Time	Title of session
09.00 – 09.30	***Registration***
09.30 - 10.45	Overview of Day Occupational Asthma
10.45 – 11.35	Inhalation injuries
11.35 – 11.50	***Coffee***
11.50 - 12.50	COPD and other occupational airway diseases Workplace spirometry and surveillance
12.50 - 13.40	***Lunch***
13.40 – 14.40	Pneumoconioses Other occupational lung disease
14.40 - 15.30	Cases, pathologies, workplaces: bringing it all together

Occupational Asthma

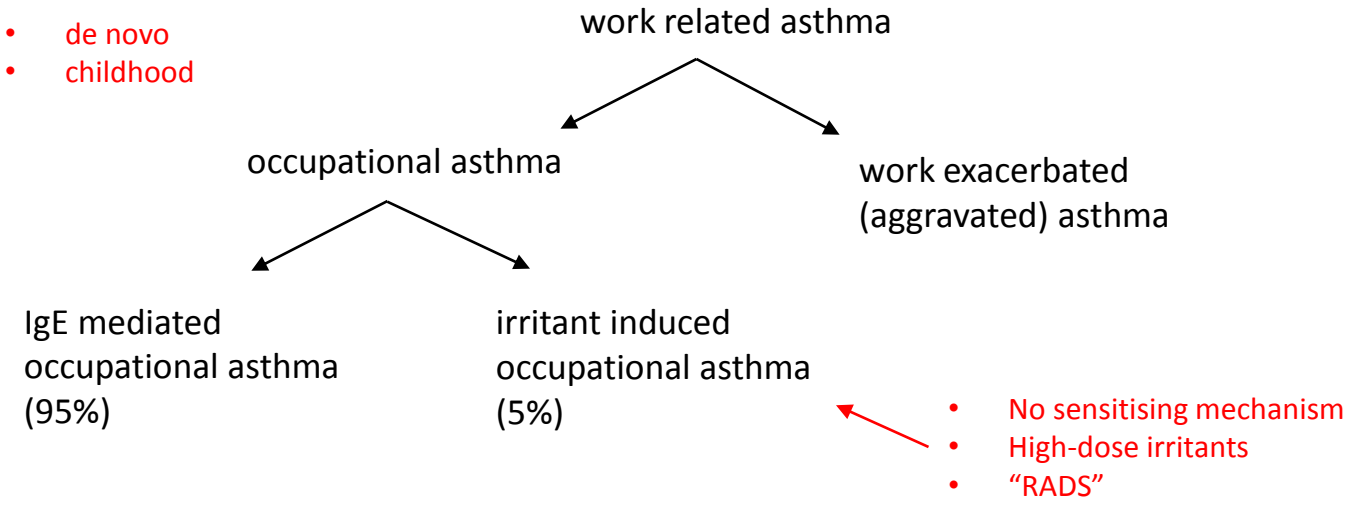
Jo S

Outline

- occupational asthma *vs* work-exacerbated asthma
- common causes of occupational asthma in UK
- risk factors
- recognition/diagnosis
- management
- outcomes
- compensation (IIDB)

Work and asthma terminology

> 4 million adults in UK receive treatment for asthma
c.10% of adult asthma is *attributable* to work



"Occupational asthma is asthma induced by inhalation of an agent in the workplace"

"Work exacerbated asthma is pre-existing asthma which is made worse by work"

Work and asthma terminology

asthma unrelated to work

- most common
- selection?

David Beckham has asthma, agent confirms

work-exacerbated asthma =
previous asthma, provoked at work

- not uncommon
- ‘irritants’

occupational asthma =
new asthma, induced at work

- sporadic
- sensitisation (95%)
- high-dose irritant (5%)

Reasons to be breathless: when is asthma occupational?

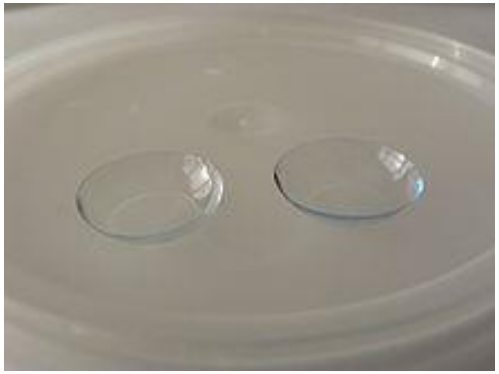
LUNGS AT WORK
www.lungsatwork.org.uk

Case: 45M

New diagnosis of adult onset asthma

Referred by OHP

Works in QC at a contact lens factory on the South Coast



LUNGS AT WORK

www.lungsatwork.org.uk

Employed since 2007 as a Technical Operative

Checking and monitoring the production of contact lenses within one of the factory areas

- supervise and monitor the technical operation of the machines (QC)
- desk based role at the end of the production line, which is arranged around his desk, within the factory
- overalls, gloves and a (FFP2) mask

Manufacture and Environment

- machine dispenses small does of pre-mixed liquid solution into wells for pressing
- product is checked then cured using UV light
- desk right next to UV light machine
- periodically replenish the liquid supply
- supplied in a sealed bottle –inserts into the machine (pierced internally)

Protection/Environment

- ingredients (unaware of integral components) have a “strong smell”
- episodes of acute self-limiting respiratory symptoms

Various narratives

Patient

“work is harming my health”
others affected

OHP

“ I am only aware of two other employees who work in a similar area with symptoms ... this is not a widespread problem.”
one known asthmatic., other work-related rhinitis under local hospital
“Neither of these employees work with sensitisers but do work with methacrylates”
no concerns about risk controls where he works having visited it, and checked the environmental monitoring results

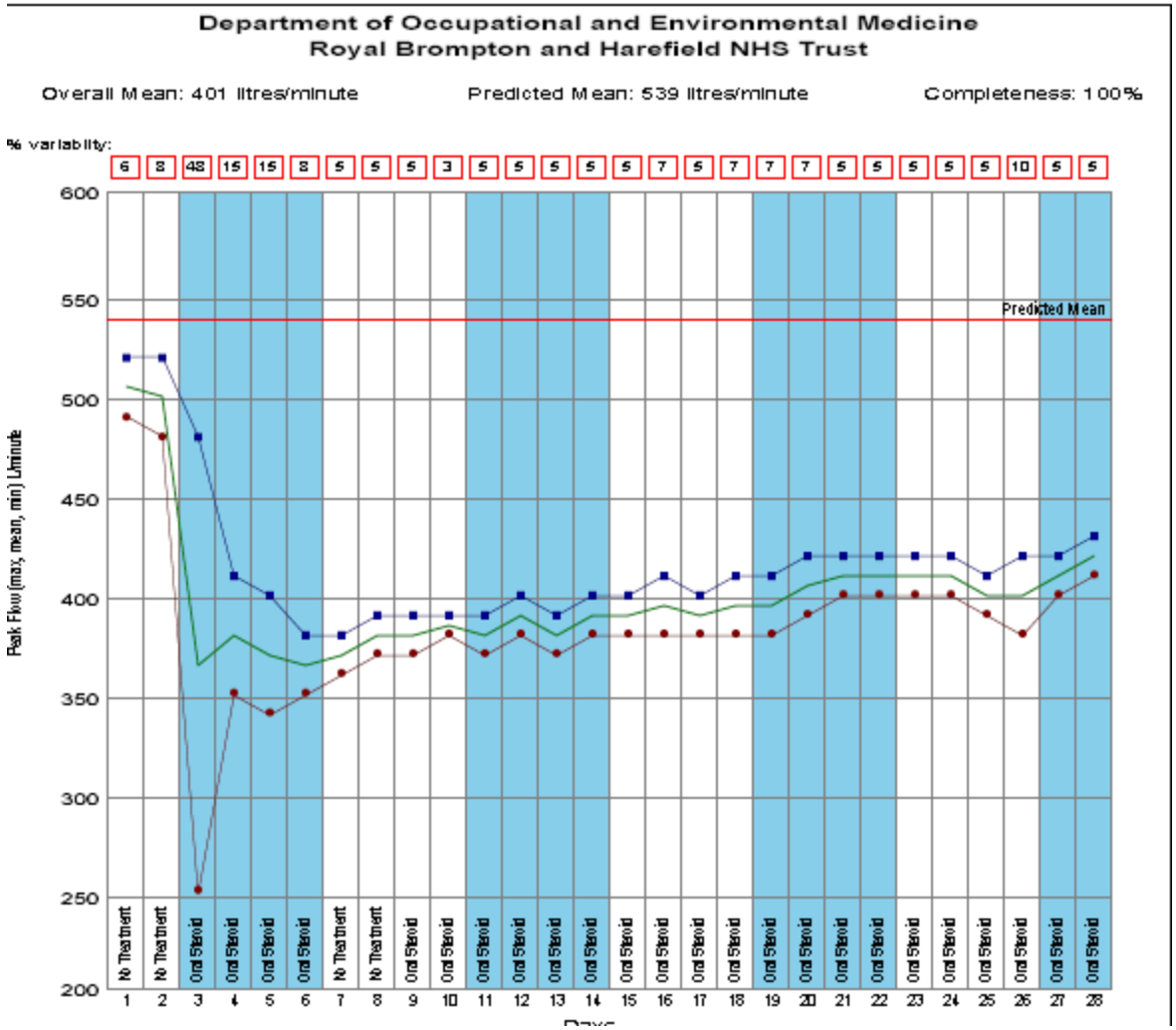
Respiratory Physician, Local Hospital

“oh yes I know that factory, I have seen a number of people who work there with respiratory (mainly airway) symptoms”

Workplace surveillance

Date	PEF	FEV/FVC
October 2008	498	59%
March 2009	630	68%
September 2009	636	61%
March 2011	506	54%
July 2011	577	58%
May 2013	334	44%
June 2013	337	47%
June 2014	424	48%

peak flows



LUNGS AT WORK
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material safety data sheet for lens ingredients...

COMFILCON A (47) PREMIX

Used in the manufacture of contact lenses.

R21: Harmful in contact with skin.

R36/37: Irritating to eyes and respiratory system.

R20/21/22: Harmful by inhalation, in contact with skin and if swallowed.

R43: May cause sensitisation by skin contact.

R36/37/38: Irritating to eyes, respiratory system and skin.

R37: Irritating to respiratory system.

R40: Limited evidence of a carcinogenic effect.

R41: Risk of serious damage to eyes.

R48/20: Harmful: danger of serious damage to health by prolonged exposure through inhalation.

Ingredients

Hazardous ingredients: N-VINYL-N-METHYLACETAMIDE 8.5-9.5%

EINECS: 221-698-5 CAS: 3195-78-6

[-] R10; [Xn] R21; [Xi] R36/37

- HYDROXYBUTYL METHACRYLATE 8.5-9.5%

  CAS: 29008-35-3

  [Xn] R20/21/22; [Sens.] R43

- POLYETHYLENE GLYCOL SUBSTITUTED POLYSILOXANYL MACROMER 39-40%

  CAS: 697234-74-5

  [Xi] R36/37/38

- POLYDIMETHYLSILOXANE METHACRYLATE DERIVATIVE 8.5-9.5%

  CAS: 697234-76-7

  [Xi] R36/37/38

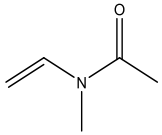
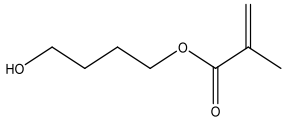
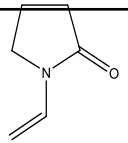
- 1-VINYL-2-PYRROLIDONE 26.5-28%

  EINECS: 201-800-4 CAS: 88-12-0

  [Xn] R20/21/22; [Xi] R37; [Xn] R40; [Xi] R41; [Xn] R48/20

Asthma Hazard Index (HI)

- Computer generated probability that a given compound is asthmagenic
- The computer uses a logistic regression equation to make a *quantitative* link between *structure* (molecular descriptors) and a*ctivity (*asthmagenic or not*)*
- The mathematical relationship is defined by the statistical comparison of molecular descriptors present in asthmagens vs controls

Chemical name	CAS	Structure	MW	HI (Jarvis et al 2005 model)	HI (Jarvis et al 2015 model)
N-Vinyl-N-Methylacetamide	3195-78-6		99	0.29	**0.37**
Hydroxybutyl methacrylate	29008-35-3		158	0.6	**1**
Polyethylene Glycol Substituted Polysiloxanyl Macromer	697234-74-5	Polymer	n/a	n/a	**n/a**
Polydimethylsiloxane methacrylate derivative	697234-76-7	Polymer	n/a	n/a	**n/a**
1-Vinyl-2-Pyrrolidone	88-12-0		111	0.32	**0.37**

Challenge test

- PC20 3.9mg/ml histamine (bronchial hyper-reactivity prior to challenge)

- No change from baseline occurred after control challenge

- Immediate fall in FEV_1 after challenge with 4 min of stirring Comfilcon solution
- Drop to 50% at 10 minutes post exposure
- Reproduced on the subsequent day, following 1 min exposure
- Drop to 26% at 15 mins post exposure
- No late response on either day

- PC20 fell steadily to 0.58mg/ml (increasing hyper-reactivity)
- Chest symptoms similar to work
- Audible expiratory wheeze on auscultation

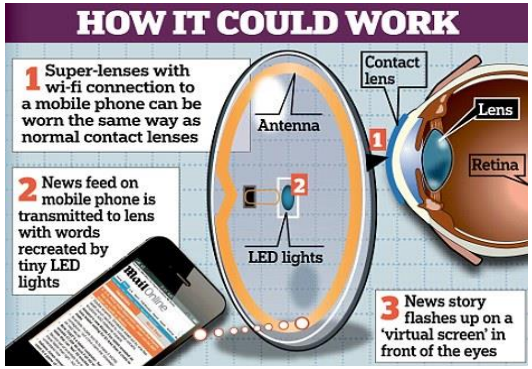
Patient input

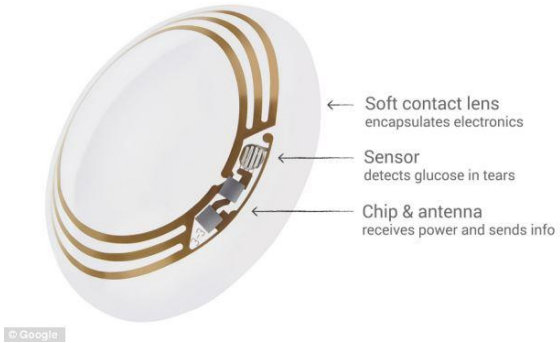
"health surveillance needs to be used efficiently and strategically to reduce or minimise possible incidences of occupational asthma" (Szram and Cullinan, via Google)

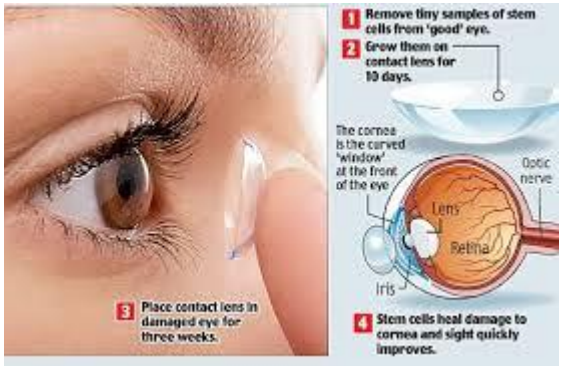
"this has great resonance in my case. I started on the agency and worked for about a year before becoming permanent. Agency workers were not included in the health surveillance programme. Hindsight is another wonderful thing and, had I had more of it 9 years ago, I would have asked questions as to why this did not happen. Many agency workers go on to permanent roles and a baseline figure for lung function testing could only be beneficial to all parties"
There were two years in which I did not get tested at all two occasions when I was tested twice in a year but this was only in response to my increasingly poor performance.
There was a clear downward trend. It may be that the drops were only small but I didn't notice a big decline in my heath until quite late in the day.

One of the questions I asked myself after seeing this graph was that it seemed pointless doing these tests if no discernable action was taken despite having increasingly poor results. It seems that the tests were only done to tick all the boxes with no material regard to the results themselves.

Life thru' a lens







Learning Points:

Chemicals are challenging

Beware acrylates

Think about surveillance

LUNGS AT WORK
www.lungsatwork.org.uk

Case 2: 29 M, supermarket scratch baker

2 yrs in a local bakery as apprentice after leaving school

8 yrs on supermarket shop floor

2 yrs ago started work as baker in his supermarket

Known cat allergy, mild hay fever

Asthma since age 5; uses blue inhaler every day

Never smoked

No previous work-related symptoms

On return to bakery:

- Breathing and fitness levels deteriorated
- Chest tightness in freezer
- Sore dry nose, sneezing
- Improves during second consecutive day at work
- No heat sealer at work

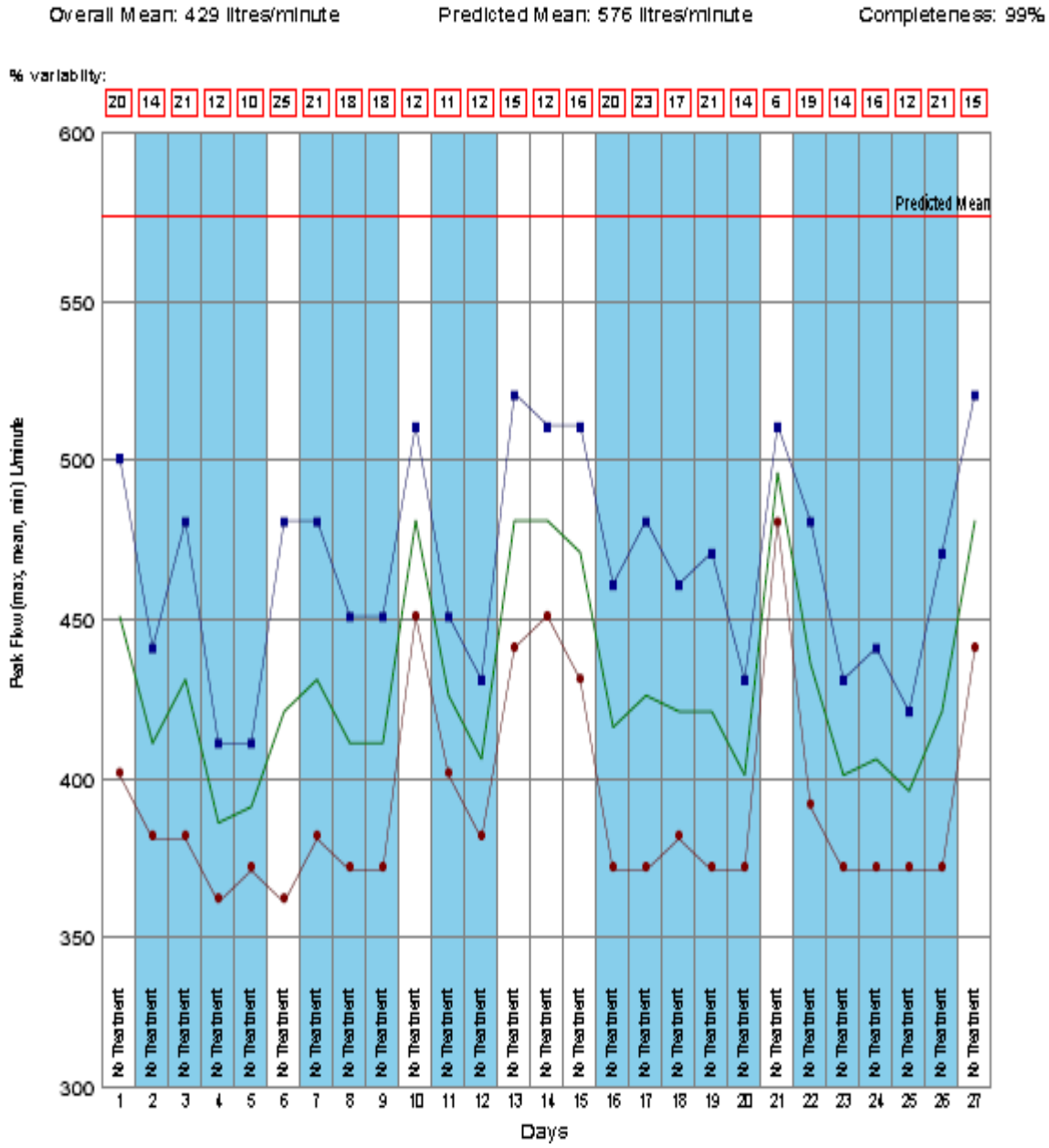
Immunology:

Skin prick tests:

- Positive to grass pollen, cat, house dust mite (='atopic')
- Negative to **flour** and to **alpha amylase**

Serum specific IgE:

- Negative to both **flour** and **alpha amylase**



- every 2-3 hours
- 4 weeks
- at work and days off
- best of 3 blows
- recorded manually

Case 2: Diagnosis of work exacerbated asthma

Asthma exacerbated by work (irritant) *(immunology negative)*

Asthma medication improved – started Symbicort

OH review with a view to reducing exposures

GP follow-up

Ineligible for Industrial Injuries Disablement Benefit

Occupational asthma or work-exacerbated asthma: some pointers

Occupational asthma or work-exacerbated asthma: some pointers

	Occupational asthma	Work-exacerbated asthma
latency (minimum)	yes (6-24 months)	no
latency (maximum)	yes	no
work - relationship	no clear differences	
eye/nose symptoms	yes (HMW)	no clear relationship
continued exposure	worsens prognosis	doesn't affect prognosis
treatment	useless	effective
RPE	often useless	effective
cure?	yes (but …)	no
legal?	yes	no
relocation	yes, major employment disruption	generally no
compensation	yes	no

Most occupational asthma arises from specific sensitisation

An agent at work is:

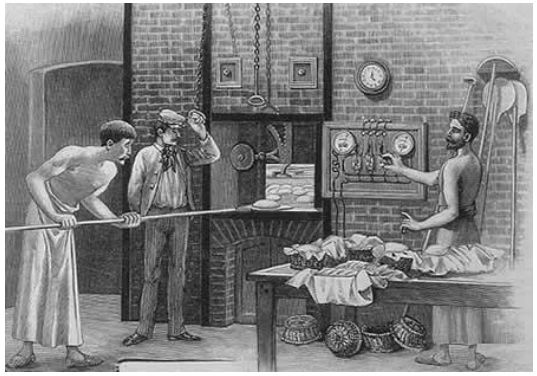
- *known* to be a respiratory sensitiser (n≈?)
- known *not* to be a respiratory sensitiser
- *not known not* to be respiratory sensitiser (tricky!)

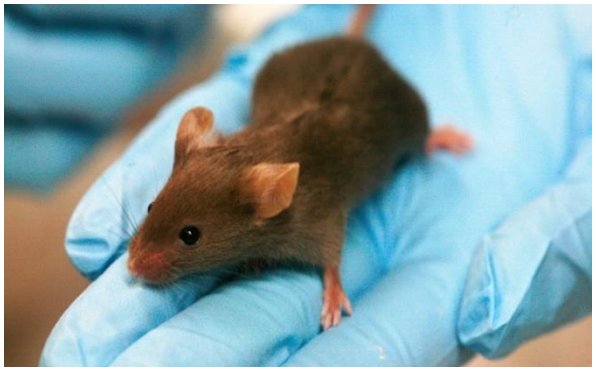
All airborne proteins are potentially sensitising agents

Many chemicals with powerful odours are NOT sensitisers

- Solvents
- Thinners
- Perfumes
- Chlorine

Be very wary of diagnosing 'occupational asthma' in anyone who is not working with a recognised respiratory sensitising agent






SAFEWAY
CYCLON
Advance
novon
Twin Tub
Logic
tablets
Washing Powder
BIOLOGICAL


SCIENCEphotoLIBRARY

Respiratory sensitising agents: high and low molecular mass

 - whole allergens

 +  - hapten-protein conjugates

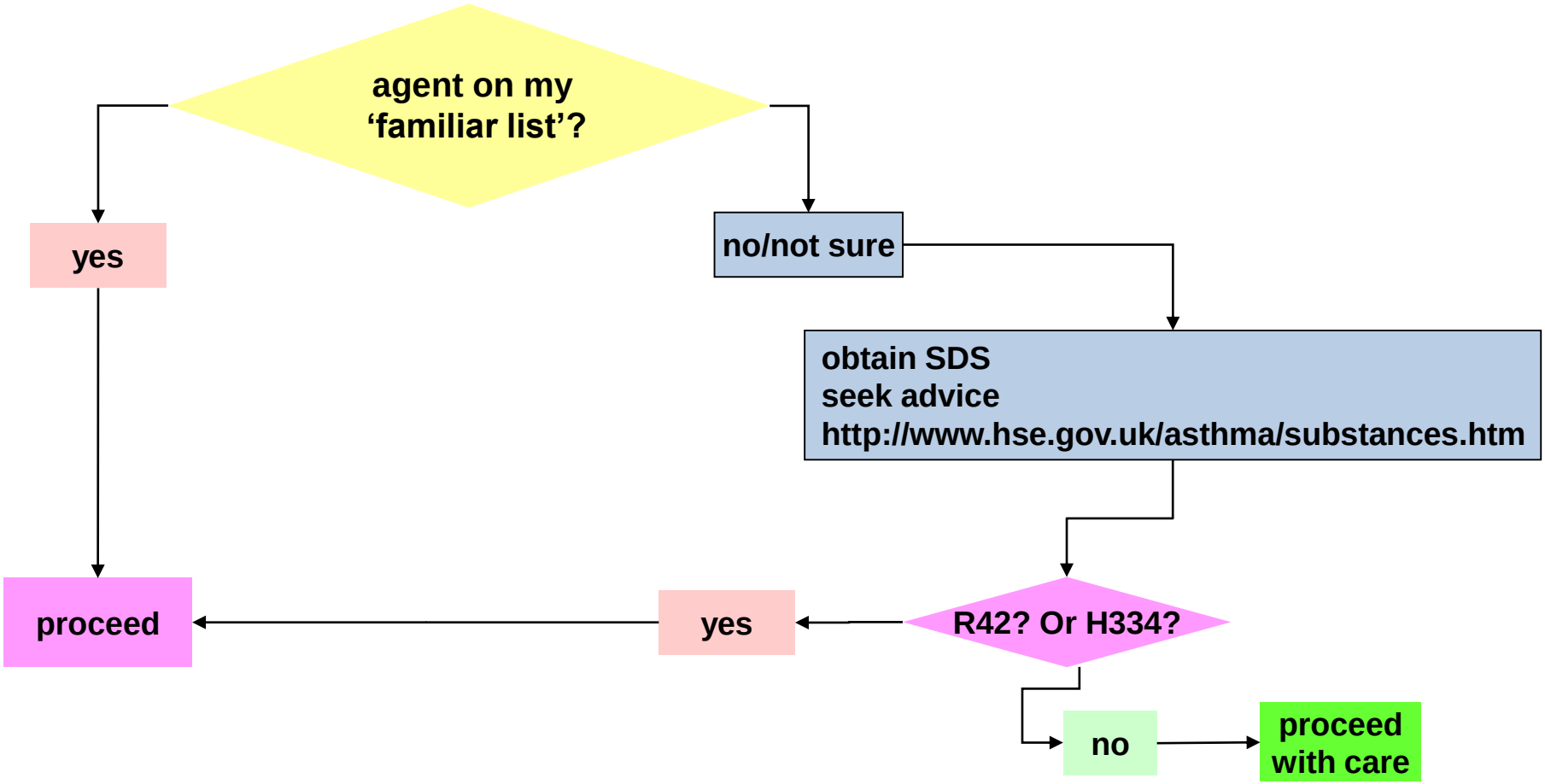
occupation	exposure(s)
baking	flour(s) alpha amylase ('improver') egg
animal work	small mammals: rat and mouse urinary proteins large mammals insects latex
food processing	seafood tea/coffee eggs flour *etc*
detergent manufacture	enzymes
health care (non-NHS)	latex

occupation	exposure(s)
spray painting	hexamethylene diisocyanate
foam manufacture	toluene diisocyanate methylene diphenyldiisocyanate
electronic engineering	colophony fume cyanoacrylate persulphate salts
woodwork	tropical wood dusts
hairdressing	persulphate salts
dentistry orthopaedics	methacrylates latex
textile printing	'reactive' dyes
precious metal refining	platinum salts

***all* have nasal sx …**
***all* induce a specific IgE response**
atopy increases risk

***some* have nasal sx …**
and *some* induce a specific IgE response

Is your patient working with a respiratory sensitising agent?



Making the diagnosis (or otherwise)

- ✓ suggestive history of work-related symptoms
- ✓ exposed to respiratory sensitiser

Are your symptoms better:
- *on days away from work*
- *on holiday*

<u>establishment of 'sensitisation'</u>

- generally for HMM ('protein') antigens
  - specific IgE *vs* SPT
  - 100% sensitive (SnNout)
  - all relevant allergens
  - experienced laboratory
- for LMM antigens seek advice (QSAR)

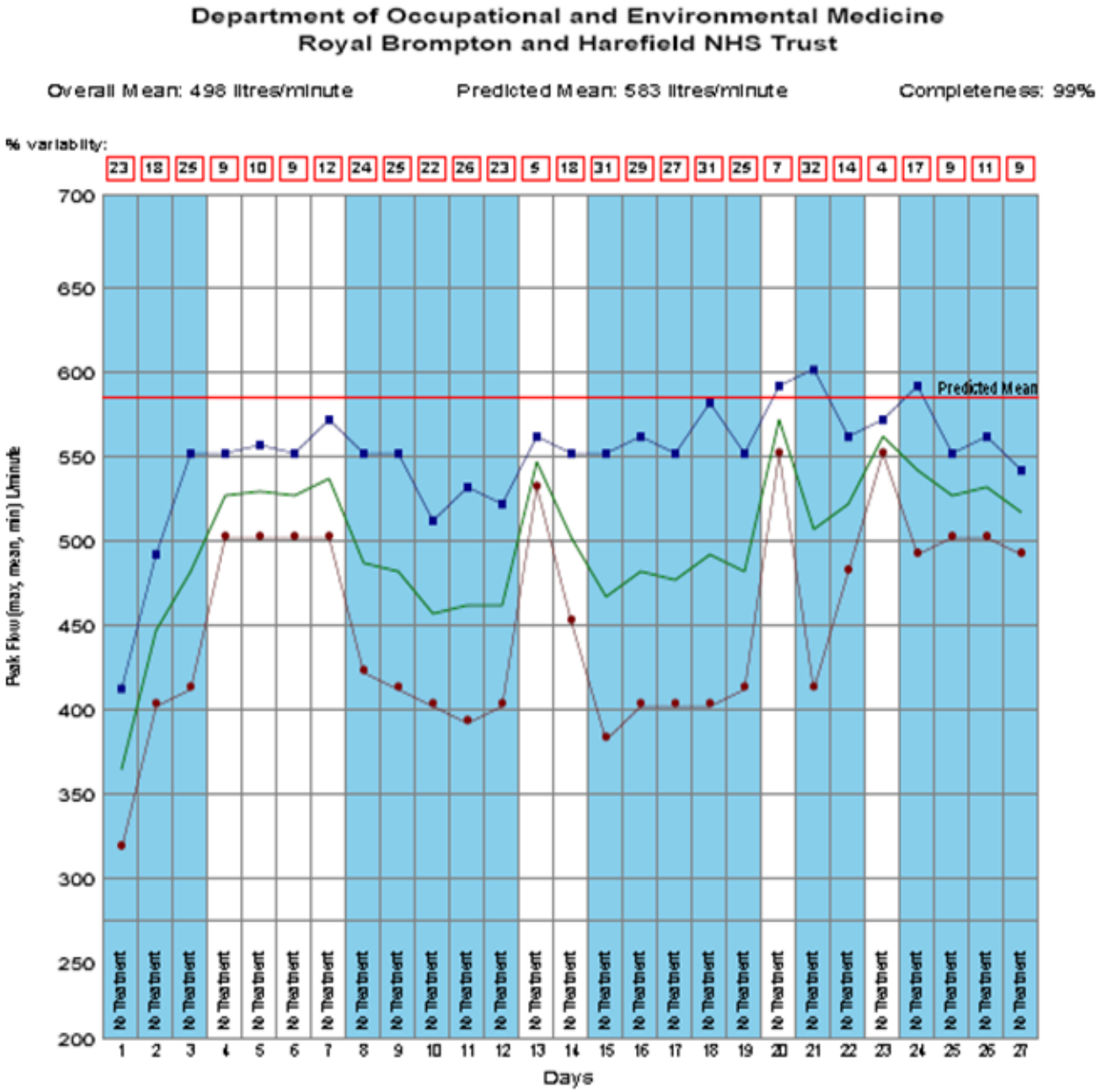
<u>establishment of 'asthma'</u>

- standard techniques

<u>establishment of physiological exposure-relationship</u>

- serial PEF (work and home)
- controlled provocation (inpatient)

A positive work related peak flow record (OA)



Work day

Day off

- every 2-3 hours
- 4 weeks
- at work and days off
- best of 3 blows
- recorded manually

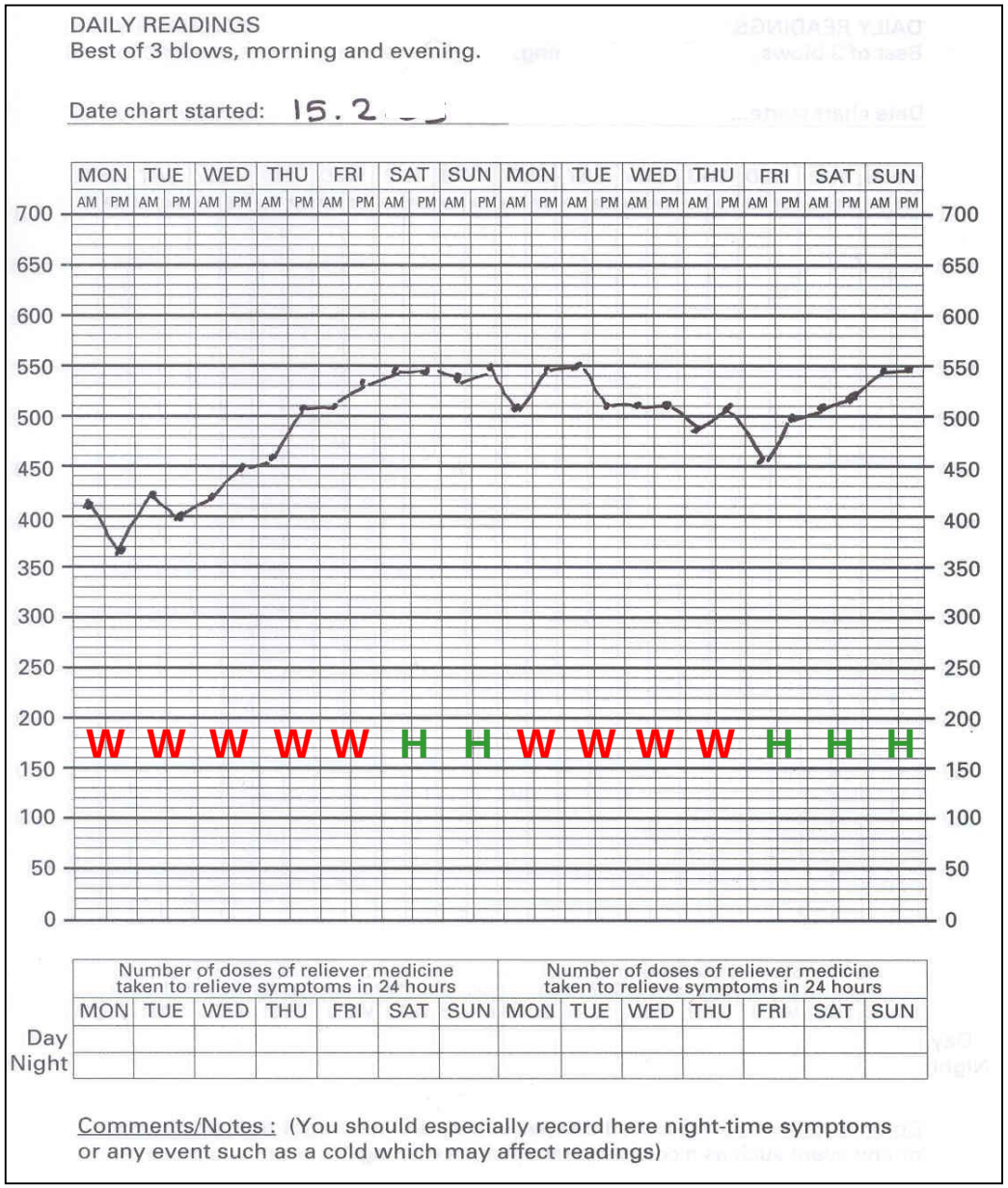
Best peak flow

Mean of all readings that day

Lowest peak flow

c.sensitivity 75%, specificity 79%

Serial measurement of peak flow



Specific inhalation testing (controlled provocation)

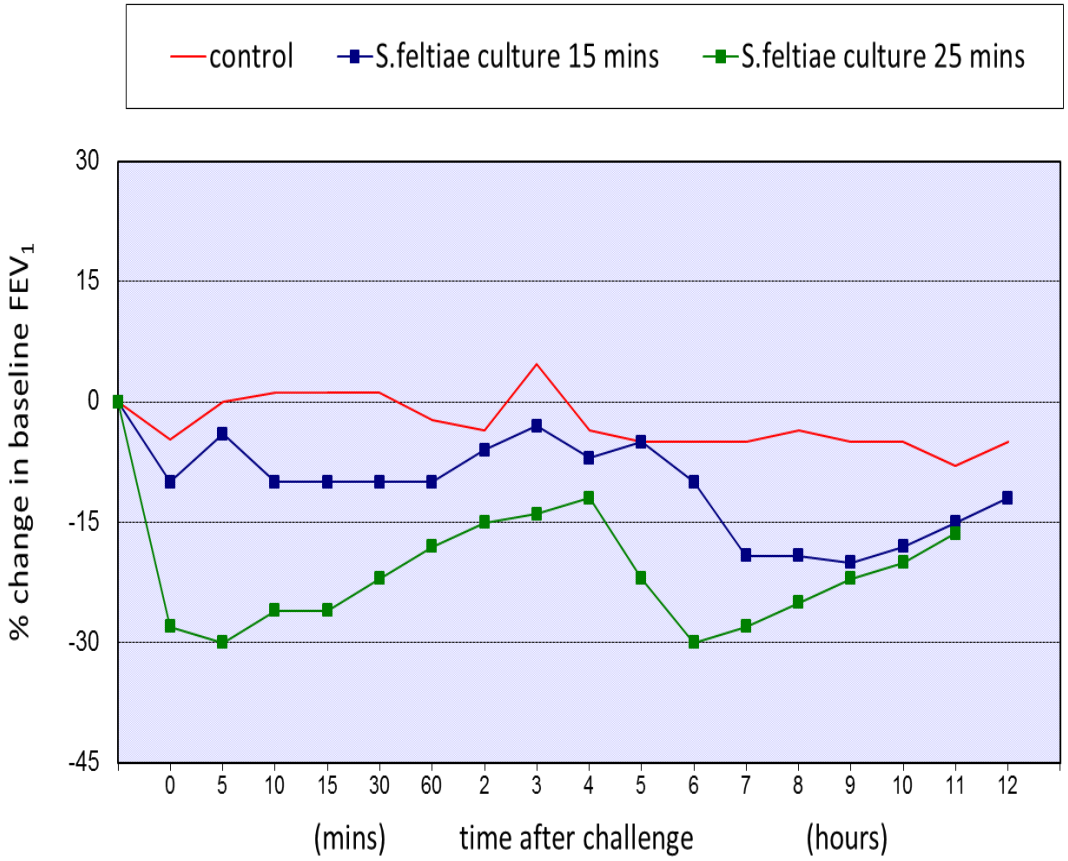
- when you need a diagnosis
- where all else fails
- new or specific agents
- not for legal reasons
- specialist++ (3 centres in the UK)

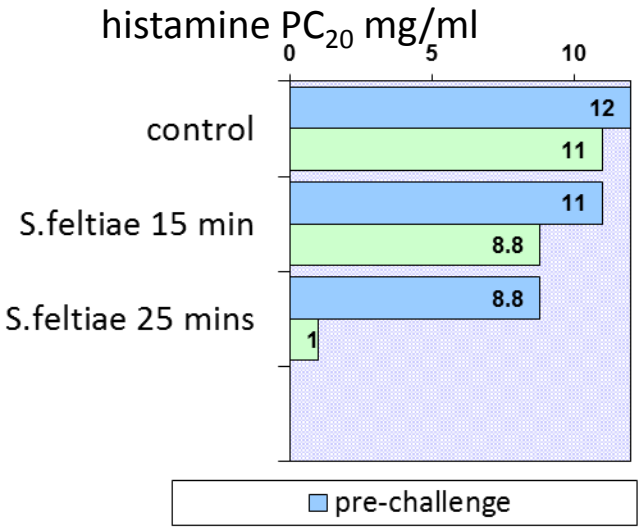
- single blind challenge series
- exposure chamber
- exposed: 15 - 25 minutes - separate days
- monitored symptoms, FEV_1 and PC_{20}


KleenGuard
A25


Sundström

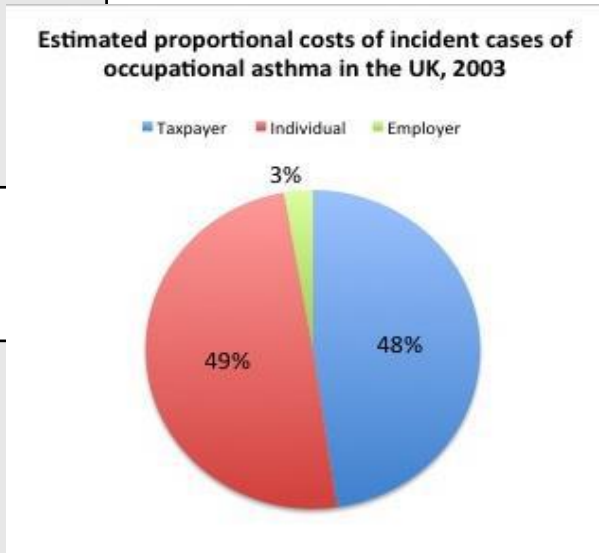
FEV1; histamine responsiveness, baseline FEV_1





Managing a case

immediate	• continuing exposure causes continuing symptoms • continuing exposure causes worse symptoms/lung fn decline • protective equipment rarely satisfactory • medical treatment usually unhelpful
mid-term	• most patients improve after exposure ceases • specific IgE antibodies fall after exposure ceases • improvement plateaus at 2 years?
socio-economic	• avoidance of exposure requires 'relocation' • re-employment more difficult (1/3 unemployed up to 6y later) • earnings often lower • dependent on occupational mobility • eligible for Industrial Injuries Disablement Benefit



c.£125,000/new case

Ayres et al., 2011

SIGN guidelines: Chapter 13 Occupational Asthma

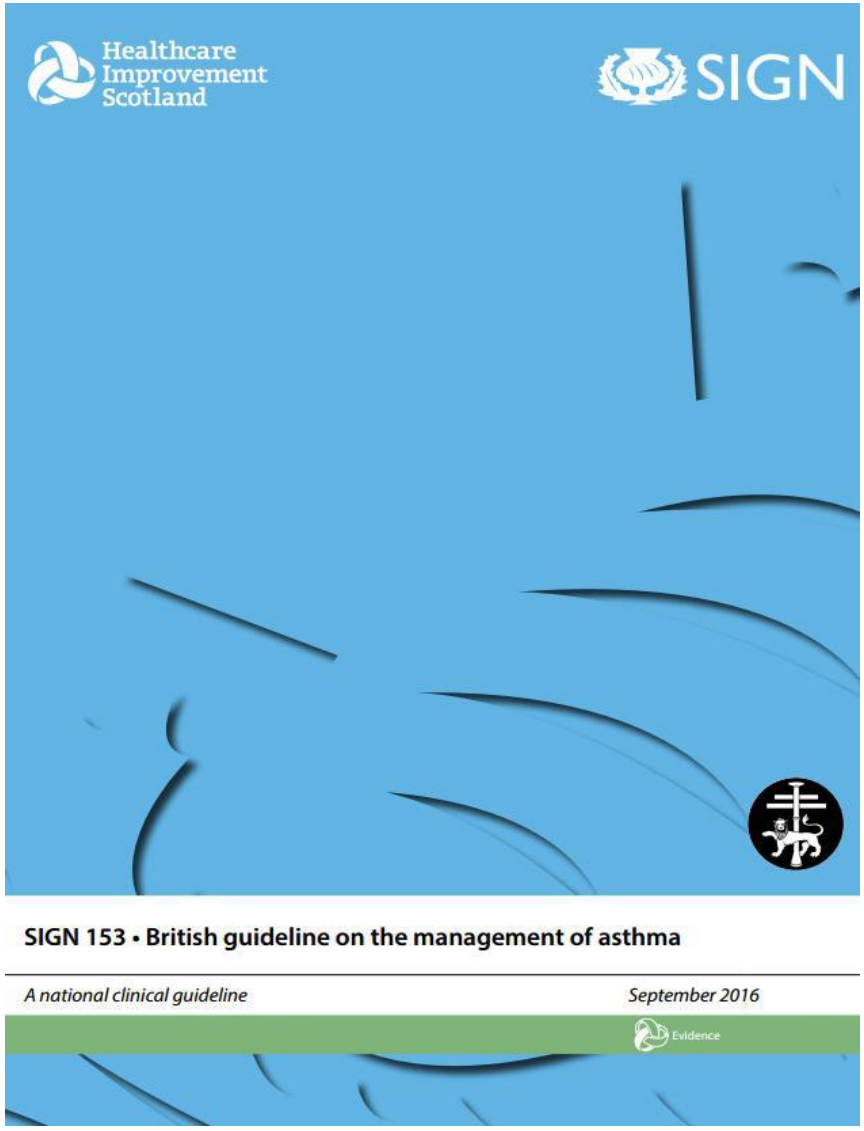
Consider occupational cause in all pts with new or reactivated asthma

Are your symptoms better:

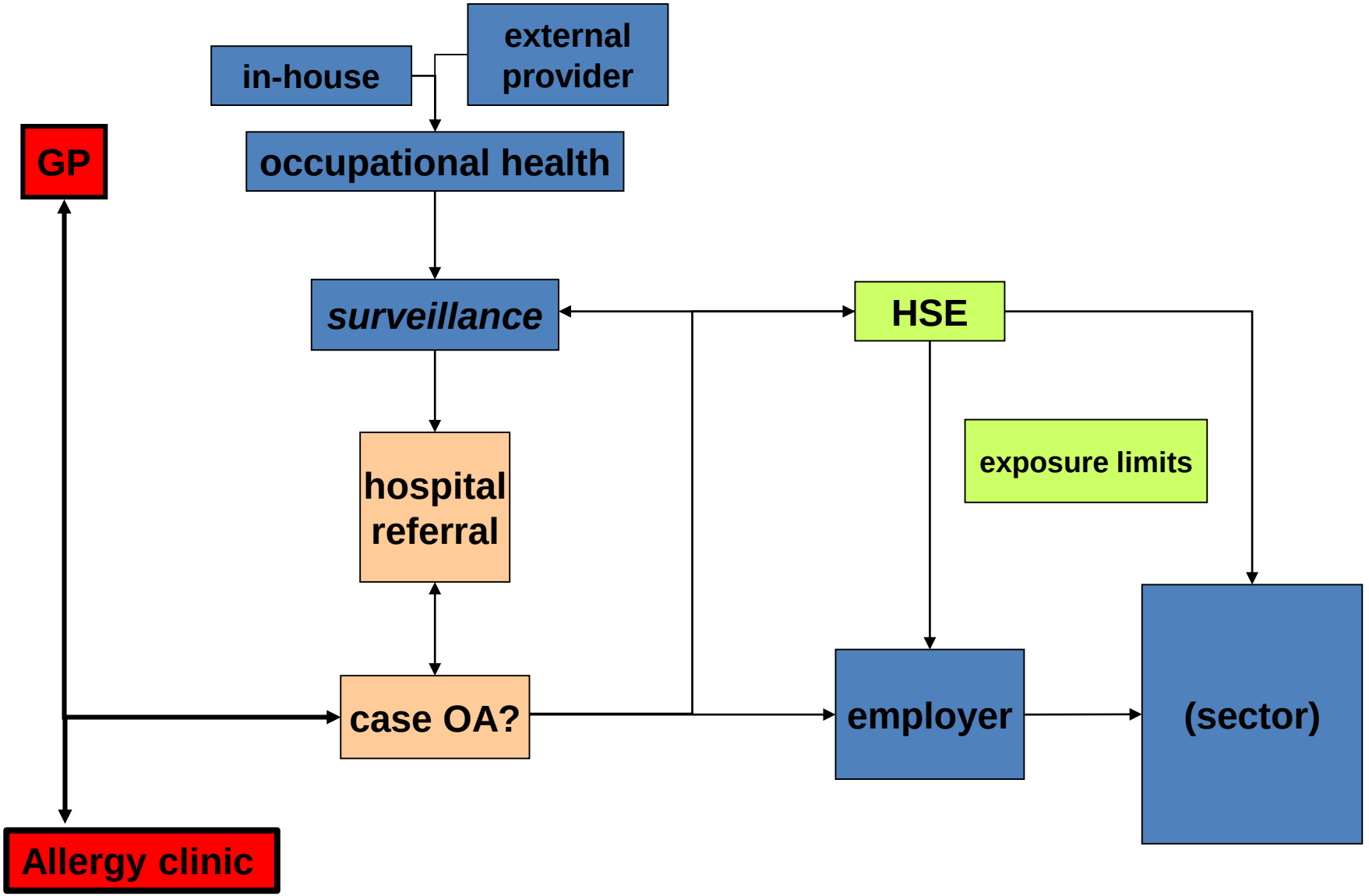
- on days away from work
- on holiday

If yes, should be investigated for OA

Positively seek OA in those with high risk occupations



Locating your patient

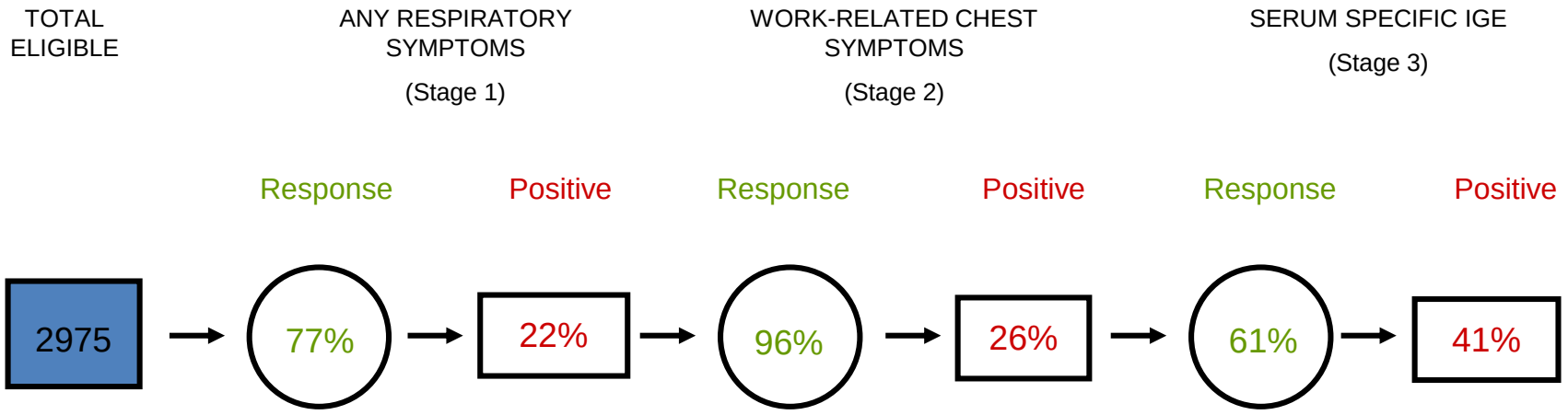


Surveillance for OA in the workplace: immunology

Platinum refining	Detergent manufacture	Baking industry	Animal research
SPT	**SPT/IgE**	**IgE**	**IgE**
high residual risk	moderate residual risk but - past epidemics	high residual risk	high residual risk
• everybody • annually	• everybody • annually	• selectively • annually	• at pre-employment
individual case recognition	individual case recognition and adjunct to exposure control	Enhanced specificity of reported symptoms	Identification of source of sensitisation (“baseline”)

Surveillance; focus on case identification rather than prevention

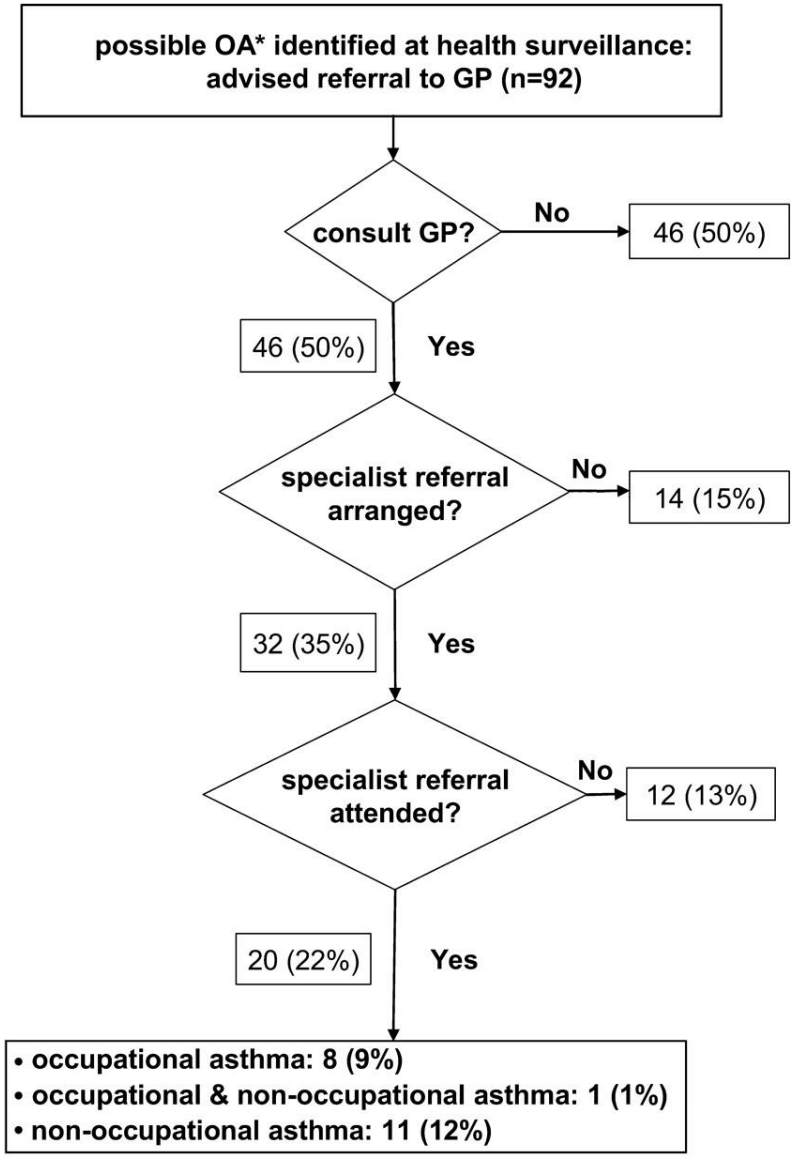
surveillance



survey

Response	93%		100%	90%	
Positive		64%	26%		32%

Surveillance; dealing with “failures”



*OA = occupational asthma

Mackie J Occup Med (Lond) 2008;58:551-555

Summary: how do I spot the case of occupational asthma in my clinic?

new, recurrent or deteriorating asthma in an employed person
eye/nasal symptoms "constant cold" "hay fever all year round"
keep having "chest infections"

Ask what they do for a job
Ask about association with work

Consider

- latency
- ocular and nasal symptoms
- days away from work (holidays)
- other exacerbating factors

Pitfalls include:

- confusing 'occupational' and 'work-exacerbated' asthma
- not identifying the responsible agent (relocation? sometimes not important (antigen mix))
- attributing cause to an agent not recognised to be a sensitiser
- removing people from work too quickly

Take a history; immunology; peak flow records; (specific inhalation challenges)

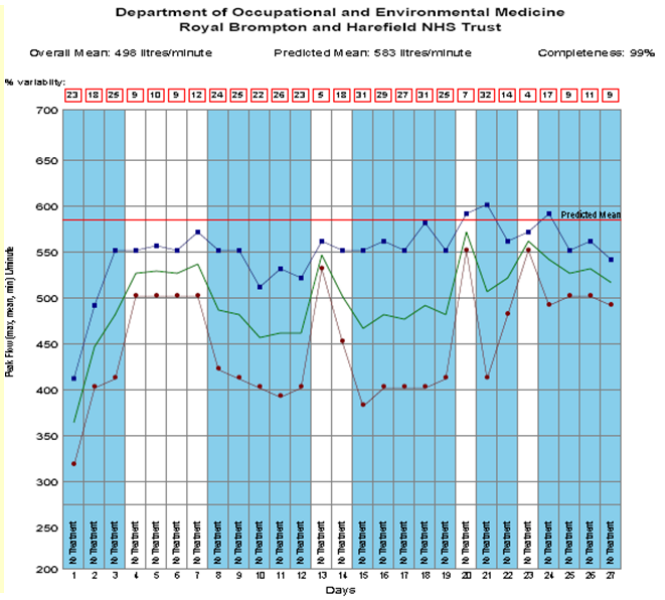
Ask for help!

Question 1

LUNGS AT WORK
www.lungsatwork.org.uk

26 year old man, history of childhood asthma – remission age 12
works for a small-scale craft baker
two chest infections in Spring; since then wheeze and chest tightness at work

skin prick tests positive to grass pollen
And wheat flour
lung function normal, no reversibility
peak flow chart:



The most likely diagnosis is:

a. **recurrence of childhood asthma**
b. **occupational asthma**
c. **post-infective bronchial hyper-reactivity**
d. **work-exacerbated asthma**
e. **seasonal asthma**

Correct answer: b. occupational asthma

What is the minimum frequency and period of serial peak flow measurement that provides the highest diagnostic value in the assessment of OA?

a) at least six times a day over six weeks
b) at least five times a day for one week
c) at least four times a day for three weeks
d) at least twice a day for four weeks
e) whatever you can persuade your patient to do

Correct answer: c. at least four times a day for three weeks

For which of the following causes of occupational asthma are there useful tests for immunological sensitisation?

a. colophony

b. iroko

c. persulphate salts

d. methylmethacrylate

e. none of the above

Correct answer: e. none of the above

Specific Inhalation challenges for OA are:

a. time consuming and not required for diagnosis in most cases
b. typically carried out in workplace settings
c. mandated in industrial injury benefit claims
d. always carried out by lung function technicians in a plethysmograph
e. commonly used to assess personal injury claims

Correct answer: a

Doctor doctor, was it my job that made me ill (is making me ill)?

- are you acting in a clinical capacity …
- … or a medico-legal capacity?

- be careful; remember anything you write may be used in ways you didn't expect
- (note GMC guidance re. letters relating to employment)

- be very wary about advising your patient to stop work

"Dear Paul

I think this is the third time you have written to me asking for more information about this man. I am afraid we do not have anything further than what I have already sent you. On the basis of those tests we thought it would be <u>prudent</u> if the patient were to avoid any further exposures at work.

If I had known what problems this would cause …."

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If I had known what problems this would cause …."

- if you are acting in a clinical capacity, you are allowed to say 'I don't know'

RIDDOR - Reporting of Injuries, Diseases and Dangerous Occurrences Regulations 2013

RIDDOR puts duties on employers, the self-employed and people in control of work premises (the Responsible Person) to report certain serious workplace accidents, occupational diseases and specified dangerous occurrences (near misses).

Incidents that happen in Northern Ireland should be reported to HSE NI.

How to control risks at work

Health and safety toolbox

Compensation

Industrial Injuries Disablement Benefit

- statutory list of 'prescribed diseases'
- 'no fault'
- not for self-employed
- DIY
- 14% threshold (NB pneumoconiosis 1%)
- ≥ c.£35 per week

and/or

Civil claim against employer

- through a lawyer (Union)
- 'personal injury'
- (any) disease *and* negligence
- statute of limitations

- asbestos-related diseases: Asbestos Victims Support Group

Prescribed respiratory diseases (IIDB)

B6	Extrinsic allergic alveolitis	D6	Nasal adenocarcinoma (wood, leather)
C4	Primary lung cancer (arsenic)	D7	Occupational asthma
C17	Chronic beryllium disease	D8	Primary lung cancer asbestos: - with asbestosis and/or - high exposure
C18	Emphysema (cadmium)	D9	Diffuse pleural thickening
D1	Pneumoconiosis	D10	Primary lung cancer (tin, some chemicals, coke oven)
D2	Byssinosis	D11	Primary lung cancer with silicosis
D3	Mesothelioma	D12	COPD (coal mine dust)
D4	Allergic rhinitis		

Compensation

Industrial Injuries Disablement Benefit
- statutory list of 'prescribed diseases'
- 'no fault'
- not for self-employed
- DIY
- 14% threshold (NB pneumoconiosis)
- ≥ c.£35 per week

and/or

Civil claim against employer
- through a lawyer (Union)
- 'personal injury'
- (any) disease *and* negligence
- statute of limitations

- asbestos-related diseases: Asbestos Victims Support Group

Reporting to understand prevalence of occupational disease: SWORD

http://research.bmh.manchester.ac.uk/epidemiology/COEH/research/thor/schemes/sword/

Surveillance of work-related and occupational respiratory disease (SWORD)

The scheme aims to determine the scale and patterns of work-related respiratory disease in the UK and to identify the agents thought to be responsible along with information on industry and occupation. Ongoing since 1988, the scheme has been funded by the Health and Safety Executive with the support of the British Thoracic Society and the Society of Occupational Medicine. Funding to continue data collection for this work runs to the end of 2017.

Approximately 418 respiratory physicians throughout the UK participate in reporting occupational respiratory disease. Twenty one of these are 'core' reporters who report every month; the remainder are sample reporters who are sampled at random and report for one month only each year.

For further details, see: Map showing distribution of SWORD reporters

The types of respiratory diseases reported include:

- Occupational asthma
- Benign and malignant pleural disease
- Mesothelioma
- Lung cancer
- Pneumoconiosis

Some resources

Guidelines:
www.bohrf.org

Specialist sites:
- www.occupationalasthma.com (Birmingham: general)
- www.remcomp.fr/asmanet/asmapro/asmawork.htm (Quebec: general)

Review articles:
- Feary J, Cullinan P. Occupational Asthma BMJ 2016 *353:i2658*
- Vandenplas O, Suojalehto H, Cullinan P. Diagnosing occupational asthma. Clin Exp Allergy. 2017;47(1):6-18
- Tarlo SM, Lemiere C. Occupational asthma. N Engl J Med. 2014;370(7):640-9

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