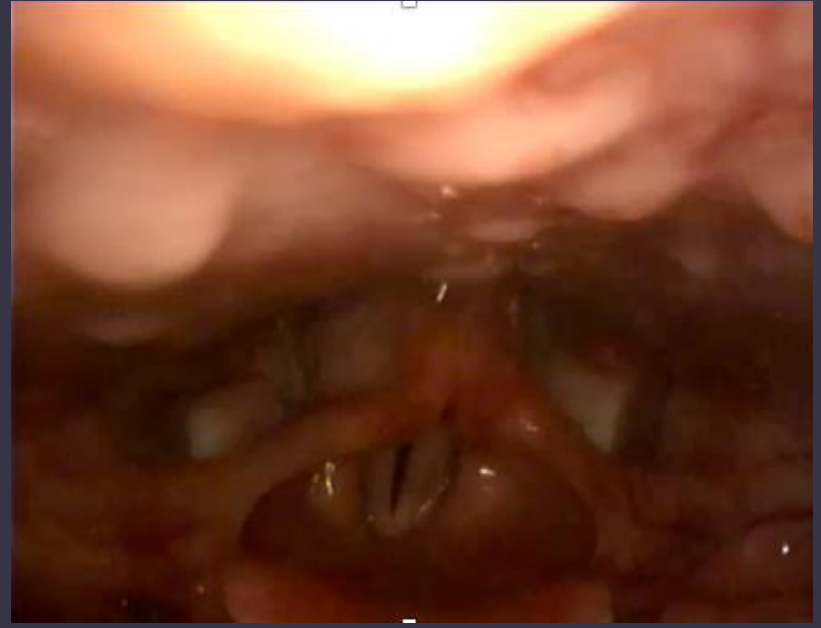
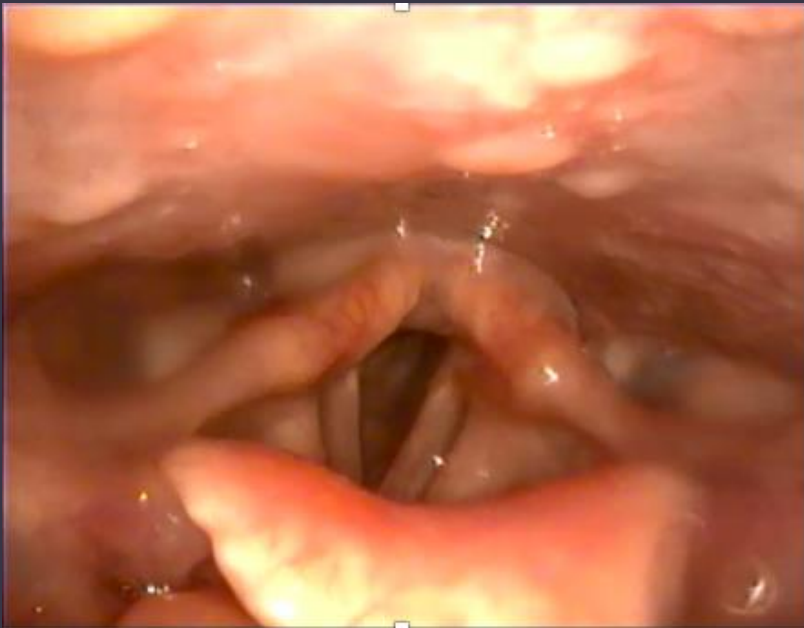


# Laryngoscopy: Quiet Respiration





# Laryngoscopy: Odour challenge



# Laryngoscopy: Phonation





# Laryngoscopy protocol

- Quiet respiration
  - Nasal vs oral
- Deep inhalation
- Phonation
  - Sustained vowels
  - High and low pitch
  - Loud and soft voice
  - Connected speech
  - Stroboscopy
- Odour challenge
- Other tasks to trigger



# Imaging

- Chest radiograph: to exclude intrathoracic cause of dyspnoea
- HRCT of upper airways to exclude subglottic stenosis, tracheal and extratracheal masses (if examination of trachea not possible during laryngoscopy)

# Tests of Movement

For breathing pattern disorders:

- Manual assessment of respiratory motion (physiotherapy)
- Structured light plethysmography
- Tidal volume traces (TV should sit in the middle of expiratory and inspiratory capacity)

# Management

- Paucity of reliable data (*Halvorsen et al 2017*)
- Lack of randomised controlled trials

# Acute Management

- Reassurance and supportive care until episode spontaneously resolves
- Respiratory manoeuvres
  - Panting, sniffing or pursed lip breathing can sometimes abort episode (activates posterior cricoarytenoid muscle causing abduction of true vocal cords)
- CPAP (continuous positive airway pressure) – some reports
- Inhalation of heliox (helium oxygen mixture) – rarely used
- Endotracheal intubation / tracheostomy is NOT recommended

# Long Term Prevention

- **\*\*\*Communicating the diagnosis\*\*\***
  - Convince patient of validity of diagnosis & symptoms
- Multidisciplinary approach
- Anti-reflux therapy
- Gabapentin/Pregabalin if significant component of chronic cough (*Gibson et al 2016*)
- **Speech pathology**
- Physiotherapy
- Psychotherapy
  - Identify psycho-social triggers

# Speech Pathology

- Goal: help patient regain laryngeal control
- Behavioural speech & voice therapy
  - Education
  - Respiratory re-training
  - Relaxation techniques
  - Vocal hygiene
  - Phonatory re-training

# Speech Pathology

- Monitoring using VCDQ or other questionnaires
- Biofeedback using videolaryngoscopy

**Table 2** Examples of strategies in the treatment programme

Component	Example
Education	No physiological benefit from cough; capacity for voluntary cough control
Strategies to reduce cough	Identify warning signs for cough and replace with modified swallow technique, pursed lip breathing exercise, or relaxed throat breath
Reduce laryngeal irritation	Increase hydration, decrease exposure to irritating stimuli
Psycho-educational counselling	Internalising locus of control; acceptance that treatment is hard work; setting realistic goals

*Vertigan et al (2016)*



# Conclusion

It was a pleasure to see [REDACTED] today, who has worked very hard in therapy for vocal cord dysfunction and has done incredibly well. She has been able to return to normal activities including sport and volunteer fire fighting, and her voice is lasting the distance in her work as a Teacher's Aide.

## **Discharge Summary**

**Problem:** vocal cord dysfunction, confirmed by scope with ENT 24/5/19 (seen during ED presentation), on a background of mild asthma since childhood.

**Assessment:** 24/4/19.

**Therapy:** 31/5/19, 7/6/19, 14/6/19, 21/6/19, 28/6/19, 12/7/19, 26/7/19, 6/9/19.

**Adherence:** diligent attendance at appointments and regular and accurate use of exercises.

**Progress:** significant improvement, normal outcome measures maintained since July.

**Outcome:** Discharge 6/9/19.

# VCD – a new epidemic???

- Increased awareness in patients of allergy / anaphylaxis
- Similar to 'rise' in food allergies
- Well covered by the media
  
- Increased awareness of VCD in clinicians (in HNE)
  
- Recent study found the prevalence of VCD in asthma patients was 25% (*Lee et al 2020 JACI*)
- Estimated prevalence of VCD in general population 5-7% (could be higher)

- “The field remains in an embryonic state with a great number of unanswered questions and hence many future research priorities” (*Hull et al 2016*)

Questions?

# References

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