ASTHMA CONTROL
GP CME South 18.8.12

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Asthma Pathophysiology

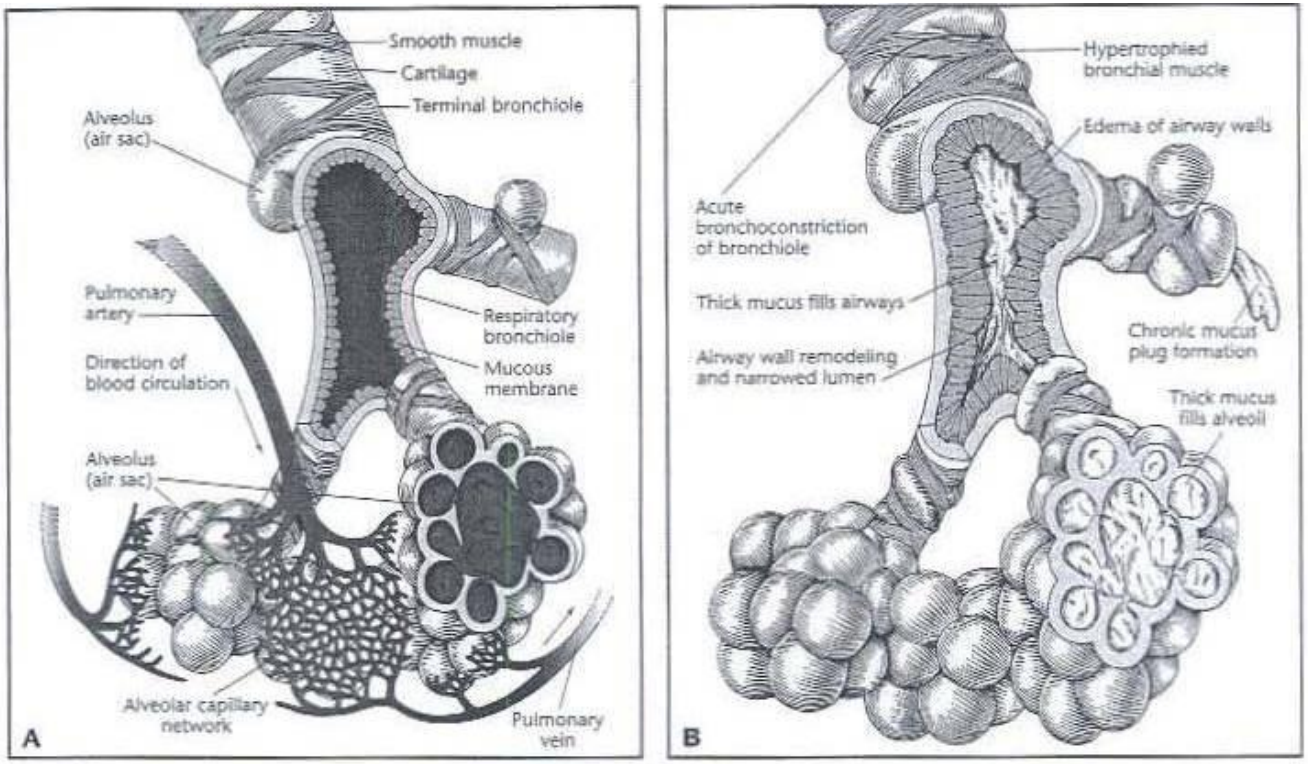


Figure 2-1. A. Normal anatomy of lung near the terminal bronchiole demonstrating the efficiency with which normal gas exchange occurs. **B.** Same region during acute asthmatic episode, demonstrating airflow obstruction in asthma. Smooth muscle along airway walls is constricted and hypertrophied. Along with extensive plugging of the airways by mucus, airway walls are thickened and edematous as a result of inflammatory changes. Eventually, airway walls may be remodeled, leading to fixed obstruction in some patients. Unchecked airway inflammation resulting in such extensive pathologic changes may cause severe hypoxemia from ventilation-perfusion mismatches and even intrapulmonary shunting.

ED Southland ‘Top 50’ missed opportunities ?

- Asthma unspecified” (9.): N=413 – 98% self referral
- “Asthma acute” : N=207 – 99% self referral
- *All asthma N=620 (5.)*

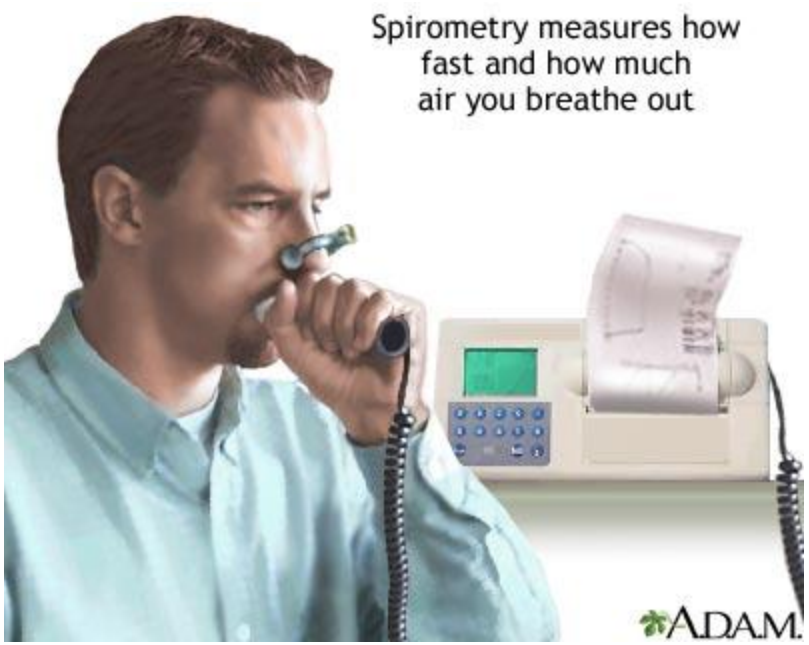
- Also “other/unspecified abn of breathing”: N=180 (74%)
- “Pneumonia, unspecified” : N=172 (81%)

ED Southland “Frequent Fliers “

- “Asthma , unspecified” (3.): N=29 80 visits
- “Asthma, acute” (11.) N=13 34 visits
- “COPD with acute exacerb” (13.) : N=11 (30)
- “COPD with acute asthma” (31.): N=7 (15)
- “COPD” (36.): N=7 (15)

- Missed opportunities – poor integration, poor LTC Mx

Not Common Enough: Spirometry tests

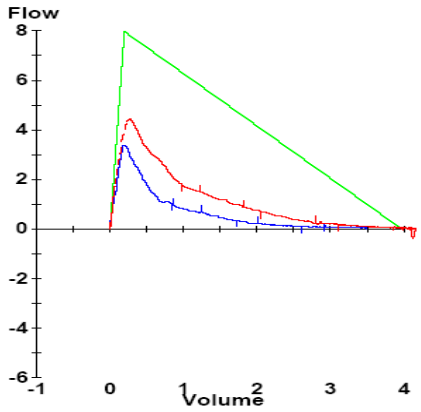


A 65 year old male smoker (45 pack yrs) with shortness of breath

Age: 65 Height(cm): 168 Weight(kg): 85.0 Body Mass Index: 30.12 Gender: Male

Spirometry
(BTPS, Ref: Hankinson/Polgar)

		REF	PRE-Rx Meas	PRE-Rx %REF	POST-Rx Meas	POST-Rx %Chg	90%C.I.
FEV1	Liters	2.94	** 1.29	** 44	** 1.83	42	0.70
FVC	Liters	3.97	3.49	88	4.16	19	0.83
FEV1/FVC	%	75	** 37		** 44		10
FEV6	Liters	3.75	** 2.51	** 67	3.37	34	0.81
FEV1/FEV6	%	78	** 51		** 54		9
FEF25-75%	L/sec	2.37	** 0.27	** 12	** 0.52	89	1.43
StdFEF25-75	L/sec	2.83	** 0.56	** 20	** 0.88	56	1.50
PEF	L/sec	7.98	** 3.41	** 43	** 4.48	31	2.07
FET100%	Sec		21.30		19.90	-7	
FVL ECode			000000		000000		



PRED___ PRE___ POST___

Medication: SALBUTAMOL

Management of asthma in Australian general practice: “Care is still not in line with clinical guidelines”

- Barton et al Prim Care Respir J 2009;18:100-5
- 247 GPs, 97 practices
- 47% asthma register, 76% access to spirometry
- 12% using spirometry routinely , 13% Asthma Action Plans, 30% inhaler technique review, 29% Ax of physical activity …

- Conclusion: “GPs are guideline fatigued”, “the majority of GL are produced by well meaning specialist oriented groups who produce GL that comprise many pages ….”

Suboptimal asthma control: prevalence, detection and consequences in general practice.

Chapman KR et al Eur Respir J 2008;31:320-25

- N=354 GPs, <50 consecutive patients for each
- N=10,428 pt s - Same questionnaire for pt and GP
- 57% attended for non-asthma reason , 26% routine asthma care, 16% urgent asthma care
- 20% SABA, 39% ICS mono-Rx, 35%, ICS+LABA, 3% no Rx, 3% other
- Patient view: 59% uncontrolled
- GP view : 42%

Suboptimal asthma control: prevalence, detection and consequences in general practice.

Chapman KR et al Eur Respir J 2008;31:320-25

- 80% no Action plan
- 32% never had inhaler technique taught
- 44% never had spirometry
- 47% “always” took meds, 10% “when remembering”, 41% when needing to
- 24% current smoker, 19% former
- Uncontrolled group: 59% had needed urgent care, “ok” control: 26%
- “excellent” control:15%

"Asthma still more questions than answers"

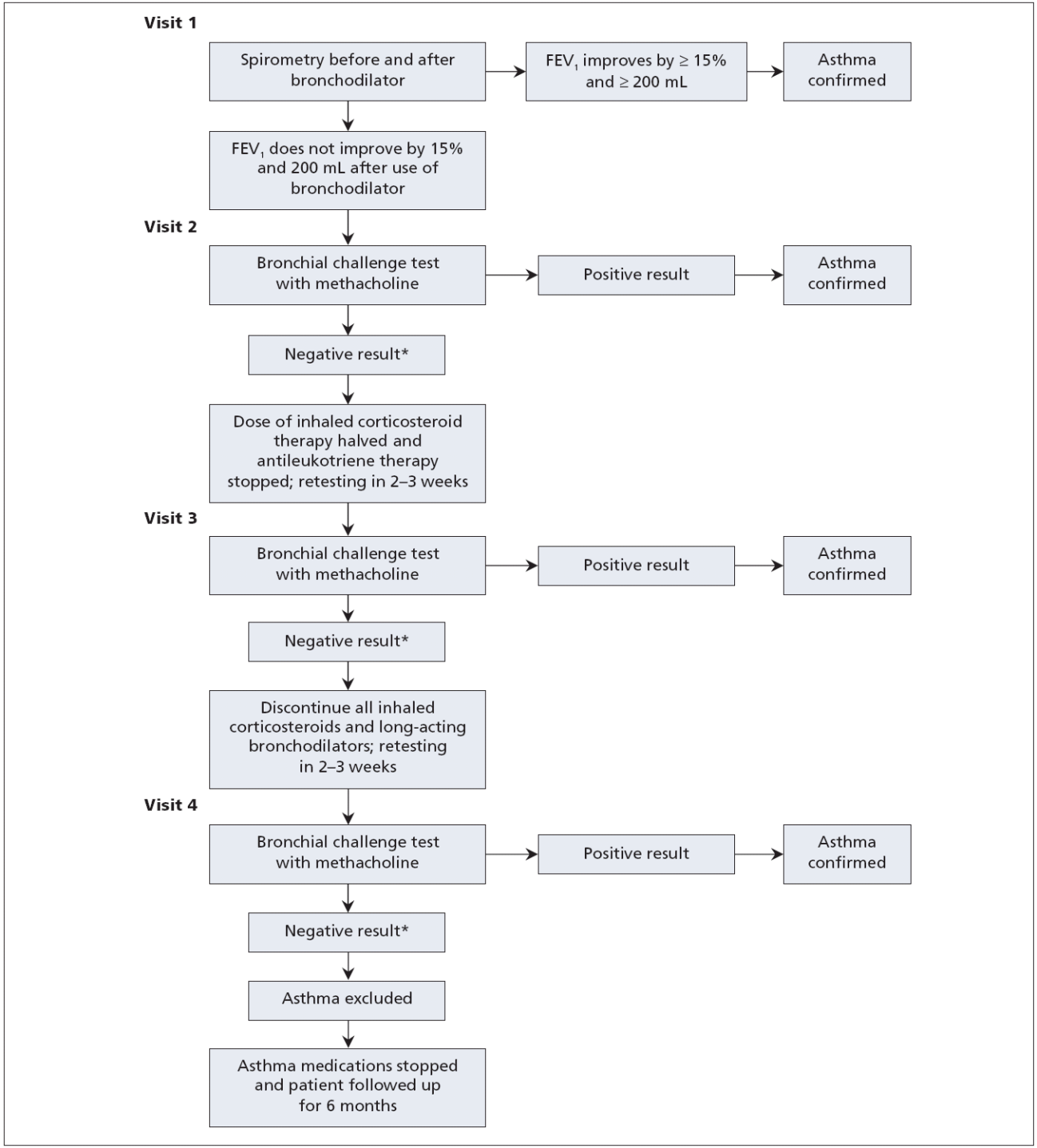
The Lancet Editorial 20 Sept 2008 + others GL often little help

- Differing clinical phenotypes, eosinophilic versus non-eosinophilic asthma
- Who gets asthma and why? e.g. birth cohort studies
- Who responds to (which) treatment? Who will have good control ?
- Genetic factors : IL4-R, hedgehog interacting protein (Chr4)
- Biomarkers : eNO, cyto-/chemokines
- New insights into risk factors: paracetamol, swimming pools, adiponectin

Diagnosing asthma

GINA update 2008 (Global Initiative for Asthma)

- Is it asthma ? *(or other cause of cough / SOB)*
- Symptoms: Worse at night, seasonal pattern, (FH of) atopy„, triggers , asthma Rx helps , “colds go to chest”
- Spirometry airflow obstruction, +>12% / 200ml after bronchodilator
- PEFR +60L/min after bronchodilator, or >20% variation day to day, or 10% with bd PEFR
- Challenge test: ? Hyper-reactivity
- Allergen skin tests or specific serum IgE
- Exhaled nitric oxide, (*sputum eosinophilia*)


Visit 1
Spirometry before and after bronchodilator
FEV1 improves by ≥ 15% and ≥ 200 mL
Asthma confirmed
FEV1 does not improve by 15% and 200 mL after use of bronchodilator
Visit 2
Bronchial challenge test with methacholine
Positive result
Asthma confirmed
Negative result*
Dose of inhaled corticosteroid therapy halved and antileukotriene therapy stopped; retesting in 2–3 weeks
Visit 3
Bronchial challenge test with methacholine
Positive result
Asthma confirmed
Negative result*
Discontinue all inhaled corticosteroids and long-acting bronchodilators; retesting in 2–3 weeks
Visit 4
Bronchial challenge test with methacholine
Positive result
Asthma confirmed
Negative result*
Asthma excluded
Asthma medications stopped and patient followed up for 6 months

Overdiagnosis of asthma in obese and nonobese adults

Shawn D. Aaron MD, Katherine L. Vandemheen BScN, Louis-Philippe Boulet MD,
R. Andrew McIvor MD, J. Mark FitzGerald MD, Paul Hernandez MD, Catherine Lemiere MD,
Sat Sharma MD, Stephen K. Field MD, Gonzalo G. Alvarez MD, Robert E. Dales MD,
Steve Doucette MSc, Dean Fergusson PhD, for the Canadian Respiratory Clinical Research Consortium

- One third of those diagnosed with asthma by their physician did not have asthma.
- Asthma is over-diagnosed

CMAJ 2008; 179:1121-31

Overdiagnosis Of Asthma In Obese And Nonobese Adults Aaron SD et al. CMAJ 2008;179:1121-31

The error of not measuring asthma, *Stanbrook M, Kaplan A CMAJ 2008;179:1099-1100*

- There is no good reason for spirometry not to be used in primary care practice.
- Doctors who do not use spirometry should not be managing asthma.
- Barriers to perform spirometry exist
- Peak flow can be a monitoring but not a diagnostic tool
- Doctors are often using *[“empirical”]*trials of treatment, which is easy but the cost can be much more than cost for spirometry

Daily Telemonitoring of Exhaled Nitric Oxide and Symptoms in the Treatment of Childhood Asthma

DeJongste et al. AJRCCM 2009;179:93-97

- Prospective, open label, randomized, parallel group study in children with atopic asthma for 30 weeks.
- Daily eNO measurements

Daily Telemonitoring of Exhaled Nitric Oxide and Symptoms in the Treatment of Childhood Asthma.

DeJongste et al. AJRCCM 2009;179:93-97

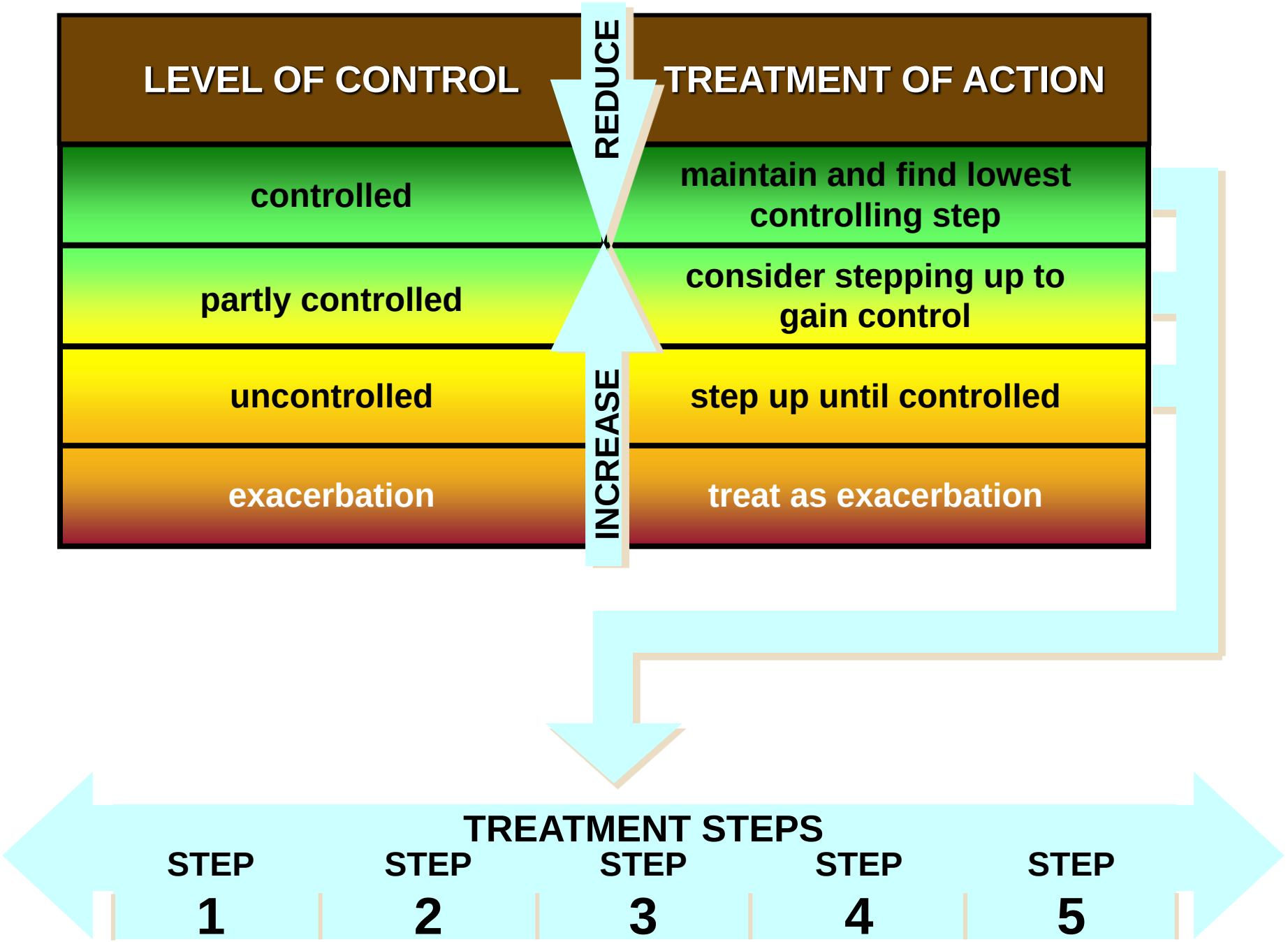
- Treatment decisions in asthma are made on the bases of lung functions and symptoms.
- Ideally we wish to treat airway inflammation with the correct dose of inhaled corticosteroids ICS
- Sputum eosinophil count and exhaled nitric oxide (eNO) levels are surrogate markers of airway inflammation.
- Proof of concept study suggests that ICS can be adjusted according to the eNO levels
- Portable eNO analyzers have become available – and so has telemonitoring.

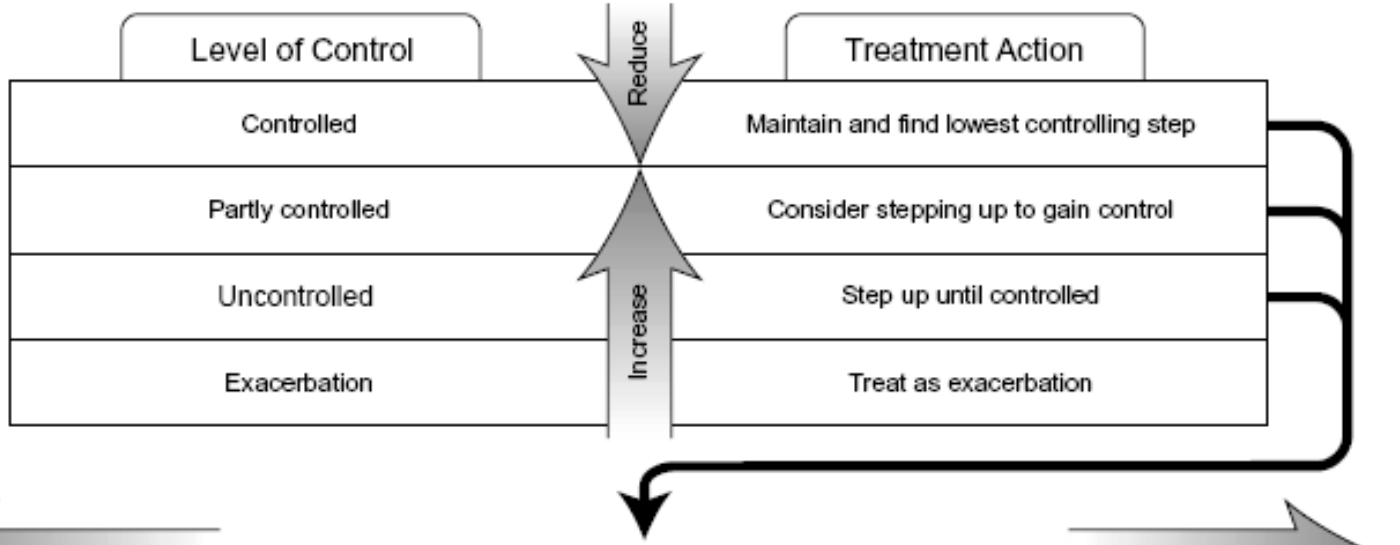
What are we trying to achieve?

- Control of symptoms
- No /less exacerbations
- Maintain pulmonary function
- Normal activity and exercise levels
- No adverse effects of therapy
- Prevent irreversible airflow limitation
- Prevent mortality

Is it controlled ?

Characteristic	Controlled (All of the following)	Partly controlled (Any present in any week)	Uncontrolled
Daytime symptoms	None (2 or less / week)	More than twice / week	3 or more features of partly controlled asthma present in any week
Limitations of activities	None	Any	
Nocturnal symptoms / awakening	None	Any	
Need for rescue / "reliever" treatment	None (2 or less / week)	More than twice / week	
Lung function (PEF or FEV_1)	Normal	< 80% predicted or personal best (if known) on any day	
Exacerbation	None	One or more / year	1 in any week


LEVEL OF CONTROL
TREATMENT OF ACTION
REDUCE
controlled
maintain and find lowest controlling step
partly controlled
consider stepping up to gain control
uncontrolled
step up until controlled
exacerbation
treat as exacerbation
INCREASE
TREATMENT STEPS
STEP 1
STEP 2
STEP 3
STEP 4
STEP 5



Reduce **Treatment Steps** **Increase**

Step 1	Step 2	Step 3	Step 4	Step 5
Asthma education Environmental control				
As needed rapid-acting β_2-agonist	As needed rapid-acting β_2-agonist			
Controller options	Select one	Select one	Add one or more	Add one or both
	Low-dose inhaled ICS*	Low-dose ICS plus long-acting β_2-agonist	Medium-or high-dose ICS plus long-acting β_2-agonist	Oral glucocorticosteroid (lowest dose)
	Leukotriene modifier Ü	Medium-or high-dose ICS	Leukotriene modifier	Anti-IgE treatment
		Low-dose ICS plus leukotriene modifier	Sustained release theophylline	
		Low-dose ICS plus sustained release theophylline		

ACT


Q1 In the **past four weeks**, how often did your asthma prevent you from getting as much done at work, school or home?
SCORE
All of the time 1
Most of the time 2
Some of the time 3
A little of the time 4
Not at all 5
Q2 During the **past four weeks**, how often have you had shortness of breath?
More than once a **day** 1
Once a **day** 2
3 to 6 times a *week* 3
Once or twice a *week* 4
Not at all 5
Q3 During the **past four weeks**, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?
4 or more times a *week* 1
2 to 3 nights a *week* 2
1 night a *week* 3
Less than 1 night a week 4
Not at all 5
Q4 During the **past four weeks**, how often have you used your reliever medication (such as your blue inhaler *or* rescue inhaler)?
3 or more times a **day** 1
1 or 2 times a **day** 2
2 or 3 times a *week* 3
Once a week or less 4
Not at all 5
Q5 How would you rate your asthma control during the **past four weeks**?
Not controlled 1
Poorly controlled 2
Somewhat controlled 3
Well controlled 4
Completely controlled 5

ACT NZMJ 10 June 2011

- BoP/ AKL GP group : Adult asthma Mx
- 50 consecutive asthma pt : ACT,Rx, ? Exacerbations, ? unplanned presentation
- Mean score 18.9
- 53% well controlled, 19% poorly controlled
- 18% better controlled than appreciated
- 36% worse control than appreciated
- Worse in Maori or ‘other’, younger, smoker, F

Action Plans: <20% of patients

Asthma Action Plan

Name	Date
Doctor	Medical Record #
Doctors Office Phone # Day	Night/Weekend
Emergency Contact	
Doctors Signature	

The Colors of a traffic light will help you use your asthma medicines.

Green means **Go Zone!**
Use preventive medicine.

Yellow Means **Caution Zone!**
Add quick relief medicine.

Red means **Danger Zone!**
Get help from a doctor.

Personal Best Peak Flow: _____

GO

You have all of these:
- Breathing is good
- No cough or wheeze
- Sleep through the night
- Can work and play

Peak flow from _____ to _____

Use these daily preventive anti-inflammatory medicines:

MEDICINE	HOW MUCH	HOW OFTEN/WHEN

For asthma with exercise, take:

CAUTION

You have any of these:
- First signs of a cold
- Exposure to known trigger
- Cough
- Wheeze
- Tight chest
- Coughing at night

Peak flow from _____ to _____

Continue with green zone medicine and add:

MEDICINE	HOW MUCH	HOW OFTEN/WHEN

CALL YOUR PRIMARY CARE PROVIDER.

DANGER

You or baby is getting worse fast:
- Medicine is not helping
- Breathing is hard and fast
- Nose opens wide
- Ribs show
- Can't talk well

Peak flow reading below _____

Take these medicines and call your doctor now.

MEDICINE	HOW MUCH	HOW OFTEN/WHEN

GET HELP FROM A DOCTOR NOW! Do not be afraid of causing a fuss. Your doctor will want to see you right away. It's important! If you cannot contact your doctor, go directly to the emergency room. DO NOT WAIT.

Make an appointment with your primary care provider within two days of an ER visit or hospitalization.

Management of “resistant” asthma - 9 steps DYM Leung

- 1. Confirm it is asthma (& exclude significant other)
- 2. Rule out psychosocial factors-Non- compliance
- 3. Review medication administration technique
- 4. Ensure good environment –i.e. antigenic exposure
- 5. Modify ICS –therapy (dose, frequency)
- 6. Maximise Rx: ICS + LABA
- 7. Written action plan
- 8. Evaluate systemic steroid pharmocokinetics & receptors (liquid preparations, bd dosing..)
- 9. Alternative anti-inflammatory / immunomodulator treatments (methotrexate, gold, IVIG)

“Asthma Plus”

- Numerous courses of prednisone for asthma “exacerbations” might make things worse!

- Obesity
- Sleep Apnea / OSA
- GERD
- Deconditioning

“Asthma Plus”

- Numerous courses of prednisone for asthma “exacerbations” might make things worse!
- Consider :
  - Smoking status
  - Rhinosinusitis
  - Vocal cord dysfunction
  - Hyperventilation….

Multiple Logistic Regression: Predicting poor control (ACQ > 1.5)

Variable		OR	95% CI	p
Rhinitis	Compared to no rhinitis:			
	Significant rhinitis	4.21	3.35 – 5.28	<.001
	Mild rhinitis	1.97	1.62 – 2.41	<.001
Smoking	Compared to never smoking:			
	Current smoker	4.30	3.50 – 5.28	<.001
	Ex smoker	1.71	1.45 – 2.01	<.001
Adherence	Compared to high adherers:			
	Low adherers	1.29	1.12 – 1.49	.001

Based on a survey of 4429 patients prescribed ICS in 83 UK general practices

Clatworthy J, Price DB et al. PCRJ 2009

This will /should work……

- Actually take the treatment
- Early recognition / mx of exacerbations
- Allergen avoidance
- Weight reduction
- Limit co-morbidities /smoking
- Exercise (but NB EIB, EIA)

Thorax 2009; 64:939-943 doi:10.1136/thx.2009.113662
Adherence to inhaled therapy, mortality and hospital admission in COPD
J Vesbo, JA Anderson, PMA Calverley, B Celli et al

- TORCH trial
- Good adherence defined >80% of study medication taken
- 4,880 (yes) vs 1232 (no) patients
- 11.3% vs 26.4% died
- 0.15 vs 0.27 annual admission rates

- **The association between increased adherence and improved mortality and reduction in hospital admissions was independent of study treatment**

Heart *2002;**88:**203-206 doi:10.1136/heart.88.2.203*

Effect of partial compliance on cardiovascular medication effectiveness

Joyce A Cramer

- The typical assessment of mediation compliance by physicians is similar to the assessment of an iceberg from the ship captain's window.
- The physician is unaware of the appropriate action to be taken.
- Instead, the physician typically prescribes even more medication as a higher dose, or an alternative or second drug.

Improving adherence

- Clarify expectations
- Involve patient /family in Rx plan development
- Explain how medication works
- Test patient's understanding
- Is treatment affordable?
- Positive reinforcement
- Address adherence during each FU
- Encourage patient to seek support (support groups, meetings…)

Treat individual patient
Stop what does not work

- Has it made a difference to you?
- Is breathing easier in any way?
- Has your sleep improved?
- Can you do some things now that you couldn't do at all before, or do the same things faster?
- Can you do the same things as before but are now less breathless when you do them?

The “non-adherent patient”

- Unintentional
- Intentional :dose, frequency,number of drugs..
- Patient beliefs about respective medication / their disease
- Difficulties with inhaler devices, complex regimen, side effects or concern of, cost, dislike, access to pharmacy …-not necessarily “irrational”

Studies of real-life inhaler technique

Reference	No. patients	Inhaler device	Inadequate technique
Erickson et al.	159	MDI	82% (>2 out of 9 steps incorrect)
Larsen et al.	12	MDI	58% actuated the MDI too early or too late
Schmid et al.	25	DPI (Turbuhaler®)	64% made errors on an 8-point scale
Shrestha et al.	125	MDI	79% made errors in series of 7 steps
Thompson et al.	72	MDI	76% made errors in series of 8 steps
van Beerendonk et al.	316	MDI (19%) or DPI (81%)	89% made at least one mistake in inhalation technique

Reviewed in Duerden M, Price D. Dis Manage Health Outcomes 2001; 9 (2)

How to improve inhaler technique

- Poor control :check technique, compliance, patient acceptance of device
- Risk factors are e.g. mix of inhaler types, more difficult devices to get right
- Observe technique , teach patient (using video demonstrations) and health care professional
- Devices to check technique and maintain trained technique: 2Tone trainer for MDIs, Mag-Flow for DPIs, Turbuhaler Whistle, Novolizer, Aerochamber Flow View

Exercise induced asthma , asthma in athletes

- "*Exercise induced Sx and signs of asthma occurring after intensive physical exercise*"
- More prevalent in elite , endurance , swimming and winter sports
- Some with "asymptomatic" exercise induced bronchocontriction EIB
- May result in chronic inflammation , remodelling
- Asthma Rx does not enhance performance if healthy
- Needs objective test= investigation(s)
- NB Bejing:19.1% of swimmers of BA- 32.9% of medals , cyclists 17.3 /28.9% !!
- Rx in "usual way"
- NZ 1 Aug 2012 Montelukast if already on ICS/LABA

Tiotropium step-up therapy for adults with uncontrolled asthma

- *NEJM 19 Sept 2010, Peters SP et al*
- N=210, 3way, 2blind, 3dummy, 14 week
- >18y, Hx asthma, +BD test or BHR, FEV1>40%, <10py smoking Hx
- All: ICS 80mcg bd run-in, if @ 4w FEV1 <70%, SABA >6/7, noct Sx>2/7
- **ICS x 2 OR add Tiotropium OR add LABA**
- Concl: T improved Sx & lung Fn more than ICSx2 , non-inferior to added LABA

Rescue use of beclomethasone and albuterol in a single inhaler for mild asthma

- *NEJM 2007;356:2040-52; Papi A et al*
- N=455; FEV1~88%, 6M, 2blind, 2 dummy
- “Step 1or Step 2 patients
- Bd P+ 250mcg B+ 100mcg A Comb PRN, bd P + A PRN, bd B + A PRN, bd Comb + A PRN
- Comb was comparable to regular , signif less cumul ICS dose (18 vs 76mg)

BTS SIGN guidelines 2009: SMART

- “ in selected adult patients at step 2-3 who are poorly controlled the use of Bud/Form in a single inhaler as rescue medication instead of a SABA, in addition to its regular use as controller therapy has been shown to be an effective regime.
- The total regular dose of ICS should not be decreased. Patients taking rescue Bud/Form should have their treatment reviewed . Careful education .. required “

Single Maintenance And Reliever Therapy

- Patients take a regular daily maintenance dose of Comb Inhaler (Bud/Form) , with additional inhalations if needed
- Patients do not require a separate SABA
- Only one inhaler where the underlying inflammation is treated with every inhalation, even when used as-needed
- Similar degree of control with lower doses of ICS (NB eg COSMOS trial (~653mcg Bud vs 583 Flu)
- Overall cost similar
- BUT: not proven for patients with poor adherence or those with problem asthma
- BUT: not currently under NZ PHARMAC criteria

Symbicort Datasheet; Barnes PJ. Eur Respir J 2007;29:587-595.

DR Taylor et al. on behalf of NZ executive TSANZ :NZMJ 7 11 2008: "as required" combination therapy… current evidence and recommendations

- In favour: varying exposure to triggers, worsening over 2-3d, many patients are non-adherent, BA monotherapy has risks of morbidity and mortality
- Assumptions / hypotheses: it is steroid-responsive, symptoms are due to increase airway inflammation, using ICS with BA will in turn reduce need for extra BA later, control is better without risking adverse effects of BA or ICS overuse

DR Taylor et al. on behalf of NZ executive TSANZ :NZMJ 7 11 2008: "*as required" combination therapy… current evidence and recommendations*

- potential problems: very high users excluded in studies (Rabe/ O' Byrne) <=10p/d), but in study high users did better on SMART- ? "real life"
- Problem asthma: frequent symptoms and poor adherence, in principle ok on SMART if certain that steroid responsive
- As yet not totally clear that ICS do always protect against risks of BA (AHS, eNO, sputum eosinophils)
- Costs: not "more expensive" counting overall cost
- PHARMAC criteria: NB these are not treatment guideline
- Caveats: still use self management plan (+ advice when to use prednisone, cap max dose of SMART at 6 (12) doses /d , still consider providing emergency reliever (+/- spacer), not appropriate in children

Cold, Damp Housing

- *P Howden-Chapman et al BMJ 26 2 2007*
- 1350 households, 4407 inhabitants, 7 low income communities: “cluster randomised study”
- Retrofitting of homes
- BR temp +0.5° C,<10 ° C for 11.7h, rel. humidity -2.3%, energy use 81/100
- OR=0.50 for fair/poor self rated health
- OR=0.57 self reported wheeze
- OR=0.47 day off school , OR=0.62 off work
- OR=0.73 for GP visit
- OR=0.53 (but NS) hospital admission

Glucocorticoid Mechanism of Action

- Cytoplasmic GC receptor-translocates to nucleus:GCRalpha-ligand complex DNA binding
- Transcription of specific target genes
- Other transcription factors CREB protein (cAMP response element binding protein), AP (activation protein), NF-kB (nuclear factor kappa B) interfere
- Increase in IL10 with inhibition of pro-inflammatory cytokine production, antigen presentation , T cell activation, mast cell and eosinophil function

Glucosteroid-resistant asthma

- Heterogeneity of mechanisms
- Acquired “type I” abnormally reduced GCR ligand and DNA binding affinity
- Reversible , and ?sustained by incubation with IL2 and IL4
- Alternative splicing of GCR pre mRNA
- Constitutive defect “type II” –low number of GCR
- In tobacco smokers: phenotypic change (neutrophils), cytokines (IL4 TNFa), GCR isoforms , pro-inflammatory transcription factors (NF-kB), decreased histone deacetylase activity

β-adrenoceptor agonists interfere with glucocorticoid receptor DNA binding in rat lung

- Matthew J. Peters, Ian M. Adcock , Carolanne R. Brown and Peter J. Barnes
- Department of Thoracic Medicine, National Heart and Lung Institute, Dovehouse Street, LondonSW3 6LY, UK

- Received 21 September 1994; revised 27 December 1994; accepted 24 January 1995

Eur J Pharmacol

Abstract

- Inhaled β2-adrenoceptor agonists are the most effective bronchodilator treatment in asthma, yet paradoxically high doses may be associated with increased asthma morbidity and mortality. Steroids are the most effective therapy in controlling asthmatic inflammation and act by binding to specific sequences of DNA (GRE), thus modulating gene transcription. We report that in rat lung, the β2-adrenoceptor agonists, salbutamol and fenoterol, decrease the binding of glucocorticoid receptors to GRE, by 46 ± 4% although it has no effect on the affinity or number of glucocorticoid receptors. The inhibition of GRE binding by salbutamol is concentration-dependent, can be blocked by propranolol and is seen following forskolin treatment. This effect appears to be due to an interaction between the glucocorticoid receptor and the transcription factor, cAMP response element binding protein (CREB), which is activated by high concentrations of β2-adrenoceptors agonists.
- We suggest that by this mechanism high doses of inhaled β2-adrenoceptor agonists may inhibit the anti-inflammatory effects of endogenous glucocorticoids and exogenous corticosteroids used for asthma therapy.

“Alternative” Asthma treatments

- Nebulised frusemide, lignocaine, heparin (for acute and chronic asthma)
- Immune modulator treatment
- Acupuncture, chiropractic or massage therapy
- Breathing exercises (Pranayama, Buteyko)
- Herbal and dietary (antioxidants, vitamins, omega3 , green lipped mussels, or elimination diets)
- Bronchial thermoplasty –radiofrequency ablation of bronchial smooth muscle tissue

Immune modulator treatment for asthma

- Methotrexate (5-50mg/week) – Increased sensitivity of lymphocytes to inhibitory effects of steroids , reduction in serum IG

  Meta-analysis , 3-4mg reduction in steroid dose, small improvement in FEV1- ?beneficial overall

- Gold: Inhibition of neutrophil and lymphocyte activity, Ab secretion. IgE induced histamine release

  Cochrane review –small reduction in steroid dose

- IVIG Immune Globulin (2g/kg /month) –mixed results in RCT but significant reduction of steroid dose in those with very high requirements before

Immune modulator treatment for asthma

- Dapsone –antimicrobial (leprosy), anti-inflammatory - ? Steroid sparing
- Colchicine -mixed results
- OH Chloroquine – 300-400mg/d – conflicting
- Macrolides (troleandomycin) - ? Reduced hepatic steroid metabolism rather than antiinflammatory /antibacterial effect
- Anti-TNF alpha agents: Infliximab (mAb) Etanercept (soluble receptor fusion protein)

Immune modulator treatment for asthma

- Cyclosporin A –altering lymphocyte IL2 4 5 production, macrophage IL1 production , apoptosis of CD4 T lymphocytes; 3-5mg /d
- SH Lock et al Am J Respir Crit Care Med 1996; 153:509-14 RCT, N=39, 36 weeks
- E Nizankowska et al Europ Respir J 1995;8:1091-9 RCT, N=34, 34 weeks
- Cochrane Review DJ Evans et al 2000 (4) “small impact but major serious adverse effects”
- CsA for atopic eczema:Meta-analysis 2007 J Schmitt et al J Europ Acad Derm Venerl 21:606-19: 15 studies, N=602- relative effectiveness 55%, no long term data on long-term effectiveness and safety !

FDA and LABA :Feb 2010

- What are the key points people should know about the safe use of LABAs in patients with asthma?
- LABAs contraindicated without asthma controller medication such as ICS
- LABAs only long-term if asthma cannot be adequately controlled on asthma controller medications.
- LABAs should be used for the shortest duration of time required to achieve control of asthma symptoms and discontinued, if possible, once asthma control is achieved.
- Pediatric and adolescent patients who require the addition of a LABA to an inhaled corticosteroid should use a combination product containing both an inhaled corticosteroid and a LABA to ensure compliance with both medications.

FDA: Inhaled Anticholinergic

- [01-14-2010] This is a Follow-Up to previous Early Communications issued in 2008 by the (FDA) describing a potential increase in the risk of stroke, heart attack, or death from a cardiovascular cause related to the use of tiotropium, which is marketed as Spiriva HandiHaler.

- FDA has now completed its review and believes the available data do not support an association between the use of Spiriva and an increased risk

FDA: Inhaled Anticholinergic

- 10/07/2008: FDA's Early Communication About an Ongoing Safety Review issued on March 18, 2008 stated that Boehringer Ingelheim, the maker of Spiriva HandiHaler (tiotropium bromide), had conducted a pooled analysis of 29 trials that suggested a small excess risk of stroke (2 cases per 1000) with tiotropium bromide over placebo.
- FDA has now received preliminary data from UPLIFT (Understanding the Potential Long-Term Impacts on Function with Tiotropium), a large, 4-year, placebo controlled clinical trial with Spiriva HandiHaler in approximately 6000 patients with chronic obstructive pulmonary disease (COPD).
- The preliminary results of UPLIFT reported by Boehringer Ingelheim to the FDA showed that there was no increased risk of stroke with tiotropium bromide (Spiriva HandiHaler) compared to placebo

Non-Pharmacological options $$

- Home oxygen (concentrator + cylinders) ~$2,500/yr
- Pulmonary rehabilitation (8weeks, 2x2h) ~ 1,000$/pt
- Acute hospital admission (5d) ~ 7,500$
- Community Spirometry 60$
- Community contract CXR ~75$

Highest evidence level for Symbicort SMART in GINA guidelines

" The use of the combination of a rapid and long-acting β_2-agonist (eformoterol) and an ICS (budesonide) in a single inhaler both as a controller and reliever is effective in **maintaining a high level of asthma control and reduces exacerbations** requiring systemic glucocorticosteroids and hospitalization **(Evidence A)**"

"Both components of budesonide-eformoterol given as needed contribute to **enhanced protection from severe exacerbations** in patients receiving combination therapy for maintenance and provide **improvements in asthma control** at relatively low doses of treatment."

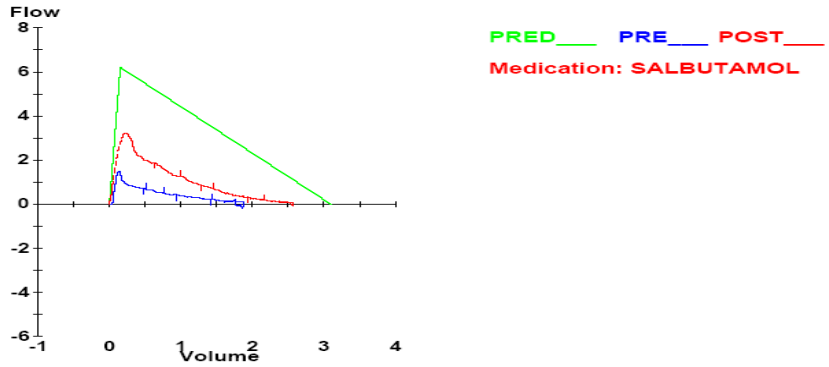
Global Initiative for Asthma, page 62, 2007. www.ginasthma.com

47 year old female smoker
You request spirometry with reversibility testing.

Age: 47 Height(cm): 152 Weight(kg): 59.0 Body Mass Index: 25.54 Gender: Female

Spirometry
(BTPS, Ref: Hankinson/Polgar)

		REF	PRE-Rx Meas	PRE-Rx %REF	POST-Rx Meas	POST-Rx %Chg	90%C.I.
FEV1	Liters	2.50	** 0.77	** 31	** 1.45	88	0.49
FVC	Liters	3.10	** 1.93	** 62	2.58	34	0.60
FEV1/FVC	%	81	** 40		** 56		10
FEV6	Liters	3.00	** 1.87	** 63	2.53	35	0.58
FEV1/FEV6	%	83	** 41		** 57		9
FEF25-75%	L/sec	2.64	** 0.39	** 15	** 0.72	82	1.08
StdFEF25-75	L/sec	2.71	** 0.40	** 15	** 0.76	89	1.11
PEF	L/sec	6.21	** 1.49	** 24	** 3.24	117	1.50
FET100%	Sec		9.05		8.19	-9	
FVL ECode			000000		000000		



Antibiotics for Respiratory Tract Infections

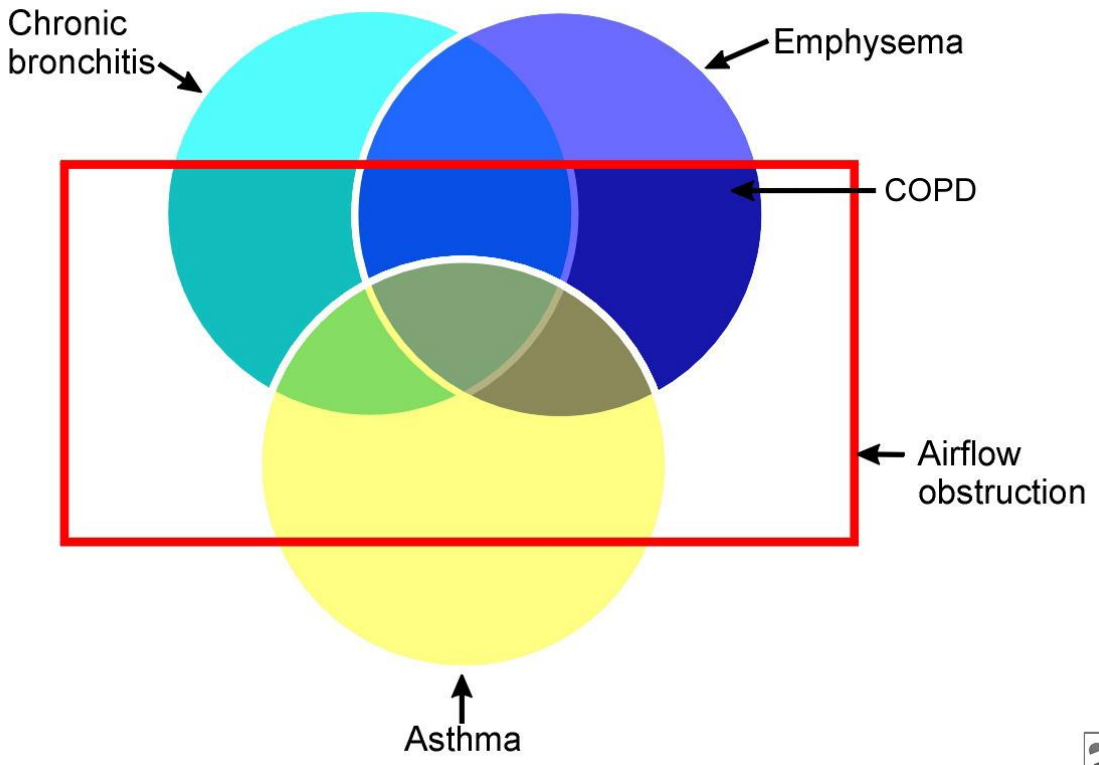
- NICE UK guideline 69 (2008) www.nice.org.uk
- Prescribing antibiotics for self-limiting RTIs in adults & children in primary care:
- > 3 months and acute otitis media/sore throat/pharyngitis/tonsillitis/ common cold/rhinosinusitis/cough/bronchitis:
- Assess, history, examination “if indicated’, address concerns and expectations - no or delayed prescribing strategy generally
- But consider immediate Rx: bilat otitis media & <2y, otorrhea, >=3 Centor tonsillitis criteria
- RTI Patients at risk of complications: systemically very unwell, serious illness, high risk of serious complications , >65y and 2+
- >80y and 1+ of : IP episode last y , diabetes, CHF, steroid Rx

Pharmaceutical options $$

- PHARMAC 2007- subsidy on Co. price
- Spiriva (1od) 70$ /30days
- Seretide 250/50 Accuhaler 49.69$ /30days
- Symbicort 200/6 (2bd) 60$ /30days
- Beclazone 250 (2bd) 22.67$ /50days
- Flixotide125 (2bd) 13.60$/ 30days
- Atrovent 20 (2qid) 16.20$ /25days
- Combivent (2qid) 12.19$ /25days
- Duolin Neb (1qid) 31.80$ /30days
- Salamol (2qid) 4.00$ /25days
- Nuelin SR 250 (1bd) 21.51$ /50days
- Prednisone 5 (1od) 0.66$ / 30days

Asthma new treatments

COPD Overlap- Phenotypes



TREATMENT OPTIONS FOR COPD