CHEST® Congress 2019 | Thailand Bangkok | 10-12 April

Practical Pulmonary Physiology (Part 1)

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Saskatoon, SK, CANADA

University of Saskatchewan

By the end of this presentation …

- Understand practical standards for the **conduct and interpretation of methacholine challenge testing**
- Appreciate the real-world utility, and limitations, of **6-minute walk testing** in the clinical setting
- Recognize **less common pulmonary function test results** that are often misdiagnosed, or delayed in correctly diagnosed

Conflict of Interest Disclosure

Consultancy

Alberta Lung Association, AstraZeneca, Boehringer-Ingelheim, Canadian Foundation for Healthcare Improvement, Chinese Committee of Health and Family Planning, GlaxoSmithKline, Health Canada, Lung Association of Saskatchewan, Mylan, Novartis, Saskatchewan Ministry of Health, Saskatchewan Health Authority, Yukon Health and Social Services

Research Funding (managed by University of Saskatchewan)

AstraZeneca, Boehringer Ingelheim, Canada Health Infoway, Canadian Institute of Health Research, GlaxoSmithKline, Lung Association of Saskatchewan, Lung Health Institute of Canada, Novartis, Sanofi, Saskatchewan Health Research Foundation, Schering-Plough

Employee

University of Saskatchewan

Case #1

60-yr-old male, normal pulmonary function, treated empirically with ICS/LABA combination and albuterol prn, is being investigated for possible asthma. After withholding inhaled medication the morning of testing, he undergoes a methacholine challenge test:

Methacholine	FEV_1 [L]	% Change
Baseline	3.36	---
0.25 mg/mL	3.46	+ 3.0%
1.0 mg/mL	3.33	- 1.0%
4.0 mg/mL	3.25	- 3.2%
16.0 mg/mL	3.28	-2.5%
After Albuterol	3.49	+ 4.0%
	PC_{20} > 32 mg/mL	

Based on the information provided, what is the next most appropriate step in management?

a. Increase the dose of ICS/LABA

b. Repeat the methacholine challenge test

c. Augment therapy with an LTRA

d. Cardiopulmonary exercise testing

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MCT - Medication Withholding Times*

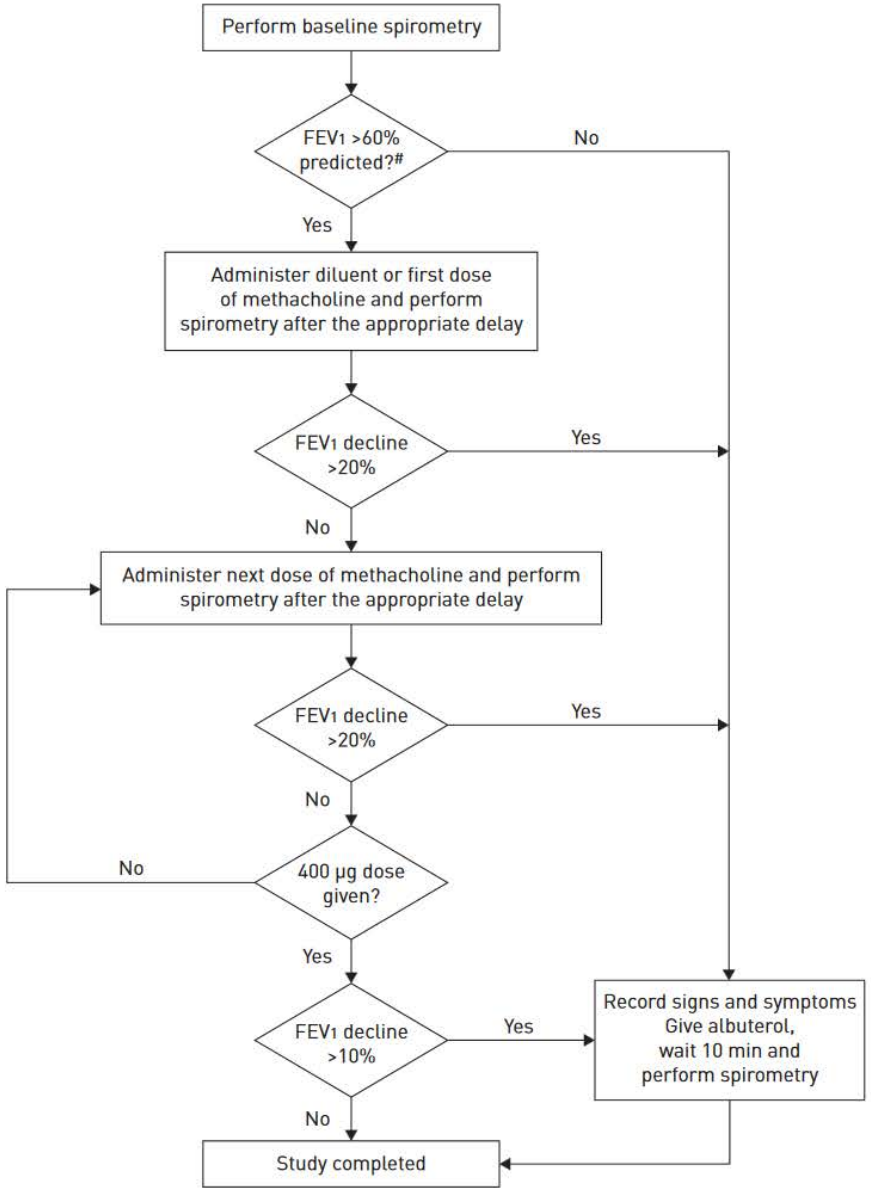
Medication	Minimum time interval from last dose to MCT h	Reference(s)
Short-acting β-agonists in conventional inhaled doses (*e.g.* albuterol 200 μg)	6	[21, 22]
Long-acting β-agonists (*e.g.* salmeterol)	36	[23, 24]
Ultra-long-acting β-agonists (*e.g.* indacaterol, vilanterol, olodaterol)	48	[25]
Ipratropium (Atrovent 40 μg)	12	[26–28]
Long-acting anti-muscarinic agents	⩾168	[29, 30]
Oral theophylline	12–24	[3]

* Inhaled corticosteroids and leukotriene modifiers have little or no effect in single dose, and do not need to be withheld unless the intent is to offload an anti-inflammatory effect – if yes, the duration of effect after regular use is uncertain, but a withhold time of 4–8 weeks is suggested.

Coates AL, et al. ERS Technical Standards – MCT. *Eur Resp J* 2017; 49:1601526

Methacholine Challenge Test repeated [after appropriately withholding medications]

Methacholine	FEV_1 [L]	% Change
Baseline	3.36	---
0.25 mg/mL	3.22	- 4.0%
1.0 mg/mL	3.00	- 10.7%
4.0 mg/mL	2.54	- 24.5%
Following Albuterol	3.44	+ 2.3%
	PC_{20} = 3.3 mg/mL	



MCT Testing Sequence

- **FEV_1 <1.5 L in adults is an additional contraindication**
- Perform post-diluent spirometry at 30 and 90 secs after the nebulization is completed - obtain an acceptable quality FEV_1 and FVC
  - this may require repeated attempts
- Calculate a **target FEV_1 that indicates a 20% fall in FEV_1 (baseline FEV_1×0.8)** using the post-diluent data value

Coates AL, et al. ERS Technical Standards – MCT. *Eur Resp J* 2017; 49:1601526

MCT – Categorization of Response

PD_{20} µmol (µg)	PC_{20} mg·mL^{-1}	Interpretation
>2 (>400)	>16	Normal
0.5–2.0 (100–400)	4–16	Borderline AHR
0.13–0.5 (25–100)	1–4	Mild AHR
0.03–0.13 (6–25)	0.25–1	Moderate AHR
<0.03 (<6)	<0.25	Marked AHR

Note: PD_{20} vs PC_{20}. **MCT testing is more useful in excluding a diagnosis of asthma** than establishing one because its –ve predictive value, when symptoms are present, is greater than its +ve predictive value. The probability that a +ve MCT reflects asthma will increase the **lower the PC_{20}** , the **higher the pre-test probability of asthma** and the **more closely the methacholine-induced symptoms mimic the naturally occurring symptoms**.

Coates AL, et al. ERS Technical Standards – MCT. *Eur Resp J* 2017; 49:1601526

Case #2

59-yr-old female performed a 6MWT for functional assessment in the setting of COPD [FEV_1 0.58L, 24% predicted]. Results are:

	Baseline Rest	End of Test
Heart Rate (/min)	97	112
Blood Pressure (mm/Hg)	120/78	142/77
SpO_2 (%)	97	96
Dyspnea (modified Borg)	1	8
Leg Fatigue (modified Borg)	0	3
Reason for Stopping		Breathing
Distance (m)		**150**
Was test d/c^{ed} prior to 6 mins?	No	
Was supplemental O_2 used?	No	
Total number of rest stops	6	

The patient's management was optimized, and she underwent a 2nd repeat 6MWT 3 months later. The results are:

	1st Test	2nd Test
Heart Rate (/min)	112	114
Blood Pressure (mm/Hg)	142/77	135/82
SpO_2 (%)	96	95
Dyspnea (modified Borg)	8	8
Leg Fatigue (modified Borg)	3	2
Reason for Stopping	Breathing	Breathing
Distance (m)	**150**	**188**
Was test d/c^{ed} prior to 6 mins?	No	No
Was supplemental O_2 used?	No	No
Total number of rest stops	6	3

Is the difference in walking distance between the 2 tests clinically important?

a. Yes
b. No
c. Can not determine from the information provided
d. Really can't say - I don't use the 6MWT very much in my clinical practice

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a. Yes

b. No

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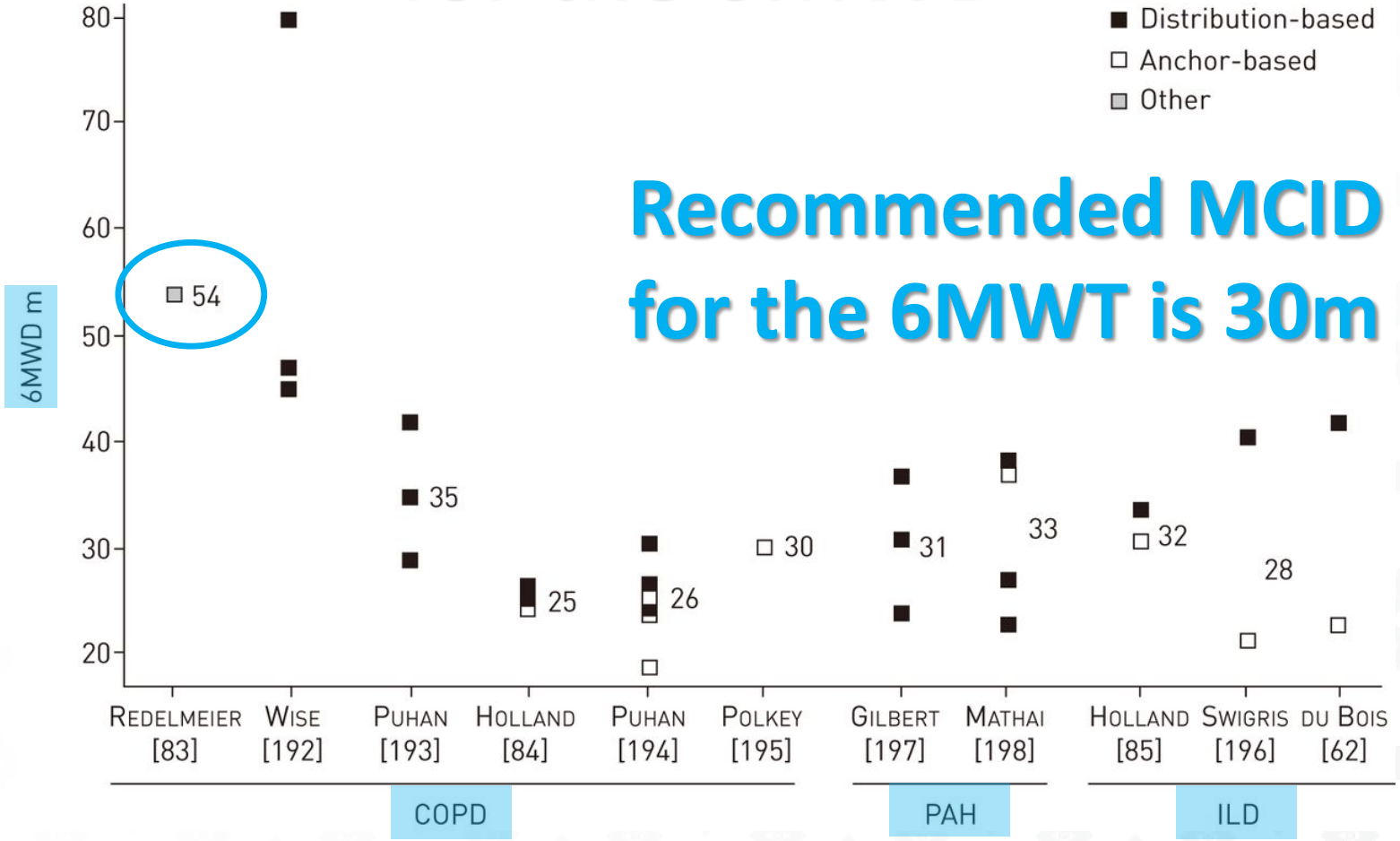
6MWT – Considerations

- is susceptible to a significant **training effect**
  - **a practice test should always be conducted**
- demonstrates a **ceiling effect** - smaller change in the 'near normal'
- **standardization [really] improves reproducibility**
  - encouragement, hallway length, walking course, etc.
- **responsive to interventions**
  - LVRS, pulmonary rehabilitation, bronchodilators, altered inspired gases, and pharmacologic therapies in varied populations
- **correlates with important outcomes**
  - hospitalization, mortality, HRQL

Singh SJ, et al. *Eur Respir J* 2014; 44:1447-1478. Holland AE, et al. *Eur Respir J* 2014; 44:1428-1446.

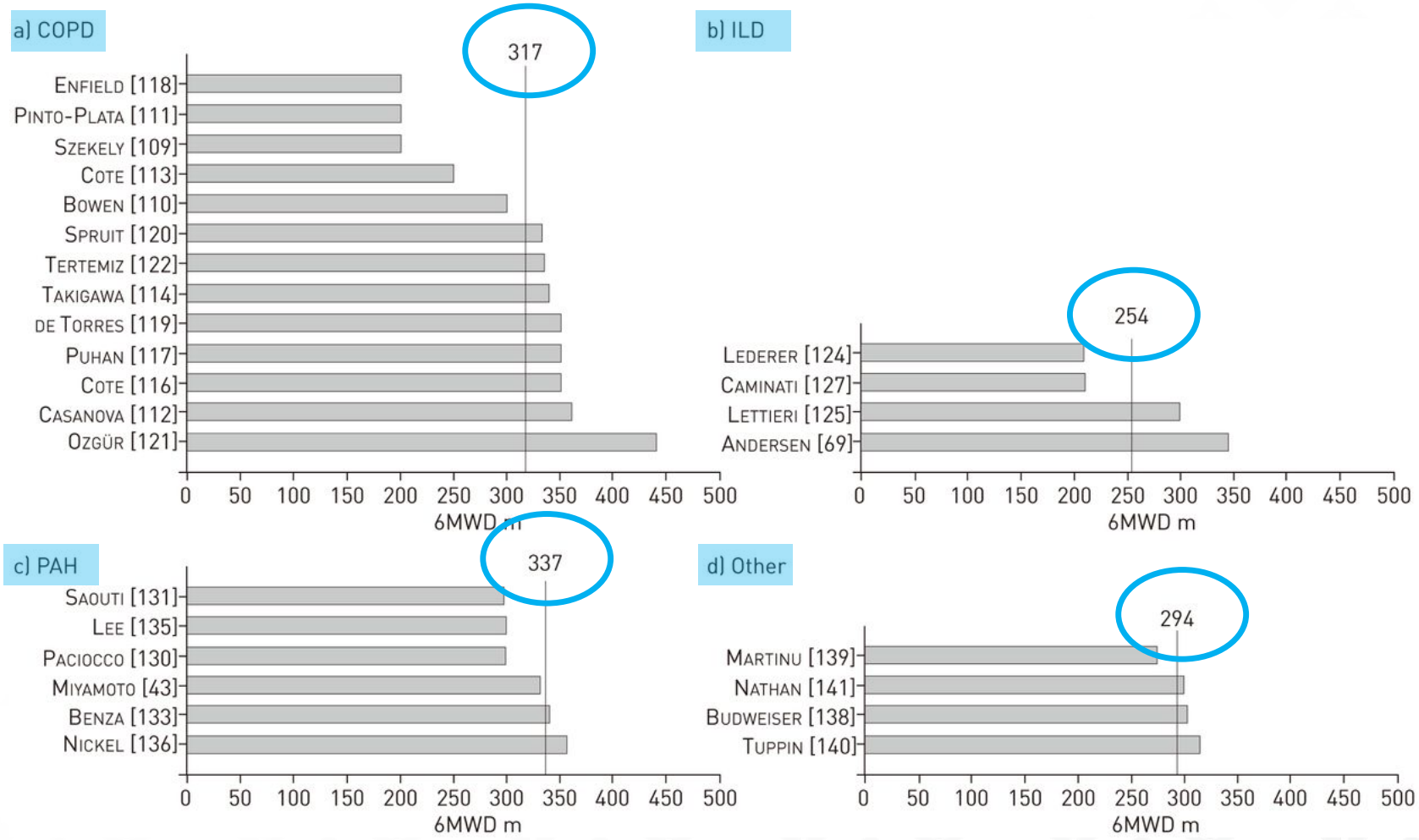
Minimal Clinically Important Difference (MCID) for the 6MWD



Recommended MCID for the 6MWT is 30m

Singh SJ, et al. *Eur Respir J* 2014; 44:1447-1478

6MWT Distance Thresholds for Increased Mortality



Singh SJ, et al. *Eur Respir J* 2014; 44:1447-1478

Effect of Methodological Variations on 6MWD

Variation in methodology	Studies n	First author [ref.]	Effect on 6MWD
Hallway *versus* treadmill	2	Stevens [14] de Almeida [15]	13–20% less on treadmill
Indoors *versus* outdoors	1	Brooks [16]	4 m (1%) more outside
Circular *versus* straight track	2	Bansal [17] Sciurba [18]	13–19 m (3–5%) more on circular track
Track length	2	Sciurba [18] Beekman [19]	No statistically significant difference in 6MWD from tracks of 15–121 m 50 m more on 30-m track compared to 10-m track
Wheeled walking aid *versus* no aid	6	Gupta [20] Honeyman [21] Probst [22] Roomi [23] Solway [24] Vaes [25]	Weighted mean 6.2% more with wheeled walker Range 2–46 m more with wheeled walker 83 m more with modern draisine compared to wheeled walker
With *versus* without oxygen	4	Davidson [26] Fujimoto [27] Rooyackers [28] Jolly [29]	12–59 m more with oxygen
Oxygen *versus* compressed air	2	Jolly [29] McDonald [30]	17–109 m more with oxygen
Carry oxygen *versus* oxygen in wheeled cart	1	Crisafulli [31]	23 m more with wheeled cart
Patient carries oxygen *versus* tester carries oxygen	1	Woodcock [32]	24 m *versus* 35 m improvement
Encouragement	1	Guyatt [33]	30.5 m more with encouragement
Instructions	1	Weir [34]	53 m further when asked to walk as "fast" as possible, rather than as "far" as possible

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Standardized Preparation for the 6MWT

"The aim of this test is to walk as far as possible for 6 minutes. You will walk this hallway between the markers, as many times as you can in 6 minutes.

I will let you know as each minute passes, and then at 6 minutes I will ask you to stop where you are. 6 minutes is a long time to walk, so you will be exerting yourself. You are permitted to slow down, to stop, and to rest as necessary, but please resume walking as soon as you are able.

Remember the objective is to walk as far as possible for 6 minutes, but don't run or jog. Do you have any questions?"

Holland AE, et al. *Eur Respir J* 2014; 44:1428-1446

Standardized Instructions for the 6MWT

1 min	*"You are doing well. You have 5 mins to go."*
2 min	*"Keep up the good work. You have 4 mins to go."*
3 min	*"You are doing well. You are halfway."*
4 min	*"Keep up the good work. You have only 2 mins left."*
5 min	*"You are doing well. You have only 1 min to go."*
6 min	*"Please stop where you are."*
If patient stops during the test, every 30s once SpO_2 ≥85%	*"Please resume walking whenever you feel able."*

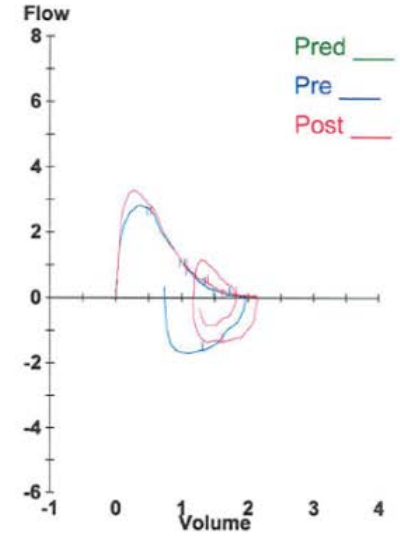
Holland AE, et al. *Eur Respir J* 2014; 44:1428-1446

Case #3

Age: 77 DOB: 06/01/1926 Gender: Female PF Reference: SHR Can.Resp.J (2004)
Height(in): 68 Height(cm): 173 Temp: 23 PBar: 720 Medication:
Weight(lb): 160 Weight(kg): 72.7 BMI: 24.29

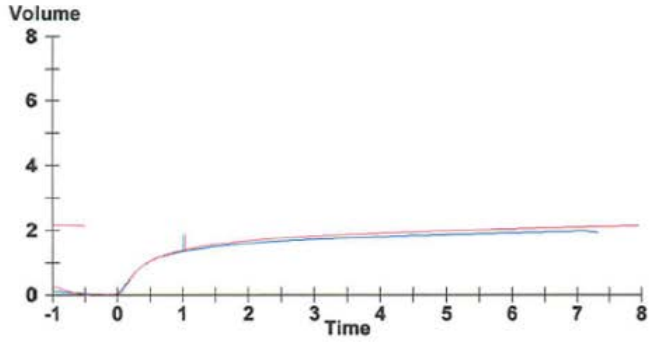
Pulmonary Function Analysis

		Pre	Ref	(Normal Range)	% Ref	Post	% Ref	%Chg
Spirometry								
FVC	Liters	1.97	3.43	(2.6 - 4.2)	57	2.15	63	9
FEV1	Liters	1.35	2.33	(1.7 - 2.9)	58	1.40	60	4
FEV1/FVC	%	69	68	(58.9 - 77.6)		65		
FEF25-75%	L/sec	0.80	1.80	(0.4 - 3.2)	44	0.72	40	-10
PEF	L/sec	2.95	5.72	(3.8 - 7.7)	52	3.28	57	11
FIVC	Liters	1.23				0.98		-20
PIF	L/sec	1.72	4.81	(3.0 - 6.6)	36	1.36	28	-21
FVL ECode		000010				001010		
Lung Volumes								
TLC	Liters	5.06	5.78	(4.8 - 6.7)	88			
VC	Liters	1.97	3.44	(2.7 - 4.2)	57			
IC	Liters	1.75	2.14	(1.7 - 2.6)	82			
FRC N2	Liters	3.31	3.17	(2.4 - 3.9)	104			
ERV	Liters	0.22	1.07	(0.8 - 1.3)	21			
RV	Liters	3.09	2.30	(1.7 - 2.9)	134			
RV/TLC	%	61	45	(35.5 - 54.7)				
Vt	Liters	0.61						
Diffusing Capacity								
DLCO	mL/mmHg/min	12.4	21.6	(15.9 - 27.3)	57			
DLCO/VA	mL/mHg/min/L	3.73	4.12	(3.0 - 5.3)	91			
VA	Liters	3.32						
IVC	Liters	1.78						
BHT	Sec	10.74						



Technologist Comments:

INTERPRETATION



77-yr-old female: unexplained shortness of breath

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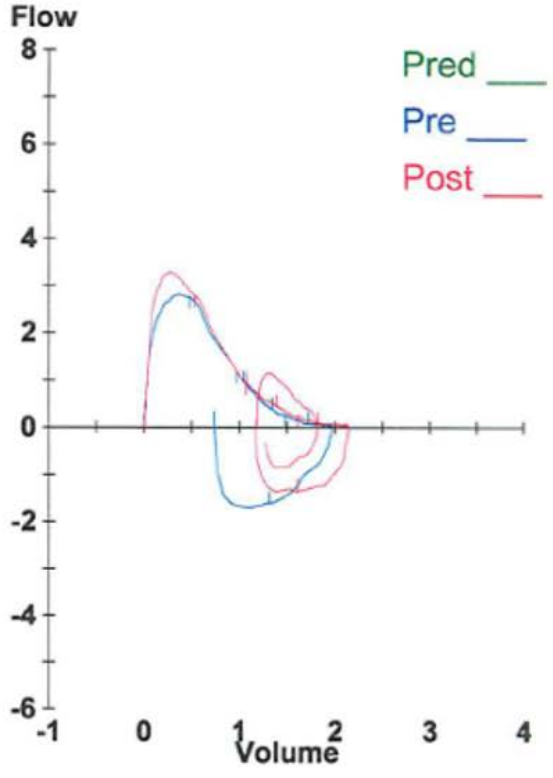

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Please Interpret These Pulmonary Function Tests:

a. Obstructive pattern

b. Restrictive pattern

c. Combined obstructive/restrictive pattern

d. Something else is going on here …

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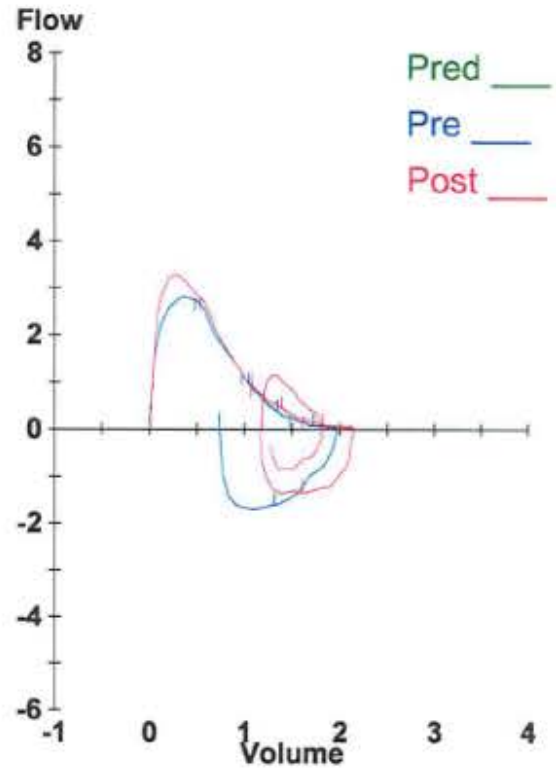
BHT	Sec	10.74						
Respiratory Muscle Force								
PI max	cmH2O	20	91	(52.8 - 129.6)	22			
PE max	cmH2O	28	51	(15.0 - 87.2)	55			



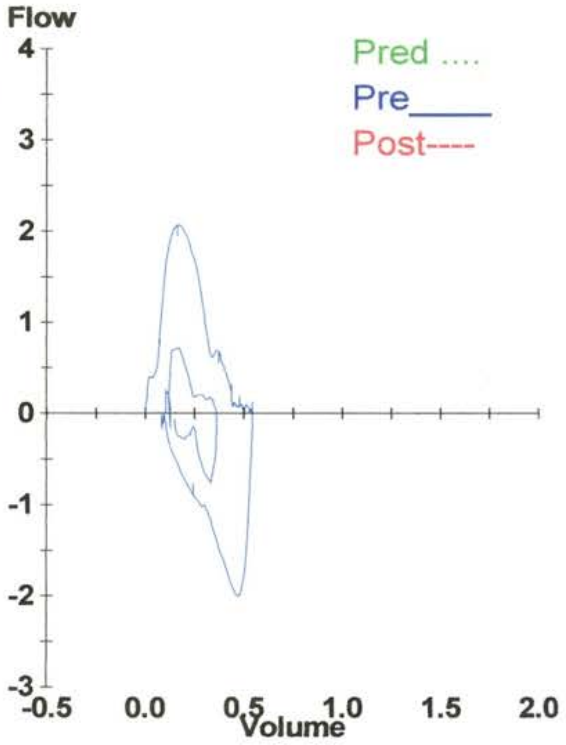
Age: 58
Height(in): 60 Height(cm): 152
Weight(lb): 78 Weight(kg): 35.5

Gender: Female
Race:
Temp: 20 PBar: 716

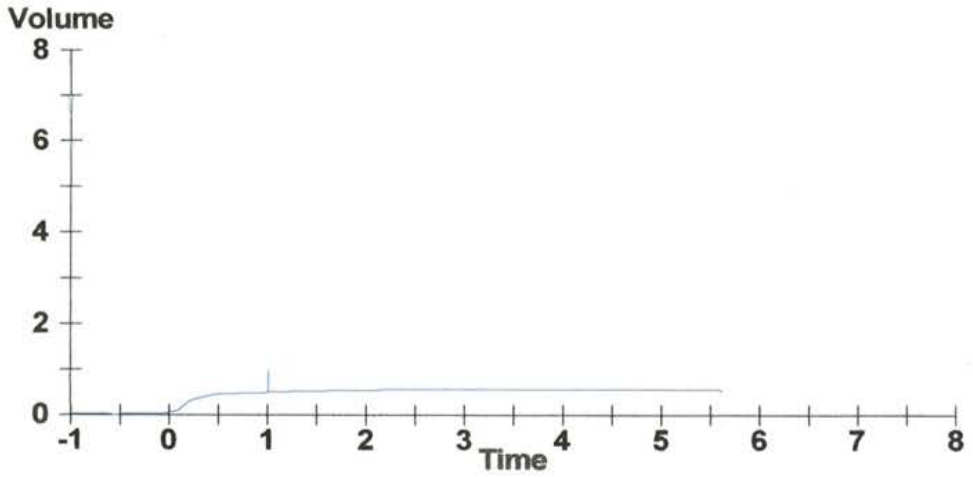
Diagnosis:
Medication: SALBUTAMOL NEB 1X 18H

Pulmonary Function Analysis

		Pre	Ref		% Ref	Post	% Ref	%Chg
Spirometry								
FVC	Liters	0.55	2.66	(1.8 - 3.5)	21			
FEV1	Liters	0.49	1.96	(1.2 - 2.7)	25			
FEV1/FVC	%	89	74	(62.8 - 85.4)				
FEF25-75%	L/sec	1.12	2.41	(0.9 - 3.9)	46			
PEF	L/sec	2.20	5.28	(2.4 - 8.1)	42			
FIVC	Liters	0.47	2.66	(1.7 - 3.6)	18			
PIF	L/sec	1.99						
FVL ECode		000001						
Lung Volumes								
VC	Liters	0.60	2.66	(1.7 - 3.6)	23			
IC	Liters	0.38	1.73	(1.3 - 2.2)	22			
ERV	Liters	0.21	0.86	(0.6 - 1.1)	24			
Respiratory Muscle Force								
PI max	cmH2O	23	74	(50.3 - 98.5)	31			
PE max	cmH2O	17	139	(98.7 - 179.9)	12			



INTERPRETATION



58-yr-old female: Post-polio kyphoscoliosis and quadriplegia

Much More Obvious, and Easier to Detect

Respiratory Muscle Pressures

- Maintain the **maximal inspiratory [or expiratory] pressure for ~2 secs**, with the largest negative [or positive] pressure sustained for 1 sec. recorded
  - **max value from 3 suitable maneuvers reported**
- Values decrease with age, and are **~1/3 lower in females when compared to men**
- In normal healthy individuals, 95% of the **test-to-test variation has a magnitude of less than 25 cmH_2O**

Respiratory Muscle Pressures [cont'd]

- **Normal MIP excludes inspiratory muscle weakness**, but a low MIP does not reliably confirm weakness
  - low +ve predictive value - variable effort/technique
- **MIP <1/3 normal predicts hypercarbic respiratory failure**
- **MEP <60 cmH_2O predicts a weak cough/difficulty clearing secretions**
- fall in FVC - upright to the supine position - correlates with significant inspiratory muscle weakness
  - when upright, a low FVC is less specific than the MIP for detecting respiratory muscle weakness

CHEST Congress 2019 | Thailand Bangkok | 10-12 April

Practical Pulmonary Physiology (Part 2)

Clayton T. Cowl, MD, MS, FCCP, FACOEM

Chair, Division of Preventive, Occupational & Aerospace Medicine
Joint Appointment, Division of Pulmonary & Critical Care Medicine
Mayo Clinic
Rochester, Minnesota USA

MAYO CLINIC

By the end of this presentation …

- Understand basic principles of **hypobaric hypoxia**
- Appreciate variables to consider when prescribing supplemental oxygen
- Recognize **symptoms of decompression illness,** findings that are often misdiagnosed, or delayed in correctly diagnosing

Conflict of Interest Disclosure

Consultancy

None

Research Funding (managed by Mayo Clinic)

U.S. Department of Labor; AVOX Incorporated (manufacturer of airline passenger and pilot quick-don oxygen masks)

Employee

Mayo Clinic

Case #4

What is happening in this photo?

What is happening in the photo?

a. Traveling to a sleep apnea convention
b. Treating “the bends”
c. Flying in an unpressurized airline cabin
d. Staying calm after a rapid decompression

What is happening in the photo?

a. Traveling to a sleep apnea convention

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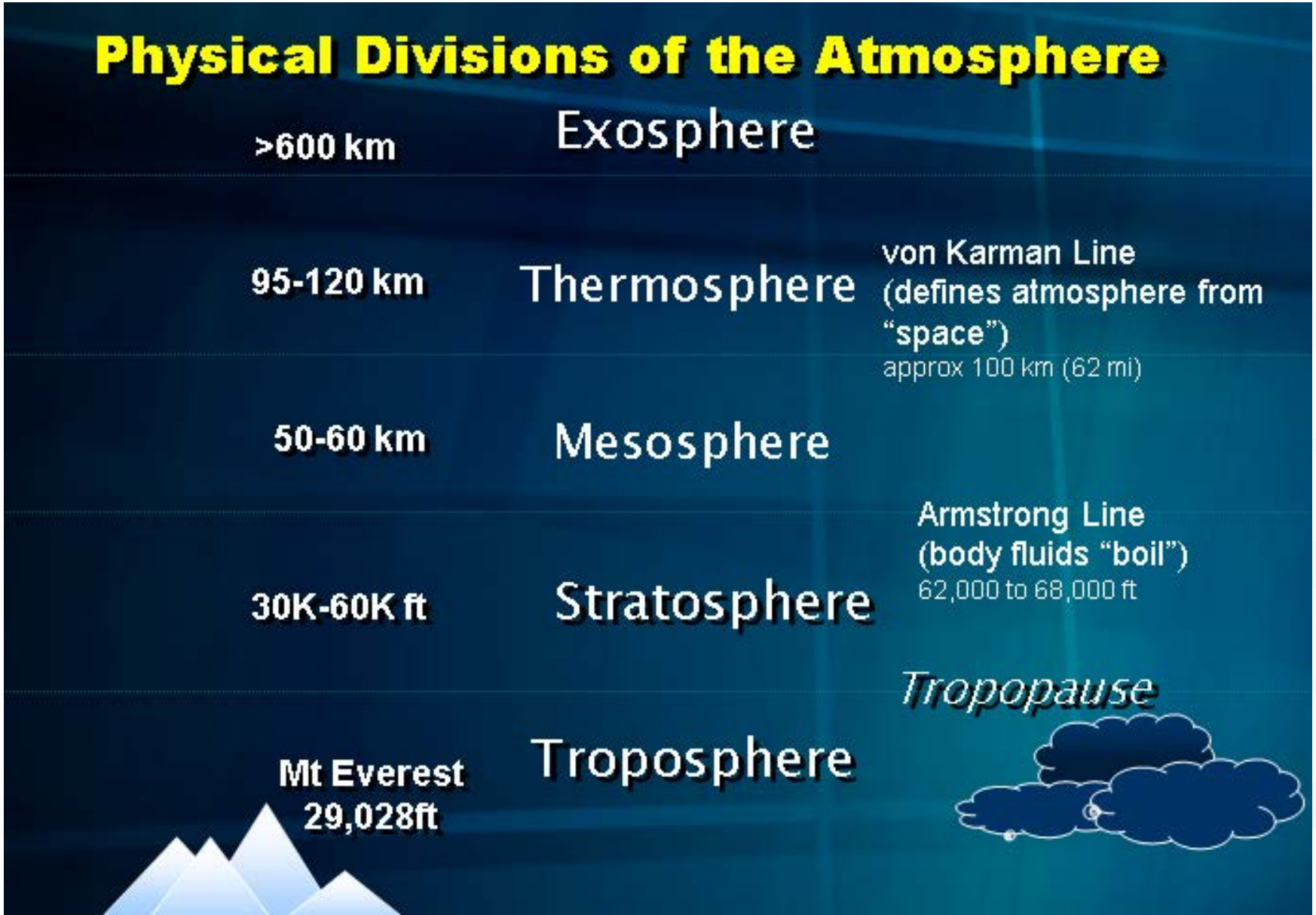
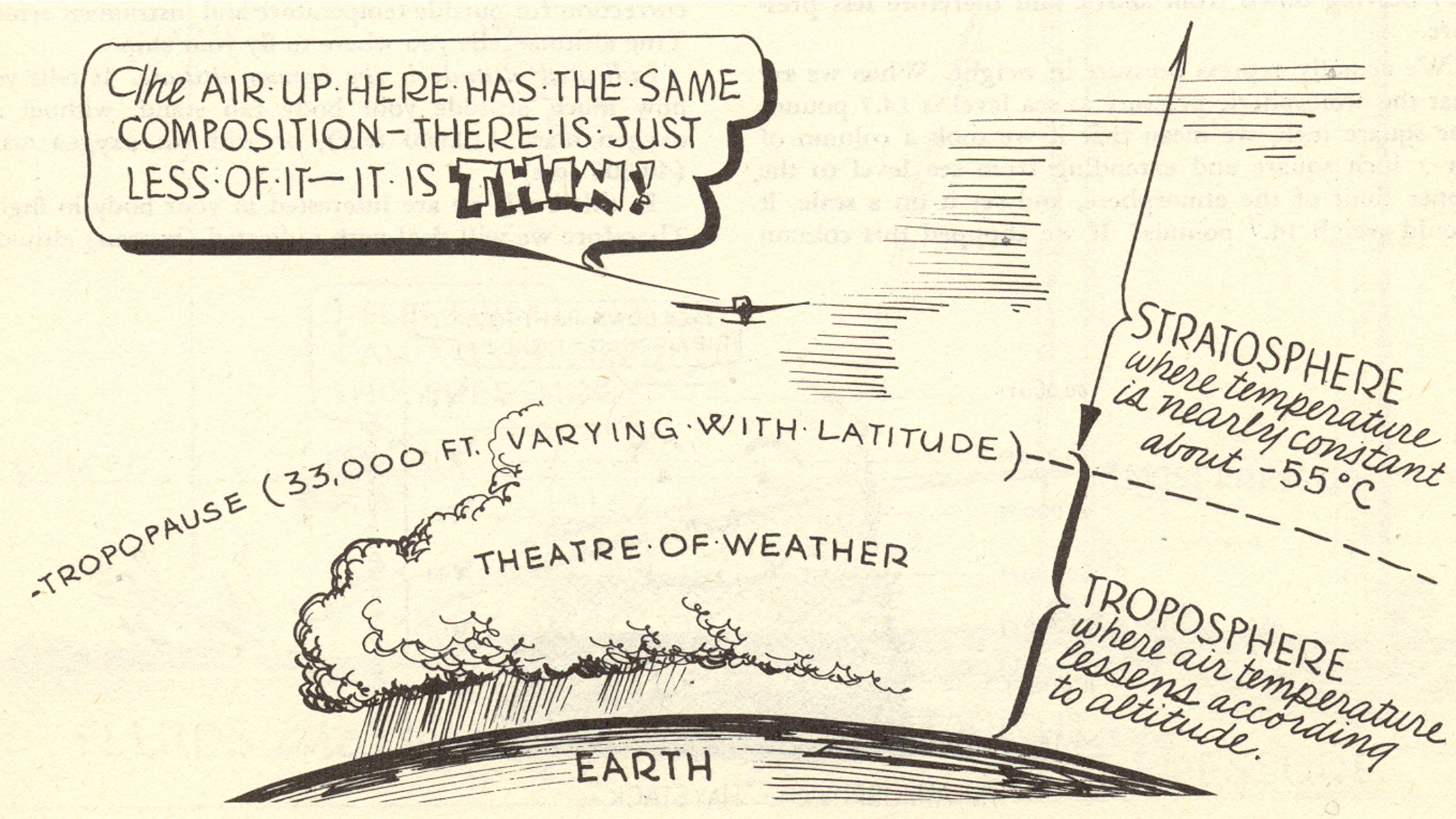
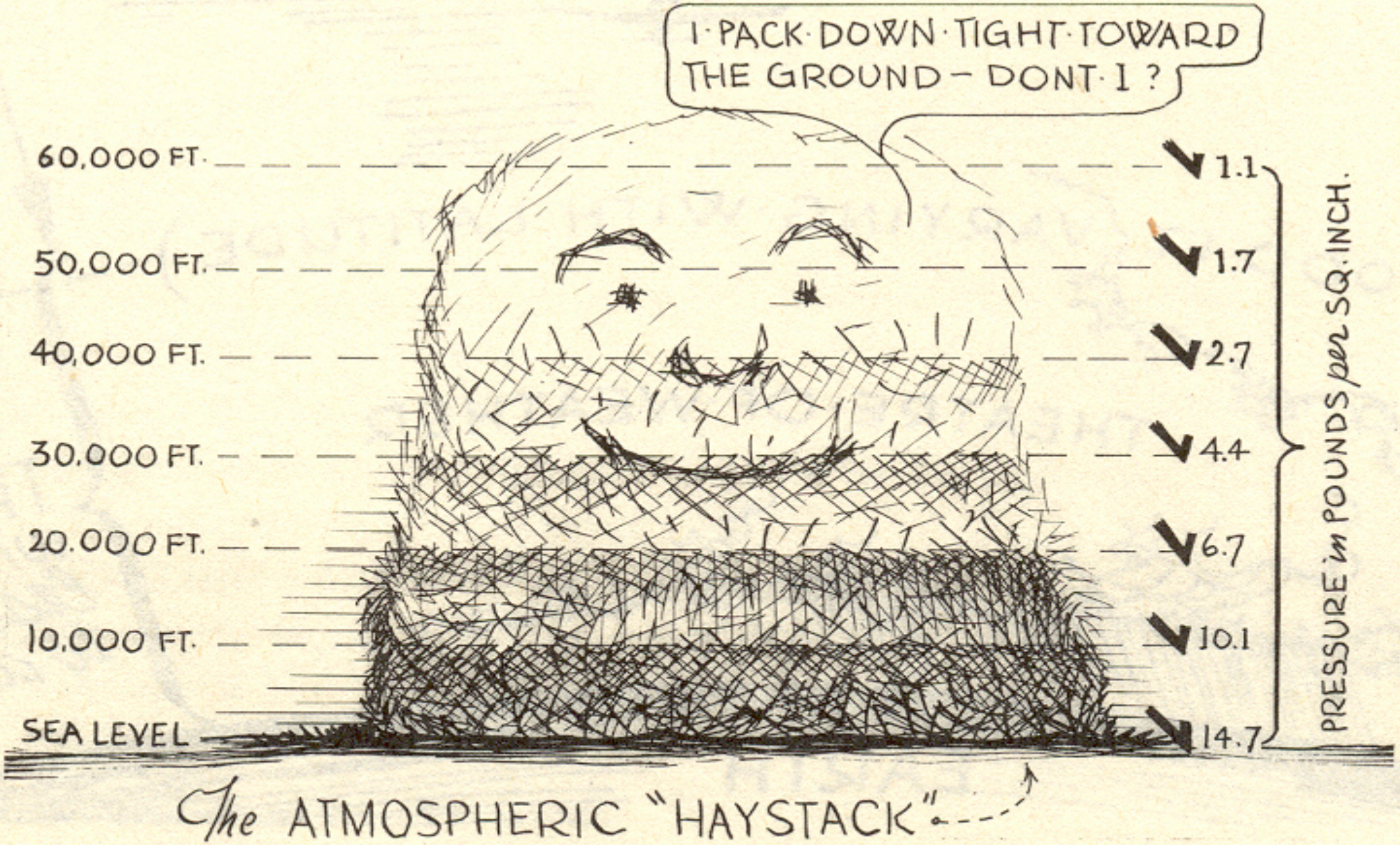
c. Flying in an unpressurized airline cabin

d. Staying calm after a rapid decompression

Stratosphere Troposphere Interactions: An Introduction
K. Mohanakumar
Springer Science & Business Media,
Jul 3, 2008 - Science



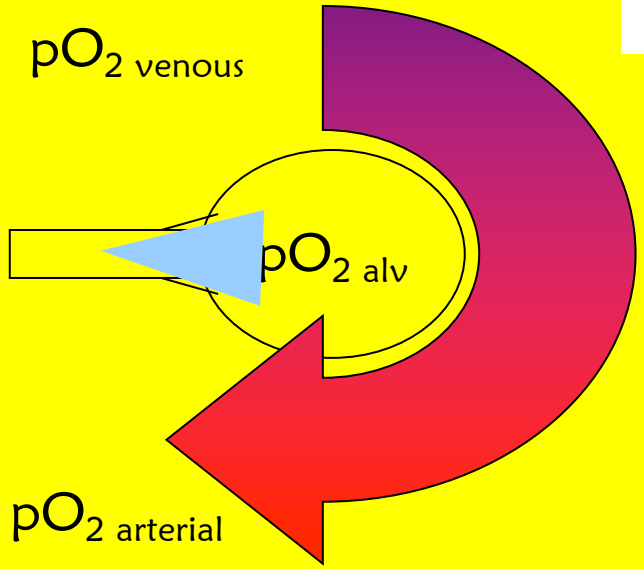

The AIR UP HERE HAS THE SAME COMPOSITION - THERE IS JUST LESS OF IT — IT IS THIN!
STRATOSPHERE where temperature is nearly constant about -55°C
TROPOPAUSE (33,000 FT. VARYING WITH LATITUDE)
THEATRE OF WEATHER
TROPOSPHERE where air temperature lessens according to altitude.
EARTH



The ATMOSPHERIC "HAYSTACK"

Gas-Exchange

Gas exchange (sea level):



$$P_{IO_2} = (P_B - P_{H_2O}) = 760\text{mmHg} - 47\text{mmHg}$$

713mmHg x 21% = 150mmHg

$$P_{AO_2} = P_{IO_2} - P_{ACO_2}\left[F_{IO_2} - \frac{(1 - F_{IO_2})}{R}\right]$$

$$R = \frac{\dot{V}_{CO_2}}{\dot{V}_{O_2}}$$ Assuming R=1, the equation becomes:

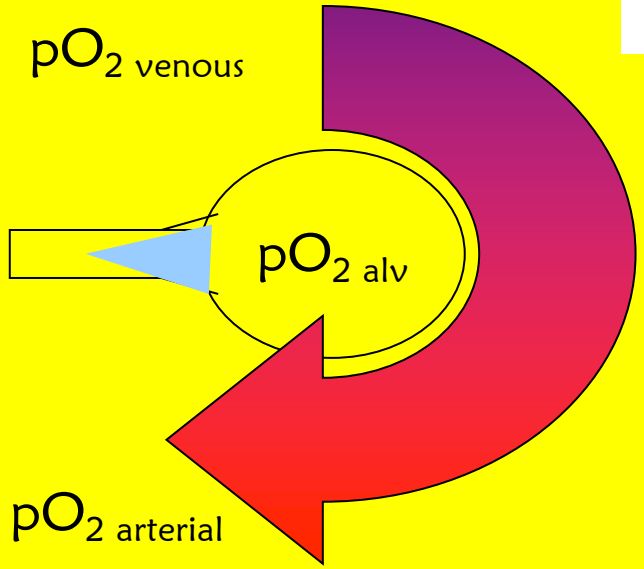
$P_{AO_2} = P_{IO_2} - P_{ACO_2}$ = 150mmHg – 40mmHg
=110mmHg

$pO_{2\ alv}$: 110mmHg
$pO_{2\ ven}$: 40mmHg
$pO_{2\ art}$: 100mmHg

ALTITUDE		PRESSURE		
feet	meters	mm Hg	in Hg	lb/in^2
0	0	760	29.92	14.69
5,000	1,525	632	24.9	12.23
10,000	3,048	523	20.58	10.11
15,000	4,572	429	16.88	8.29
20,000	6,096	349	13.74	6.75
25,000	7,620	282	11.09	5.45
30,000	9,144	226	8.87	4.36
35,000	10,668	179	7.04	3.46
40,000	12,192	141	5.53	2.72
45,000	13,716	111	4.35	2.14
50,000	15,240	87.3	3.44	1.69
55,000	16,764	68.8	2.71	1.33
60,000	18,288	54.1	2.14	1.05
65,000	19,812	42.3	1.66	0.8164
70,000	21,336	33.3	1.32	0.6494
75,000	22,860	26.2	1.03	0.5057
80,000	24,384	20.7	0.82	0.4028
85,000	25,908	16.4	0.644	0.3165
90,000	27,432	13	0.508	0.2496
95,000	28,956	10.3	0.404	0.1988

Gas-Exchange

Gas exchange (sea level):



$$P_{IO_2} = (P_B - P_{H_2O}) = 760\text{mmHg} - 47\text{mmHg}$$

713mmHg x 21% = 150mmHg

349-47=302

302 x .21 = 63

$$P_{AO_2} = P_{IO_2} - P_{ACO_2}\left[F_{IO_2} - \frac{(1 - F_{IO_2})}{R}\right]$$

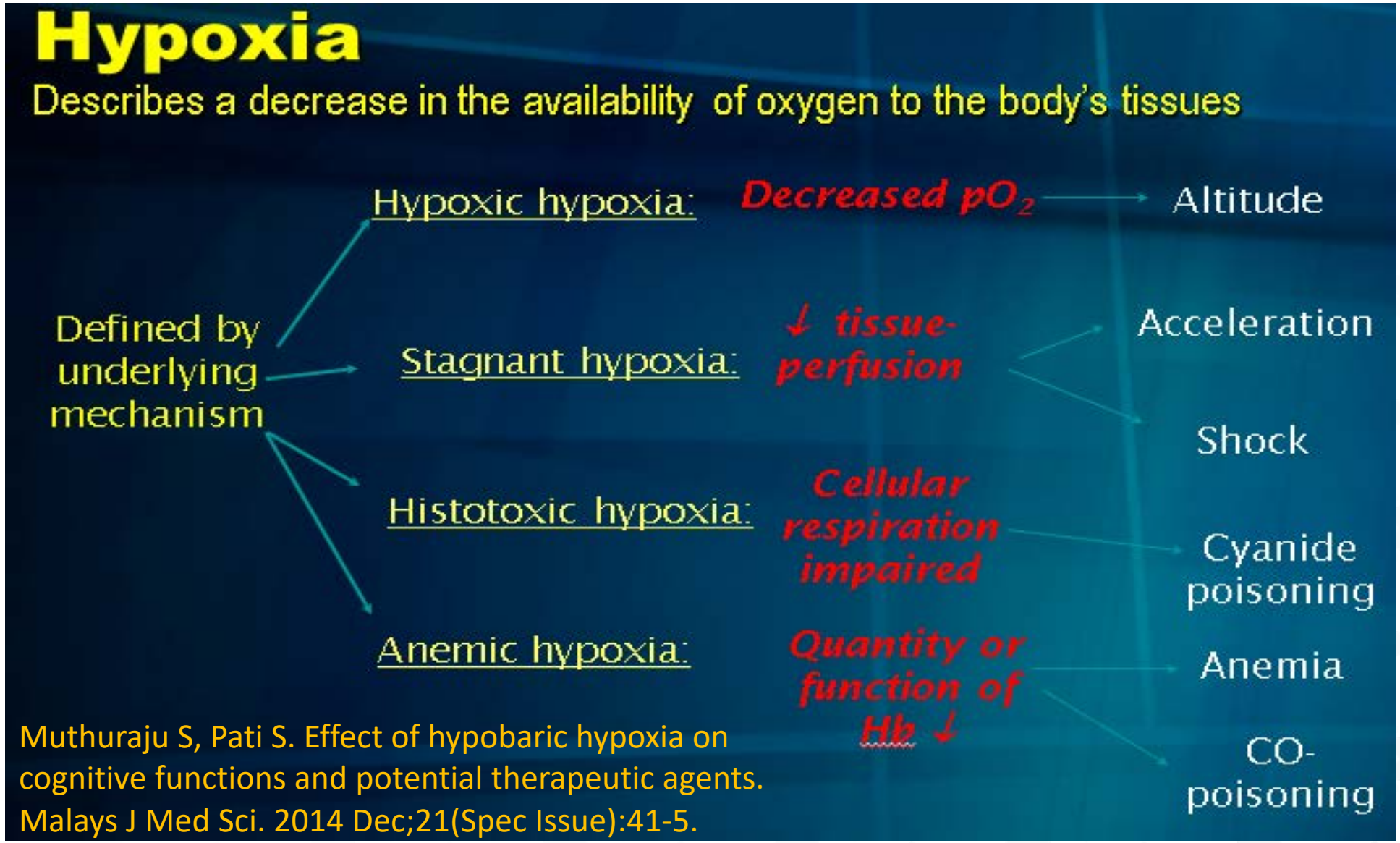
$$R = \frac{\dot{V}_{CO_2}}{\dot{V}_{O_2}}$$

Assuming R=1, the equation becomes:

$P_{AO_2} = P_{IO_2} - P_{ACO_2}$ = 150mmHg – 40mmHg
=110mmHg

63 – 40 = 23 mmHg

$pO_{2\ alv}$: 110mmHg
$pO_{2\ ven}$: 40mmHg
$pO_{2\ art}$: 100mmHg



Muthuraju S, Pati S. Effect of hypobaric hypoxia on cognitive functions and potential therapeutic agents. Malays J Med Sci. 2014 Dec;21(Spec Issue):41-5.

Case #5

You are asked to see a 63-year-old man on the lung transplant list with interstitial lung disease. An oxygen titration study reveals that he requires 6-7 L/min supplemental oxygen via nasal cannula at rest with slightly greater flow with minimal exertion. He wants to travel to visit his children at their home in the mountains (8,000 ft/2,438 m).

What would be the most appropriate advice?

a. Approve travel by air using a portable oxygen concentrator

b. Recommend traveling by car and using pursed lip breathing until stationary concentrator can be set up at destination

c. Suggest no travel by patient at any time

d. Have patient use tank oxygen while traveling with backup stationary concentrator at destination

What would be the most appropriate advice?

a. Approve travel by air using a portable oxygen concentrator

b. Recommend traveling by car and using pursed lip breathing until stationary concentrator can be set up at destination

c. Suggest no travel by patient at any time

d. Have patient use tank oxygen while traveling with backup stationary concentrator at destination

Oxygen Concentrator

- Provides 95% pure O2
- Never requires refill
- Maximum flow rates 5-10 L/min
- Runs on electricity and has alarm if power fails
- Back-up oxygen needs to be in place in the home for use during equipment or power failure

Home Transfill Oxygen Systems (HTF)

- Unlimited oxygen supply
- Refillable cylinders
- Reduced storage requirements for oxygen cylinders
- Reduced electrical costs
- Operates in conjunction with oxygen concentrator

Liquid oxygen systems

- Requires scheduled refills with liquid oxygen (75 lbs O_2 = 4-8 days)
- Portable unit is refilled from a stationary unit
- Delivery system required for oxygen mask and high-flow patients
- More cumbersome and less availability than other systems
- Is not flammable, but is concentrated and can be dangerous if coming in contact with organic substances

Portable O_2 gas delivery system

- Use for portability outside of the home (with conserving device can last 4-12 hours on 2 L / min)
- Cylinders weigh 7-11 pounds
- Transported by cart or carry strap
- Cylinders last 3-5 hours on 2L/min depending on cylinder size
- Can be used as a backup system to a concentrator
- Conserving device attachment requires oximetry testing to confirm setting that maintains O_2 saturation

Case #6

A 37-year-old woman comes to your office after vacationing in the Caribbean where she and her significant other went diving. There was a discount by the dive outfitter if they would dive three days in a row. The last dive concluded on a Friday morning and they departed for home by air that evening. Upon their return home, she noted severe joint pain in her left hip and right shoulder. She was unaware of any trauma to these areas. No bruising or limitation in range of motion is noted on exam. Her lungs are clear and there are no other abnormalities.

What would be the most appropriate next step?

a. Immediately provide the patient 1L/min of supplemental oxygen via nasal cannula

b. Apply 100% FiO2 and refer for hyperbaric oxygen therapy

c. Perform a joint aspiration and inject with corticosteroids

d. Prescribe 800 mg of ibuprofen and have patient call if pain worsens

What would be the most appropriate next step?

a. Immediately provide the patient 1L/min of supplemental oxygen via nasal cannula

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d. Prescribe 800 mg of ibuprofen and have patient call if pain worsens

Decompression illness ("The Bends")

Type I DCS

- Musculoskeletal pain and mild cutaneous symptoms such as itching and mild rashes (as distinct from a clear mottled or marbled and sometimes raised discoloration of the skin — a condition that is known as *cutis marmorata* that may occur prior to development of the more serious symptoms of Type 2 DCS).
- Less common but still associated with Type 1 DCS is obstruction of the lymphatic system, which can result in swelling and localized pain in the tissues surrounding the lymph nodes — such as in the armpits, groin or behind the ears.
- Symptoms can build in intensity, but does not typically increase upon movement of the affected joint, although holding the limb in one position rather than another may reduce discomfort. Such pain can ultimately be quite severe.

Decompression illness ("The Bends")

Type II DCS

- Considered more serious and symptoms may develop quickly or slowly and fall into three categories: neurological, inner ear and cardiopulmonary.
- Neurological symptoms: numbness; paresthesia, or an altered sensation, such as tingling; muscle weakness; an impaired gait, or difficulty walking; problems with physical coordination or bladder control; paralysis; or a change in mental status, such as confusion or lack of alertness.
- Inner-ear symptoms may include ringing in the ears, known as "tinnitus"; hearing loss; vertigo or dizziness; nausea; vomiting; and impaired balance.
- Cardiopulmonary symptoms, known commonly as "the chokes," include a dry cough; chest pain behind the sternum, or breastbone; and dyspnea.


N167C

Thank you for your attention!