

**Pharmacology Update:
Gastroenterology, Pulmonary and
Infectious Diseases**

**Wendy L. Wright,
DNP, ANP-BC, FNP-BC FAANP, FAAN, FNAP**
Adult / Family Nurse Practitioner
Owner - Wright & Associates Family Healthcare
Amherst, New Hampshire
Owner- Wright & Associates Family Healthcare
Concord, NH
Owner – Partners in Healthcare Education, PLLC

Wright, 2021

1

Disclosures

- **Speaker Bureau: Sanofi-Pasteur, Merck, Pfizer, AbbVie, Biohaven**
- **Consultant: Sanofi-Pasteur, Pfizer, Merck, GlaxoSmithKline**

Wright, 2021

2

Objectives

Upon completion, the participant will be able to:

- Discuss latest statistics pertaining to asthma, COPD, GI disorders, and emerging infectious diseases
- Discuss pharmacologic treatment options for patients with the above conditions
- Compare and contrast various pharmacologic treatment options for patients with the above conditions

Wright, 2021

3

Asthma

Wright, 2021

4

4

Asthma is...

- Derived from the Greek word for panting or breathlessness
- Recurrent airflow obstruction caused by chronic airway inflammation with a superimposed bronchospasm
- Leads to... wheezing, breathlessness and a cough

Guidelines for the Diagnosis and Management of Asthma—Update on Selected Topics 2002. NIH, NHLBI. June 2002. NIH publication no. 02-5075.

Wright, 2021

5

5

Prevalence of Asthma

- Impacts approximately 19 million individuals in the United States (18 and older)
- Most common chronic disease of childhood affecting 5.5 million children
- Increasing incidence of this disease
 - 76% increase in the prevalence of asthma within the past decade

<https://www.cdc.gov/nchs/fastats/asthma.htm> accessed 04-01-2021

Wright, 2021

6

6

Impact of Asthma

- 9.8 million visits to providers office annually
- 1.6 million ED visits annually
 - 189,000 hospitalizations
- 3524 deaths annually (2019)
 - Highest rates: adults (5x more likely than children to die)
- Children: boys > girls
- Adults: women > men

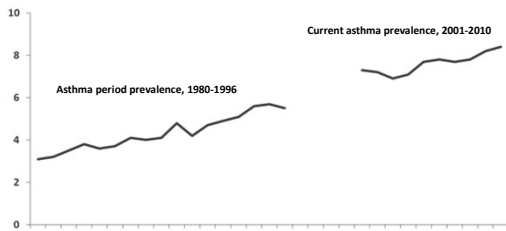
<https://www.cdc.gov/nchs/fastats/asthma.htm> accessed 04-01-2021

Wright, 2021

7

7

Asthma Period Prevalence and Current Asthma Prevalence: United States, 1980-2010



The percentage of the U.S. population with asthma increased from 3.2% in 1980 to 5.5% in 1996 and 7.3% in 2001 to 8.4% in 2010.

8

Pathophysiology of Asthma

- Likely genetic predisposition with environmental triggers
- Genetic predisposition
 - Chromosome: 5Q31-Q33
- Results from repeated exposure to allergens in the individual already equipped with the genetic predisposition
- Upon exposure to an allergen, there is a release of IgE antibodies
- IgE antibody binds with the antigen

Wright, 2021

9

9

Pathophysiology of Asthma

- IgE/allergen complex - then attaches itself to the mast cells on the nasal and bronchial mucosa
- Release of numerous chemical mediators

Wright, 2021 10

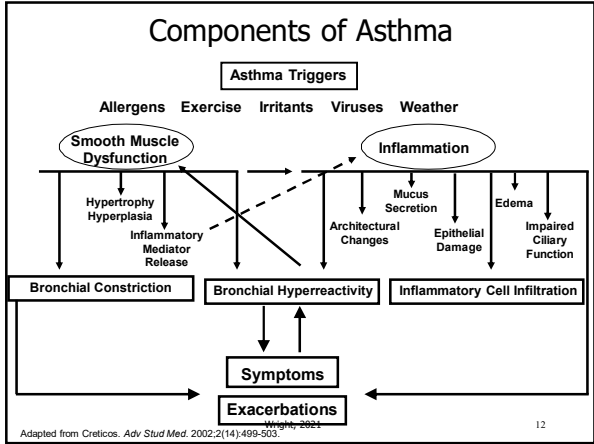
10

Histamine

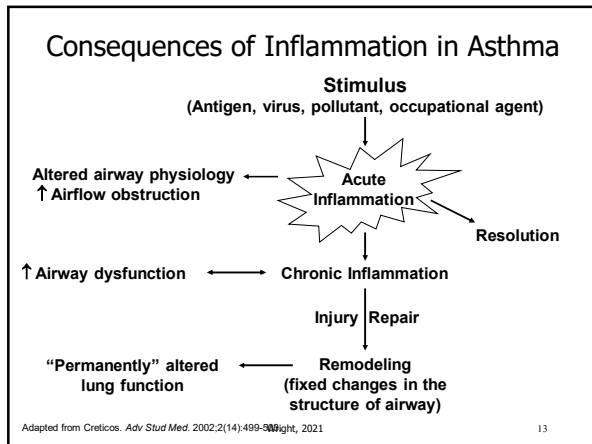
- Histamine is stored mainly in the mast cell
 - Circulated in the blood via the basophil
- Causes an increase in blood flow to the affected area.
 - Responsible for the increased nasal discharge, edematous mucous membranes, sneezing, itchy nose and eyes, and hives
 - Also associated with airway inflammation and bronchoconstriction

Adapted from Creticos. Adv Stud Med. 2002;2(14):499-503. Wright, 2021 11

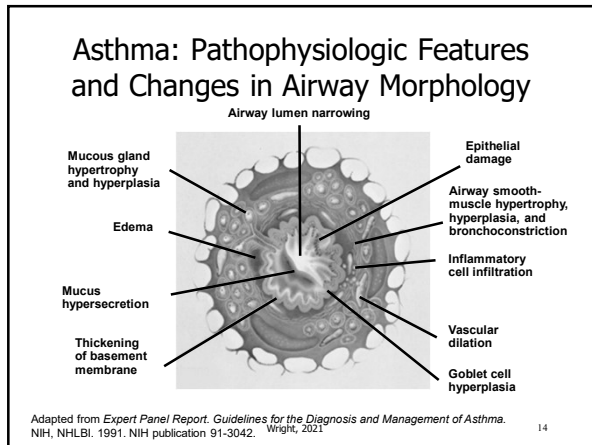
11



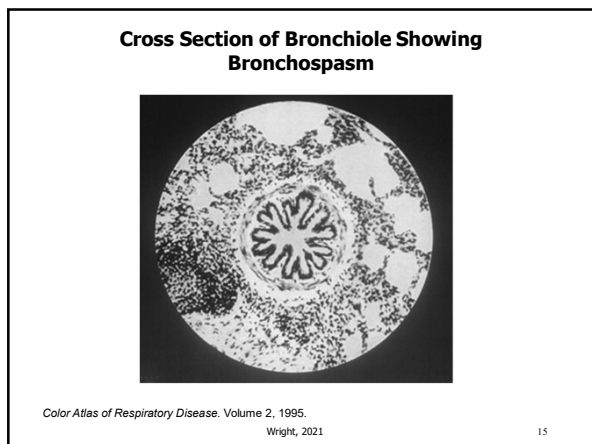
12



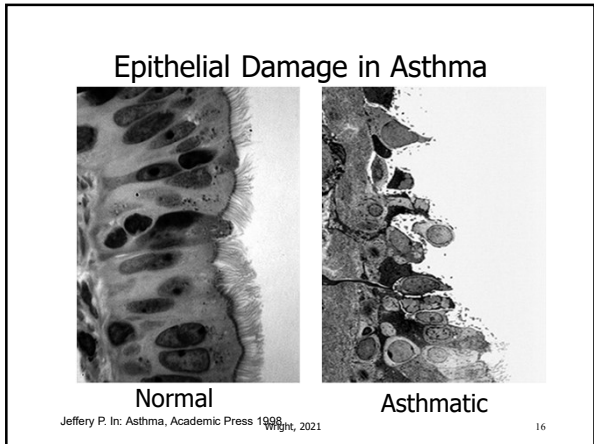
13



14



15



16



17

Asthma is...

- A disease of:
 - Inflammation
 - Primary Process
 - Hyperresponsiveness
 - Airway bronchoconstriction
 - Excessive mucous production

Wright, 2021

18

Diagnosis of Asthma

Wright, 2021 19

19

M.E.

- 21-year-old female
 - C/o shortness of breath with running; present x months. Accompanied by coughing.
 - Denies CP, audible wheezing, runny nose, dizziness.
 - Has not been previously evaluated
 - Nonsmoker
 - Bronchiolitis: infancy

Wright, 2021 20

20

Diagnosis of Asthma

- History and Physical Examination
- Spirometry is needed to make diagnosis
- Monitoring:
 - Peak Flow Meters

Wright, 2021 21

21

Important:

2% of individuals who present with asthma symptoms have a significant cardiorespiratory condition (other than asthma)

<https://www.aafp.org/afp/2020/0615/p762.html> accessed 04-01-2021

Wright, 2021

22

22

Symptoms and Signs of Asthma in Children and Adults

- Coughing, particularly at night or after exercise
- Wheezing
- Chest tightness
- SOB
- Cold that lingers x months

Wright, 2021

23

23

Methods for Measuring Airway Caliber



Maximum PEF
airflow achieved
Home

FVC, FEV₁,
FEF_{25%-75%}
Office/Clinic

Airway
Resistance
Clinic/Laboratory

Wright, 2021

24

24

M.E. (continued)

- VSS
- Lungs clear
- Heart: S1, S2, RRR; no S3 or S4; no murmurs
- Spirometry (Quality A)
 - FEV1: 72% predicted
 - FEV1/FVC ratio: 94% predicted

Wright, 2021 25

25

Diagnosis

- Diagnosis:
 - Improvement of 12% or more in FEV1 and 200 mL from baseline after bronchodilator OR
 - 20% improvement in PEFR post bronchodilator

<https://www.aafp.org/afp/2020/0615/p762.html> accessed 04-01-2021

Wright, 2021 26

26

M.E. (continued)

- Baseline spirometry (Quality A)
 - FEV1: 72% predicted
 - FEV1/FVC ratio: 94% predicted
- Post-bronchodilator
 - FEV1: 90% (up 18%)
 - FEV1/FVC ratio: 95%

Wright, 2021 27

27

Classification of Asthma Severity (Youths ≥ 12 Years of Age and Adults)						
Initial Diagnosis: Determine Severity and Treatment Needed						
Components of Severity		Persistent				
Symptoms	Intermittent	Mild	Moderate	Severe		
		<2 days/week but not daily	Daily	Throughout the day		
Impairment Short-acting beta ₂ -agonist use for symptom control (not prevention of EIB) Normal FEV₁/FVC: 8-19 y 85% 20-59 y 80% 60-80 y 70%	Nighttime awakenings	≤2x/month	3-4x/month	>1x/week but not nightly	Often 7x/week	
	Interference with normal activity	None	Minor limitation	Some limitation	Extreme limitation	
	Lung function	Normal FEV ₁ between exacerbations	FEV ₁ >80% predicted	FEV ₁ >60% but <80% predicted	FEV ₁ <60% predicted	
		FEV ₁ /FVC normal	FEV ₁ /FVC normal	FEV ₁ /FVC reduced ≥5%	FEV ₁ /FVC reduced >5%	
Risk	Exacerbations requiring oral systemic corticosteroids	0-1/year (see note)	≥2/year (see note)			
		Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. Relative annual risk of exacerbations may be related to FEV ₁ .				
Recommended Step for Initiating Treatment		Step 1	Step 2	Step 3	Step 4	
		In 2 to 6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.				

28


M.E. (continued)

- **Diagnosis:**
–Moderate Persistent Asthma
- **Plan: Step 3 Care**

29

Asthma

- Hyperinflation
- Diaphragm is down to the 11th ribs
- Most patients with asthma have normal x-rays

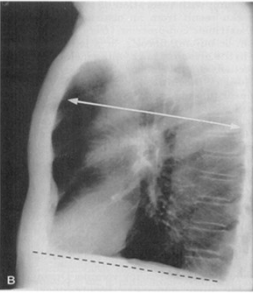


Wright, 2021

30

Chronic Asthma Changes

- Increased AP Lateral diameter
- The way you know that AP/Lat diameter is increased by this clear space between the sternum and the ascending aorta
- Flat diaphragms



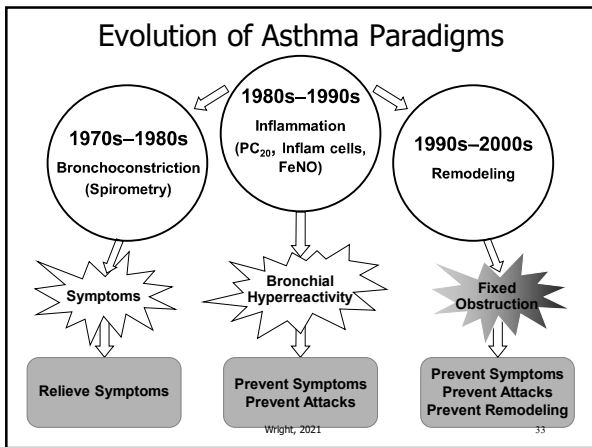
31

31

Treatment of Asthma

Wright, 2021 32

32



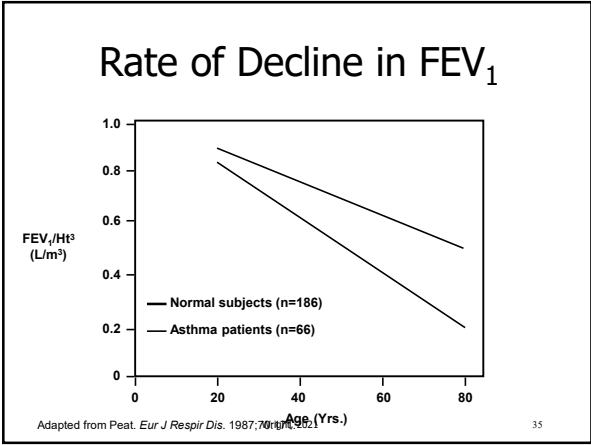
33

Childhood Asthma Control Can Predict Adult Lung Status

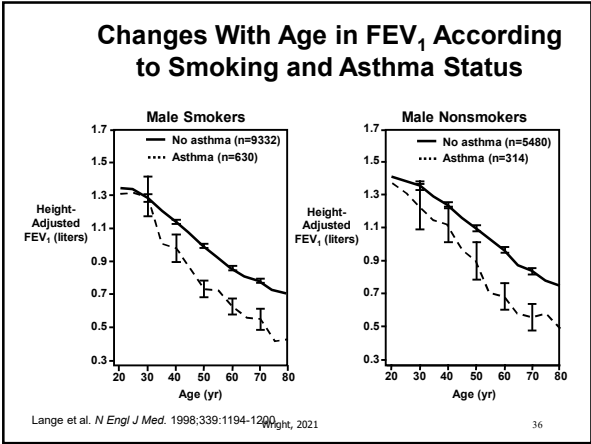
- Study of 119 asthmatic children during 1966 and 1969
- Ages: 5-14 were evaluated using FEV1
- Follow-up performed 17-18 years later and 27-28 years later
- Children who were well controlled during childhood had the smallest decline in total lung volume during adulthood

Wright, 2021 34

34



35



36

Table 10-14: Classification of Asthma Severity (Youths ≥ 12 Years of Age and Adults)

Initial Diagnosis: Determine Severity and Treatment Needed						
Components of Severity		Persistent				
Symptoms	Intermittent	Mild		Moderate	Severe	
		<2 days/week	>2 days/week but not daily	Daily	Throughout the day	
Impairment Normal FEV ₁ /FVC: 8-19 y 85% 20-39 y 80% 40-59 y 75% 60-80 y 70%	Nighttime awakenings	≤2x/month	3-4x/month	>1x/week but not nightly	Often 7x/week	
	Short-acting beta ₂ -agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not >1x/day	Daily	Several times per day	
	Interference with normal activity	None	Minor limitation	Some limitation	Extreme limitation	
	Lung function	Normal FEV ₁ between exacerbations				
		FEV ₁ >80% predicted	FEV ₁ >80% predicted	FEV ₁ >60% but <80% predicted	FEV ₁ <60% predicted	
	FEV ₁ /FVC normal	FEV ₁ /FVC normal	FEV ₁ /FVC reduced 5%	FEV ₁ /FVC reduced >5%		
Risk	Exacerbations requiring oral systemic corticosteroids	0-1/year (see note)		≥2/year (see note)		
		Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. Relative annual risk of exacerbations may be related to FEV ₁ .				
Recommended Step for Initiating Treatment	Step 1	Step 2	Step 3	Step 4 and consider short course of oral systemic corticosteroids		
	In 2 to 6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly. ^{17,21}					

37



<https://www.nhlbi.nih.gov/health-topics/all-publications-and-resources/2020-focused-updates-asthma-management-guidelines>

Wright, 2021

38

38

Indoor Allergen Mitigation

- Can be very helpful for individuals with allergic component
- Recommend air purifiers, mattress and pillow covers, HEPA filters

Wright, 2021

39

39

Stepwise Approach Ages 0 – 4 Years

Figure 1.B: Stepwise Approach for Management of Asthma in Individuals Ages 0-4 Years

Intermittent Asthma		Management of Persistent Asthma in Individuals Ages 0-4 Years					
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6	
Preferred	PRN SABA and/or At the start of RTI, Add short-acting beta ₂ agonist ICS*	Daily low-dose ICS and PRN SABA	Daily medium-dose ICS and PRN SABA	Daily medium-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA	
Alternative		Daily formoterol† or budesonide and PRN LABA		Daily medium-dose ICS + formoterol† and PRN LABA	Daily high-dose ICS + formoterol† and PRN LABA	Daily high-dose ICS + Montelukast† and oral systemic corticosteroid and PRN SABA	

For children age 4 years only, see Step 3.

Assess Control

- First check adherence, inhaler technique, environmental factors, and comorbid conditions.
- Step up if needed; reassess in 4-6 weeks.
- Step down if possible if asthma is well controlled for at least 3 consecutive months.
- Consult with asthma specialist if Step 4 or higher is required. Consider consultation at Step 2.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta₂ agonist; SABA, inhaled short-acting beta₂ agonist; RTI, respiratory tract infection; PRN, as needed.

* Updated based on the 2020 guidelines.

† Omnidex and Montelukast were not considered for this update and/or have limited availability for use in the United States. The FDA issued a boxed warning for montelukast in March 2020.

Wright, 2021

40

40

Stepwise Approach Ages 5 – 11 Years

Figure 1.C: Stepwise Approach for Management of Asthma in Individuals Ages 5-11 Years

Intermittent Asthma		Management of Persistent Asthma in Individuals Ages 5-11 Years					
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6	
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA	Daily and PRN low-dose ICS/formoterol† or low-dose LABA	Daily and PRN medium-dose ICS/formoterol† or medium-dose LABA	Daily high-dose ICS-LABA and PRN LABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA	
Alternative		Daily LTRA, or formoterol† or budesonide† or PRN LABA	Daily medium-dose ICS and PRN LABA† or	Daily medium-dose ICS and PRN LABA† or	Daily high-dose ICS-LABA† or daily high-dose ICS-LABA† and PRN LABA	Daily high-dose ICS-LABA† + formoterol† or oral high-dose ICS + formoterol† + oral systemic corticosteroid and PRN SABA	

Step 4 is considered maintenance therapy for children ages 5-11 years. For children ages 5-11 years, Step 4 is considered maintenance therapy for children ages 5-11 years.

Assess Control

- First check adherence, inhaler technique, environmental factors, and comorbid conditions.
- Step up if needed; reassess in 2-6 weeks.
- Step down if possible if asthma is well controlled for at least 3 consecutive months.
- Consult with asthma specialist if Step 4 or higher is required. Consider consultation at Step 3.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta₂ agonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta₂ agonist.

* Updated based on the 2020 guidelines.

† Omnidex, Nedocadilil, TruScribe, and Theophylline were not considered for this update and/or have limited availability for use in the United States, and/or have an increased risk of adverse consequences and need for monitoring that make their use less desirable. The FDA issued a boxed warning for montelukast in March 2020.

‡ Omnidex is the only asthma biologic currently FDA-approved in the US.

Wright, 2021

41

41

Stepwise Approach Ages 12 Years and Older

Figure 1.D: Stepwise Approach for Management of Asthma in Individuals Ages 12 Years and Older

Intermittent Asthma		Management of Persistent Asthma in Individuals Ages 12 Years and Older					
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6*	
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA	Daily and PRN low-dose ICS/formoterol† or low-dose LABA	Daily and PRN medium-dose ICS/formoterol† or medium-dose LABA	Daily high-dose ICS-LABA and PRN LABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA	
Alternative		Daily LTRA, or formoterol† or budesonide† or PRN LABA	Daily medium-dose ICS and PRN LABA† or	Daily medium-dose ICS and PRN LABA† or	Daily high-dose ICS-LABA† or daily high-dose ICS-LABA† and PRN LABA	Daily high-dose ICS-LABA† + formoterol† or oral high-dose ICS + formoterol† + oral systemic corticosteroid and PRN SABA	

Step 4 is considered maintenance therapy for children ages 12 years and older. For children ages 12 years and older, Step 4 is considered maintenance therapy for children ages 12 years and older.

Assess Control

- First check adherence, inhaler technique, environmental factors, and comorbid conditions.
- Step up if needed; reassess in 2-6 weeks.
- Step down if possible if asthma is well controlled for at least 3 consecutive months.
- Consult with asthma specialist if Step 4 or higher is required. Consider consultation at Step 3.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta₂ agonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta₂ agonist.

* Updated based on the 2020 guidelines.

† Omnidex, Nedocadilil, TruScribe, and Theophylline were not considered for this update, and/or have limited availability for use in the United States, and/or have an increased risk of adverse consequences and need for monitoring that make their use less desirable. The FDA issued a boxed warning for montelukast in March 2020.

‡ Omnidex is the only asthma biologic currently FDA-approved in the US.

Wright, 2021

42

42

M.E. (continued)

- Where do we go with her?
- Plan:
 - ICS with LABA (formoterol)
 - Return for f/u in 4 - 6 weeks
 - If well-controlled, continue x 3 months
 - If not well-controlled, step up care

Wright, 2021 43

43

Major Focus in EPR-3

- Controlling asthma is a major focus of the EPR-3 guidelines

Wright, 2021

44

Assessing Asthma Control
(Youths ≥12 Years of Age and Adults)

Follow-up Visits: Determine Level of Control and Treatment Needed				
Components of Control	Well-controlled	Not Well-controlled	Very Poorly Controlled	
Impairment	Symptoms	≤2 days/week	>2 days/week	Throughout the day
	Nighttime awakenings	≤2 x/month	1-3x/week	≥4x/week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short-acting beta ₂ -agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week	Several times per day
	FEV ₁ or peak flow	>80% predicted/personal best	60-80% predicted/personal best	<60% predicted/personal best
	Validated Questionnaires ATAQ ACQ ACT	0 ≤0.75* ≥20	1-2 ≥1.5 16-19	3-4 N/A ≤15
Risk	Exacerbations	0-1/year ≥2/year (see note) Consider severity and interval since last exacerbation		
	Progressive loss of lung function Treatment-related adverse effects	Evaluation requires long-term follow-up care Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk.		

*ACT values of 0-7.0, 1-4 are indicators for poor, not well-controlled asthma. Wright, 2021
Note: EIB, exercise-induced bronchospasm; FEV₁, forced expiratory volume in 1 second. See Figure 3-8 for full name and source of ATAQ, ACQ, ACT.

45

**Monitoring Control in Clinical Practice:
Asthma Control Test™ for Patients Aged ≥12 Years¹**

1. In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work, school or at home?
 All of the time Most of the time Some of the time A little of the time None of the time

2. During the past 4 weeks, how often have you had shortness of breath?
 More than once a day Once a day 3 to 6 times a week Once or twice a week Not at all

3. During the past 4 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 nights a week 2 or 3 nights a week Once a week Once or twice Not at all

4. During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?
 3 or more times per day 1 or 2 times per day 2 or 3 times per week Once a week or less Not at all

5. How would you rate your asthma control during the past 4 weeks?
 Not controlled at all Poorly controlled Somewhat controlled Well controlled Completely controlled

Level of Control Based on Composite Score²

≥20 = **Controlled**

16-19 = **Not Well Controlled**

≤15 = **Very Poorly Controlled**

Regardless of patient's self assessment of control in Question 5

1. Asthma Control Test™ copyright, QualityMetric Incorporated 2002, 2004. All rights reserved.
 2. Available at: <http://www.nhlbi.nih.gov/od/asthma/asthmaexp/0responpage.cfm>, Wright, 2021

46

Short -Acting Beta-2 Agonists

- Albuterol (Proventil HFA, Ventolin HFA, ProAir HFA, Xopenex HFA)
 - 90mcg/puff, 200 puffs
 - 1 - 2 puffs every 4-6 hours or 2 puffs 15 minutes before exercise
 - Onset: 5 minutes
- Generic albuterol HFA is now available

Wright, 2021

47

Short-Acting Beta-2 Agonists

- Usage of these medications more than 2 times/week is indicative of poor control
- 1 inhaler = 200 inhalations

Wright, 2021

48

Controller Medications

Wright, 2021 49

49

Maintenance or Prevention is the Key

- Good management is the key to preventing exacerbations and hospitalizations

Wright, 2021 50

50

Inhaled Corticosteroids

- Most potent and effective anti-inflammatory medication currently available

Wright, 2021 51

51

Inhaled Corticosteroids

- Examples
 - Beclomethasone (QVAR)
 - Budesonide (Pulmicort)
 - Fluticasone (Flovent, ArmonAir, Arnuity Ellipta)
 - Mometasone (Asmanex)
 - Ciclesonide (Alvesco)

Wright, 2021 52

52

Comparative Daily Doses: ICS

ESTIMATED COMPARATIVE DAILY DOSAGES: INHALED CORTICOSTEROIDS FOR LONG-TERM ASTHMA CONTROL

Daily Dose	0-4 years of age			5-9 years of age			≥10 years of age		
	Low	Medium	High	Low	Medium	High	Low	Medium	High
Beclomethasone HFA	N/A	N/A	N/A	80-160 mcg	160-320 mcg	320 mcg	80-160 mcg	160-320 mcg	320-640 mcg
40 mcg/actuator				1-2 puffs, 2x/day	2-4 puffs, 2x/day	4 puffs, 2x/day	1-2 puffs, 2x/day	2-4 puffs, 2x/day	4-8 puffs, 2x/day
80 mcg/actuator				1 puff, 2x/day	2 puffs, 2x/day	4 puffs, 2x/day	1 puff, 2x/day	2 puffs, 2x/day	4 puffs, 2x/day
Budesonide DPI	N/A	N/A	N/A	80-160 mcg	160-320 mcg	320 mcg	80-160 mcg	160-320 mcg	320-640 mcg
80 mcg/inhalation				1-2 inhaler, 2x/day	2-4 inhaler, 2x/day	4 inhaler, 2x/day	1-2 inhaler, 2x/day	2-4 inhaler, 2x/day	4-8 inhaler, 2x/day
160 mcg/inhalation				1-2 inhaler, 2x/day	2-4 inhaler, 2x/day	4 inhaler, 2x/day	1-2 inhaler, 2x/day	2-4 inhaler, 2x/day	4-8 inhaler, 2x/day
Budesonide Nebuizer	0.25-0.5 mg	0.5-1 mg	1-2 mg	0.5 mg	1 mg	2 mg	N/A	N/A	N/A
0.25 mg	0.5 mg/2 puffs	1 mg/2 puffs	2 mg/2 puffs	1 puff, 2x/day	1 puff, 2x/day	2 puffs, 2x/day			
0.5 mg	1 puff, 2x/day	2 puffs, 2x/day	4 puffs, 2x/day	1 puff, 2x/day	2 puffs, 2x/day	4 puffs, 2x/day			
1 mg	2 puffs, 2x/day	4 puffs, 2x/day	8 puffs, 2x/day	2 puffs, 2x/day	4 puffs, 2x/day	8 puffs, 2x/day			
Fluticasone HFA	N/A	N/A	N/A	80-160 mcg	160-320 mcg	320 mcg	80-160 mcg	160-320 mcg	320-640 mcg
80 mcg/actuator				1-2 puffs, 2x/day	2-4 puffs, 2x/day	4 puffs, 2x/day	1-2 puffs, 2x/day	2-4 puffs, 2x/day	4-8 puffs, 2x/day
160 mcg/actuator				1 puff, 2x/day	2 puffs, 2x/day	4 puffs, 2x/day	1 puff, 2x/day	2 puffs, 2x/day	4 puffs, 2x/day
Mometasone HFA	N/A	N/A	N/A	100 mcg	200-400 mcg	400 mcg	100 mcg	200-400 mcg	400-800 mcg
100 mcg/actuator				1 puff, 2x/day	2 puffs, 2x/day	4 puffs, 2x/day	1 puff, 2x/day	2 puffs, 2x/day	4 puffs, 2x/day
200 mcg/actuator				1 puff, 2x/day	2 puffs, 2x/day	4 puffs, 2x/day	1 puff, 2x/day	2 puffs, 2x/day	4 puffs, 2x/day

https://www.nhlbi.nih.gov/files/docs/guidelines/asthma_qrg.pdf

53

To Reduce Side Effects of Inhaled Corticosteroids

- Administer with spacers or holding chambers
- Rinse mouth after inhalation
- Use lowest possible dose to maintain control
- Children - monitor growth

Wright, 2021 54

54

Schenkel, E. et. al

- 98 patients randomized to either placebo or mometasone furoate aqueous nasal spray
- Ages: 3 - 9 years
- After 1 year, there was no suppression of height in the children using the nasal corticosteroid when compared with the child using placebo

Pediatrics Vol 105 No. 2 February 2000, p. 22

Wright, 2021

55

55

Remember...

- Poorly controlled asthma often delays growth
- In general, children with asthma tend to have longer periods of reduced growth rates prior to puberty

Wright, 2021

56

56

Leukotriene Receptor Antagonists

- Cysteinyl leukotriene production in the body has been associated with airway edema, smooth muscle constriction and the inflammatory process
- These medications block the leukotriene receptors which in turn is able to prevent inflammation and bronchoconstriction

Wright, 2021

57

57

Leukotriene Receptor Antagonists

(Zafirlukast) Accolate

- 10mg bid for ages 5-11
- 20mg bid for 12 and older
- Studied in children as young as 5
- Avoid food 1 hour before and 2 hours after taking: Food decreases the bioavailability of Accolate
- Metabolism: Metabolized through the CY P450 2C9 and 3A4 pathways
 - Major pathways in the body
 - Numerous other medications use this same pathway

Wright, 2021

58

58

Zafirlukast (Accolate)

- Drug/Drug Interactions
 - Aspirin: Increased zafirlukast levels by 40%
 - Erythromycin: 40% decrease in zafirlukast
 - Theophylline: Postmarketing reports of increased theophylline levels
 - Coumadin: 35% increase in PT/INR

Wright, 2021

59

59

Zafirlukast (Accolate)

- Side effects
 - Headache (12.9%)
 - Dizziness
 - Nausea
 - Churg Strauss syndrome
- Pregnancy: B
- Precautions
 - Not for an acute exacerbation

Wright, 2021

60

60

Montelukast (Singulair)

- (Montelukast) Singulair
 - 4 mg Granules once daily: 12 – 23 months
 - 4 mg tablet for children 2 - 5 years of age
 - 5mg qhs for ages 6-14
 - 10mg qhs for ages 15 and older

Wright, 2021

61

61

Montelukast (Singulair)

- Drug Interactions
 - Metabolized through CYP2A6 (minor pathway)
 - Phenobarbital: decreases montelukast but no dosage adjustment is required
- Side effects: headache, fatigue, dizziness, Churg-Strauss
- Precautions
 - Not for an acute exacerbation
- Category: B

Wright, 2021

62

62

Updates

- Montelukast (Singulair)
 - FDA strengthened warnings re: serious behavior changes and mood changes

Wright, 2021

63

63

Methylxanthines

- Theophylline
 - Theo-24, Theo-Dur, Uni-Dur, Slo-Bid
 - Bronchodilates and increases the force with which the diaphragm contracts
 - 6 years and older
 - Difficult to manage and as a result has not really gained wide spread acceptance
 - Indicated for individuals with moderate to severe asthma
 - Numerous drug interactions

64

64

Theophylline

- Numerous medications, foods and chemicals interact with theophylline
 - All of the following decrease theophylline levels
 - Smoking (cigarettes and marijuana)
 - High protein/low carbohydrate diet
 - Phenytoin
 - Phenobarbital
 - Carbamazepine
 - Ketoconazole
 - Diuretics

Wright, 2021

65

65

Theophylline

- Theophylline levels (normal 6-15mcg/dL)
 - 15-25: GI upset, N/V, diarrhea, abdominal pain
 - 25-35: Tachycardia, occasional PVC's
 - >35: Ventricular tachycardia, seizures
- Category: C

Wright, 2021

66

66

Long-Acting Beta-2 Agonists

- Salmeterol (Serevent)
 - Diskus
 - ≥ 4 years of age-1 puff po q 12 hours
 - No role for acute exacerbations
 - Seems to help children affected by the nocturnal cough and wheezing
 - Good for prevention of exercise induced asthma

Wright, 2021 67

67

Long-Acting Beta-2 Agonists

- Formoterol (Foradil, Perforomist)
 - ≥ 5 years of age: 1 inhalation every 12 hours
 - May be used for prevention of EIB
- Olodaterol (Striverdi Respimat)
 - Indicated for COPD only
- Indacaterol (Arcapta Neohaler)
 - Indicated for COPD only

Wright, 2021 68

68

LABA

- ~~REMOVED: FDA warning regarding increased deaths in patients treated with LABA~~
- Should be used only with inhaled corticosteroid in the patient with asthma

www.fda.gov/CDER/Drug/infopage/LABA/default.htm accessed 07-20-2010

Wright, 2021 69

69

Combination Products

- Fluticasone/salmeterol (Advair, AirDuo, Wixela Inhub)
- Budesonide/formoterol (Symbicort)
- Mometasone/formoterol (Dulera)
- Fluticasone/vilanterol (Breo Ellipta)

Wright, 2021 70

70

Monoclonal Antibodies

Wright, 2021 71

71

Omalizumab (Xolair)

- Indicated for adults and adolescents (6 and older) with moderate to severe persistent asthma who have a positive skin test or *in vitro* reactivity to a perennial aeroallergen
- And...whose symptoms are inadequately controlled with inhaled corticosteroids
- SC injection (weight and IGE based)
- Every 2 – 4 weeks
- Warning: anaphylaxis

Wright, 2021 72

72

Omalizumab (Xolair)

- Recombinant DNA-derived humanized IgG1 monoclonal antibody that selectively binds to human immunoglobulin E (IgE).
- Inhibits the binding of IgE to the high-affinity IgE receptor on the surface of mast cells and basophils
- Limits the degree of release of mediators of the allergic response.

Wright, 2021

73

73

Eosinophilic phenotypes

- Interleukin-4/13 antagonist
 - Dupilumab (Dupixent)
- Interleukin-5 antagonists
 - Mepolizumab (Nucala)
 - Reslizumab (Cinqair)
 - Benralizumab (Fasenra)

Wright, 2021

74

74

LAMA

- LAMA
 - Long acting bronchodilator
 - Increasing/emerging role in the management of asthma
 - Controller medication
 - LAMA are only added to patient with poorly controlled asthma after LABA/ICS is in place

Wright, 2021

75

75

LAMA

- Caution: urinary retention and glaucoma
- Approved LAMA
 - Tiotropium bromide: approved 6 years of age and older - asthma

Wright, 2021

76

76

Triple Drug Therapy

- Fluticasone, umeclidinium, and vilanterol (Trelegy Ellipta)
 - 1 inhalation daily

Wright, 2021

77

77

Fractional Exhaled Nitric Oxide

- Nitric oxide can be measured in exhaled breath
- Measure of airway inflammation
- Used:
 - When diagnosis is uncertain
 - In children 4 years of age and younger with recurrent wheezing

<https://www.nhlbi.nih.gov/health-topics/all-publications-and-resources/2020-focused-updates-asthma-management-guidelines>

Wright, 2021

78

78

Fractional Exhaled Nitric Oxide

- FeNO > 50 ppb (or > 35 ppb in children ages 5 – 12 years) are consistent with elevated T2 (Type 2) inflammation and support diagnosis of asthma
- Allergic rhinitis can increase FeNO levels as well; interpret cautiously

<https://www.nhlbi.nih.gov/health-topics/all-publications-and-resources/2020-focused-updates-asthma-management-guidelines>

79

79

FeNO Testing



© MRCO FOUNDATION FOR MEDICAL EDUCATION AND RESEARCH. ALL RIGHTS RESERVED.

Wright, 2021

80

80

Last....

- Don't forget to treat the nose
- 85% of individuals with asthma have concomitant allergic rhinitis

Wright, 2021

81

81

Allergic Facies



82
fig

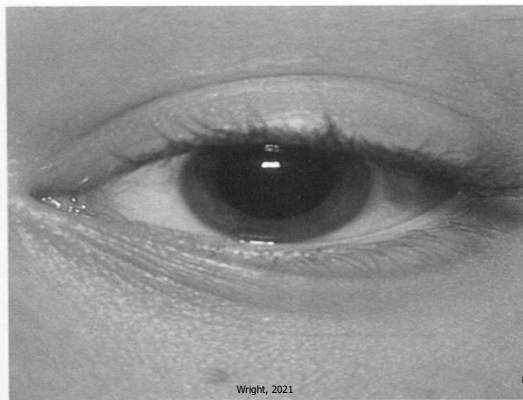
82



Wright, 2021

83

83



Wright, 2021

84

84

Consider Immunotherapy

- SCIT
- SLIT
- Consider as an adjunct for individuals with significant or unresponsive allergens/allergic rhinitis

Wright, 2021

85

85

Acute Asthma Exacerbation Management

Wright, 2021

86

86

Severity of Acute Exacerbations

FIGURE 5-1. CLASSIFYING SEVERITY OF ASTHMA EXACERBATIONS IN THE URGENT OR EMERGENCY CARE SETTING

Note: Patients are instructed to use quick-relief medications if symptoms occur or if PEF drops below 80 percent predicted or personal best. If PEF is 50–79 percent, the patient should monitor response to quick-relief medication carefully and consider contacting a clinician. If PEF is below 50 percent, immediate medical care is usually required in the urgent or emergency care setting; the following parameters describe the severity and likely clinical course of an exacerbation.

	Symptoms and Signs	Initial PEF (or FEV ₁)	Clinical Course
Mild	Dyspnea only with activity (assess tachypnea in young children)	PEF ≥70 percent predicted or personal best	<ul style="list-style-type: none"> • Usually cared for at home • Prompt relief with inhaled SABA • Possible short course of oral systemic corticosteroids
Moderate	Dyspnea interferes with or limits usual activity	PEF 40–69 percent predicted or personal best	<ul style="list-style-type: none"> • Usually requires office or ED visit • Relief from frequent inhaled SABA • Oral systemic corticosteroids; some symptoms last for 1–2 days after treatment is begun
Severe	Dyspnea at rest; interferes with conversation	PEF <40 percent predicted or personal best	<ul style="list-style-type: none"> • Usually requires ED visit and likely hospitalization • Partial relief from frequent inhaled SABA • Oral systemic corticosteroids; some symptoms last for >3 days after treatment is begun • Adjunctive therapies are helpful
Subse^c: Life threatening	Too dyspneic to speak; peripneic	PEF <25 percent predicted or personal best	<ul style="list-style-type: none"> • Requires ED hospitalization; possible ICU • Minimal or no relief from frequent inhaled SABA • Intravenous corticosteroids • Adjunctive therapies are helpful

Key: ED, emergency department; FEV₁, forced expiratory volume in 1 second; ICU, intensive care unit; PEF, peak expiratory flow; SABA, short-acting beta₂-agonist

<http://www.nhlbi.nih.gov/guidelines/asthma/asthsumm.pdf> accessed 06-15-2019, Wright, 2021

87

Acute Asthma Exacerbation

- Measure FEV1
- Inhaled short acting beta 2 agonist: Up to three treatments of 2-4 puffs by MDI at 20 minute intervals OR a single nebulizer
- Can repeat x 1 – 2 provided patient tolerates
- Prednisone
 - What dose and schedule??

Wright, 2021

88

88

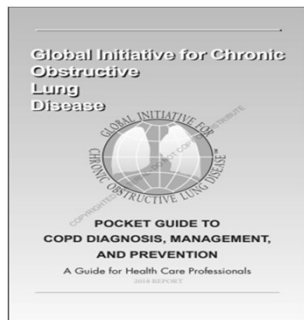
COPD

Wright, 2021

89

89

Global Initiative for Chronic Obstructive Lung Disease, 2018



Wright, 2021

90

90

Case Study

- 55 year old male
- Presents with 3 year history of worsening SOB on exertion
 - Denies chest pain, diaphoresis, palpitations, lightheadedness
- Smoker x 35 years; 1 ppd

Wright, 2021 91

91

Case Study

- PMH
 - Asthma in childhood
- ROS
 - Wheezing with exercise and URI's
 - Sputum production every morning

Wright, 2021 92

92

Case Study

- Physical examination
 - VS: 128/78, Pulse: 88, RR: 20, Temp: 97.2
 - HEENT: normal
 - Heart: S1, S2, RRR; no S3, S4, murmurs
 - Lungs: clear, but diminished
 - O2 sat – 97% on RA

Wright, 2021 93

93



COPD Definition

▶ Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.

94



Definition and Overview

OVERALL KEY POINTS:

- ▶ The most common respiratory symptoms include dyspnea, cough and/or sputum production.
- ▶ The main risk factor for COPD is tobacco smoking but other environmental exposures such as biomass fuel exposure and air pollution may contribute.

95



Chronic Obstructive Pulmonary Disease (COPD)

- ▶ COPD is currently the fourth leading cause of death in the world.¹
- ▶ COPD is projected to be the 3rd leading cause of death by 2020.²
- ▶ More than 3 million people died of COPD in 2012 accounting for 6% of all deaths globally.
- ▶ Globally, the COPD burden is projected to increase in coming decades because of continued exposure to COPD risk factors and aging of the population.

1. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; 380: 209-249.
2. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med* 2006; 3(11): e142.

96



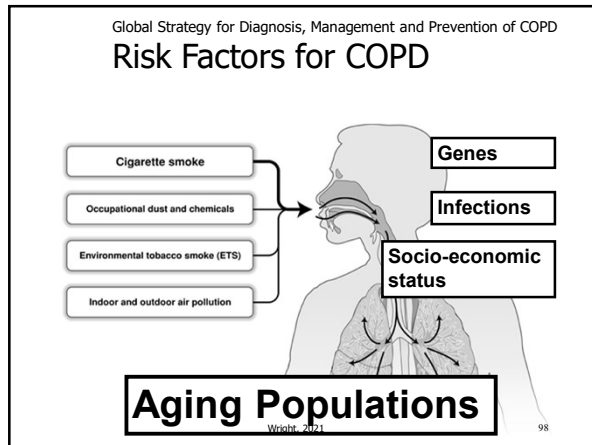
Economic and Social Burden

Economic burden of COPD

- ▶ COPD is associated with significant economic burden.
- ▶ COPD exacerbations account for the greatest proportion of the total COPD burden.
- ▶ USA:
 - Direct costs of COPD are \$32 billion
 - Indirect costs \$20.4 billion.

© 2017 Global Initiative for Chronic Obstructive Lung Disease Wright, 2021 97

97




98

Alpha-1 antitrypsin deficiency (AATD)

- Alpha-1 antitrypsin deficiency (AATD) screening
 - Screen all individuals with COPD, particularly those who live in areas of high prevalence
 - Levels < 20% may suggest familial homozygous deficiency and family members should be screened

<https://goldcopd.org/wp-content/uploads/2018/02/WMS-GOLD-2018-Feb-Final-to-print-v2.pdf>
Wright, 2021 99

99



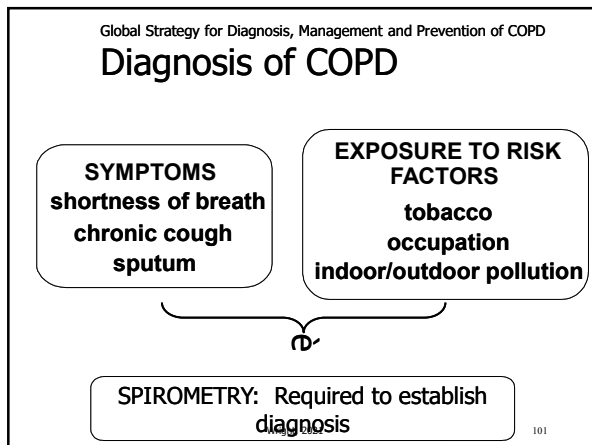
Diagnosis and Initial Assessment

OVERALL KEY POINTS:

- ▶ COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease.
- ▶ Spirometry is required to make the diagnosis; the presence of a post-bronchodilator FEV₁/FVC < 0.70 confirms the presence of persistent airflow limitation.
- ▶ The goals of COPD assessment are to determine the level of airflow limitation, the impact of disease on the patient's health status, and the risk of future events (such as exacerbations, hospital admissions, or death), in order to guide therapy.

© 2017 Global Initiative for Chronic Obstructive Lung Disease 100

100



101

Global Strategy for Diagnosis, Management and Prevention of COPD

Assessment of Airflow Limitation: Spirometry

- Spirometry should be performed after the administration of an adequate dose of a short-acting inhaled bronchodilator to minimize variability.
- A post-bronchodilator FEV₁/FVC < 0.70 confirms the presence of airflow limitation.
- Where possible, values should be compared to age-related normal values to avoid overdiagnosis of COPD in the elderly.

Wright, 2021 102

102

Spirometry Testing

- CPT codes

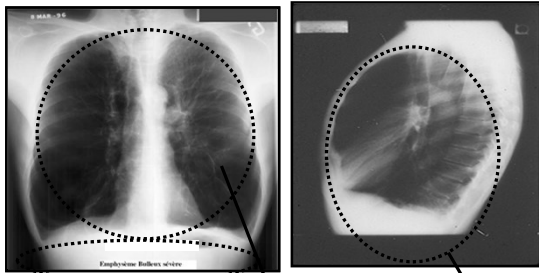
- 94010: \$32.84 (FEV1/FVC)
- 94060: \$56.65 (spirometry before and after bronchodilator)
- 94375: \$36.81 (flow loop)
- 94620: \$64.59 (pulmonary stress test)

Wright, 2021

103

103

Utilized with permission from Fitzgerald Health Education Associates, 2007



Low, Flattened Diaphragm Increased A-P Diameter
Air Trapping

Wright, 2021

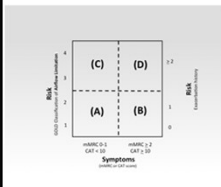
104

104

Global Strategy for Diagnosis, Management and Prevention of COPD

Combined Assessment of COPD

When assessing risk, choose the **highest** risk according to GOLD grade or exacerbation history



Patient	Characteristic	Spirometric Classification	Exacerbations per year	mMRC	CAT
A	Low Risk Less Symptoms	GOLD 1-2	≤ 1	0-1	< 10
B	Low Risk More Symptoms	GOLD 1-2	≤ 1	≥ 2	≥ 10
C	High Risk Less Symptoms	GOLD 3-4	≥ 2	0-1	< 10
D	High Risk More Symptoms	GOLD 3-4	≥ 2	≥ 2	≥ 10

Wright, 2021

105

105

Global Strategy for Diagnosis, Management and Prevention of COPD
Assessment of COPD

■ Assess symptoms

Use the COPD Assessment Test(CAT)
or
mMRC Breathlessness scale

Wright, 2021 106

106

Global Strategy for Diagnosis, Management and Prevention of COPD
Assessment of Symptoms

COPD Assessment Test (CAT): An 8-item measure of health status impairment in COPD (<http://catestonline.org>).

Breathlessness Measurement using the Modified British Medical Research Council (mMRC) Questionnaire: relates well to other measures of health status and predicts future mortality risk.

Wright, 2021 107

107

CAT: What are the questions?

Example: I am very happy X I am very sad

QUESTION	SCORE
I breathe enough	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> I cough all the time
I have no phlegm (sputum) in my chest at all	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> My chest is completely full of phlegm (sputum)
My chest does not feel tight at all	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> My chest feels very tight
When I walk up a hill or one flight of stairs I am out of breath	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> When I walk up a hill or one flight of stairs I am very breathless
I am not limited doing any activities at home	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> I am very limited doing activities at home
I am confident leaving my home despite my lung condition	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> I am not at all confident leaving my home because of my lung condition
I sleep soundly	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> I don't sleep soundly because of my lung condition
I have lots of energy	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> I have no energy at all

TOTAL SCORE

Reproduced from: COPD Assessment Test Healthcare Professional User Guide
Wright, 2021

108

108

Classification of Severity of Airflow Limitation in COPD*

In patients with $FEV_1/FVC < 0.70$:

- GOLD 1: Mild $FEV_1 \geq 80\%$ predicted
- GOLD 2: Moderate $50\% \leq FEV_1 < 80\%$ predicted
- GOLD 3: Severe $30\% \leq FEV_1 < 50\%$ predicted
- GOLD 4: Very Severe $FEV_1 < 30\%$ predicted

**Based on Post-Bronchodilator FEV_1*

Wright, 2021

109

109

Case Study

- Spirometry Test Results

- FEV1

- Pre-bronchodilator: 2.22 L (69%)
- Postbronchodilator: 243 L (76%)
- Change: 9%

- FVC

- Pre: 4.22 L (107%)
- Post: 4.45 L (113%)
- Change: 5%

Wright, 2021

110

110

Case Study

- Spirometry Test Results

- FEV1/FVC

- Pre: 53%
- Post: 55%

- CAT test: 12

Wright, 2021

111

111

Global Strategy for Diagnosis, Management and Prevention of COPD

Combined Assessment of COPD

When assessing risk, choose the **highest** risk according to GOLD grade or exacerbation history

Patient	Characteristic	Spirometric Classification	Exacerbations per year	mMRC	CAT
A	Low Risk Less Symptoms	GOLD 1-2	≤ 1	0-1	< 10
B	Low Risk More Symptoms	GOLD 1-2	≤ 1	≥ 2	≥ 10
C	High Risk Less Symptoms	GOLD 3-4	≥ 2	0-1	< 10
D	High Risk More Symptoms	GOLD 3-4	≥ 2	≥ 2	≥ 10

Wright, 2021 112

112

ABCD Assessment Tool

Figure 2.4. The refined ABCD assessment tool

© 2017 Global Initiative for COPD. Obstructive Lung Disease 113

113

What Patient Type is Our Patient?

- A
- B
- C
- D

Wright, 2021 114


114

What Would You Initiate?

- What would you do?
- Which medication would you choose??

Wright, 2021 115

115




Evidence Supporting Prevention & Maintenance Therapy

OVERALL KEY POINTS (1 of 3):

- ▶ Smoking cessation is key. Pharmacotherapy and nicotine replacement reliably increase long-term smoking abstinence rates.
 - ▶ The effectiveness and safety of e-cigarettes as a smoking cessation aid is uncertain at present.
- ▶ Pharmacologic therapy can reduce COPD symptoms, reduce the frequency and severity of exacerbations, and improve health status and exercise tolerance.
- ▶ Inhaler technique needs to be assessed regularly.

© 2017 Global Initiative for Asthma (GINA) 2021 Obstructive Lung Disease 116

116



Evidence Supporting Prevention & Maintenance Therapy

OVERALL KEY POINTS (2 of 3):

- ▶ Influenza vaccination decreases the incidence of lower respiratory tract infections.
- ▶ Pneumococcal vaccination decreases lower respiratory tract infections.
- ▶ Pulmonary rehabilitation improves symptoms, quality of life, and physical and emotional participation in everyday activities.
- ▶ In patients with severe resting chronic hypoxemia, long-term oxygen therapy improves survival.

© 2017 Global Initiative for Asthma (GINA) 2021 Obstructive Lung Disease 117

117

Global Strategy for Diagnosis, Management and Prevention of COPD
Therapeutic Options: COPD Medications

Beta ₂ -agonists
Short-acting beta ₂ -agonists
Long-acting beta ₂ -agonists
Anticholinergics
Short-acting anticholinergics
Long-acting anticholinergics
Combination short-acting beta ₂ -agonists + anticholinergic in one inhaler
Methylxanthines
Inhaled corticosteroids
Combination long-acting beta ₂ -agonists + corticosteroids in one inhaler
Systemic corticosteroids
Phosphodiesterase-4 inhibitors

Wright, 2021 118

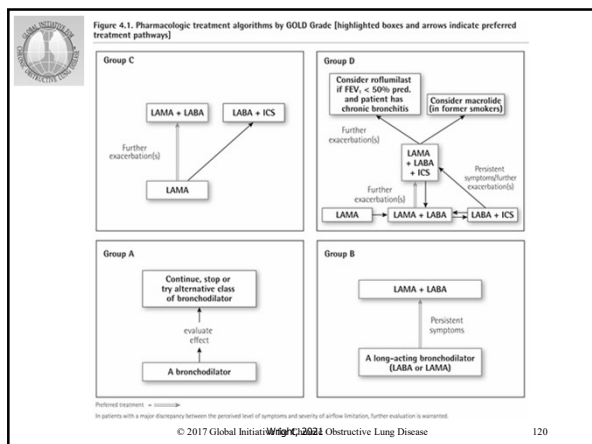
118

Global Strategy for Diagnosis, Management and Prevention of COPD
Manage Stable COPD: Non-pharmacologic

Patient Group	Essential	Recommended	Depending on local guidelines
A	Smoking cessation (can include pharmacologic treatment)	Physical activity	Influenza vaccination Pneumococcal vaccination
B, C, D	Smoking cessation (can include pharmacologic treatment) Pulmonary rehabilitation	Physical activity	Influenza vaccination Pneumococcal vaccination

Wright, 2021 119
© 2014 Global Initiative for Chronic Obstructive Lung Disease

119



120

Pharmacologic treatment algorithms

Group A

- ▶ All Group A patients should be offered bronchodilator treatment based on its effect on breathlessness. This can be either a short- or a long-acting bronchodilator.
- ▶ This should be continued if symptomatic benefit is documented.

© 2017 Global Initiative for Asthma (GINA) Obstructive Lung Disease 121

121

Pharmacologic treatment algorithms

Group B

- ▶ Initial therapy should consist of a long acting bronchodilator. Long-acting inhaled bronchodilators are superior to short-acting bronchodilators taken as needed i.e., *pro re nata* (prn) and are therefore recommended.
- ▶ There is no evidence to recommend one class of long-acting bronchodilators over another for initial relief of symptoms in this group of patients. In the individual patient, the choice should depend on the patient's perception of symptom relief.
- ▶ For patients with persistent breathlessness on monotherapy the use of two bronchodilators is recommended.

© 2017 Global Initiative for Asthma (GINA) Obstructive Lung Disease 122

122

Pharmacologic treatment algorithms

Group B (continued)

- ▶ For patients with severe breathlessness initial therapy with two bronchodilators may be considered.
- ▶ If the addition of a second bronchodilator does not improve symptoms, we suggest the treatment could be stepped down again to a single bronchodilator.
- ▶ Group B patients are likely to have comorbidities that may add to their symptomatology and impact their prognosis, and these possibilities should be investigated.

© 2017 Global Initiative for Asthma (GINA) Obstructive Lung Disease 123

123

Group C

► Initial therapy should consist of a single long acting bronchodilator. In two head-to-head comparisons the tested LAMA was superior to the LABA regarding exacerbation prevention, therefore we recommend starting therapy with a LAMA in this group.

► Patients with persistent exacerbations may benefit from adding a second long acting bronchodilator (LABA/LAMA) or using a combination of a long acting beta₂-agonist and an inhaled corticosteroid (LABA/ICS). As ICS increases the risk for developing pneumonia in some patients, our primary choice is LABA/LAMA.

```
graph LR
    LAMA --> LABA_LAMA[LABA + LABA]
    LAMA --> LABA_IC[LABA + ICS]
    LABA_LAMA --> LABA_IC
    LABA_LAMA ==> PT[Preferred treatment]
```

© 2017 Global Initiative for Asthma Obstructive Lung Disease 124

124

Group D

► We recommend starting therapy with a LABA/LAMA combination because:

- In studies with patient reported outcomes as the primary endpoint LABA/LAMA combinations showed superior results compared to the single substances. If a single bronchodilator is chosen as initial treatment, a LAMA is preferred for exacerbation prevention based on comparison to LABAs (for details see GOLD 2017 Chapter 3).
- A LABA/LAMA combination was superior to a LABA/ICS combination in preventing exacerbations and other patient reported outcomes in Group D patients (for details see GOLD 2017 Chapter 3).
- Group D patients are at higher risk of developing pneumonia when receiving treatment with ICS.

```
graph LR
    LAMA --> LABA_LAMA[LABA + LABA]
    LABA_LAMA --> LABA_LAMA_IC[LABA + LABA + ICS]
    LABA_LAMA_IC ==> PT[Preferred treatment]
    LABA_LAMA --> Consider[Consider inhaled corticosteroid (ICS) if FEV<sub>1</sub> < 50% pred. and patient has chronic bronchitis]
    LABA_LAMA --> Consider2[Consider mucolytic (in former smokers)]
    Consider --> LABA_LAMA_IC
    Consider2 --> LABA_LAMA_IC
```

© 2017 Global Initiative for Asthma Obstructive Lung Disease 125

125

Group D (continued)

► In some patients initial therapy with LABA/ICS may be the first choice. These patients may have a history and/or findings suggestive of asthma-COPD overlap. High blood eosinophil counts may also be considered as a parameter to support the use of ICS, although this is still under debate

► In patients who develop further exacerbations on LABA/LAMA therapy we suggest two alternative pathways:

- Escalation to LABA/LAMA/ICS. Studies are underway comparing the effects of LABA/LAMA vs. LABA/LAMA/ICS for exacerbation prevention.
- Switch to LABA/ICS. However, there is no evidence that switching from LABA/LAMA to LABA/ICS results in better exacerbation prevention. If LABA/ICS therapy does not positively impact exacerbations/symptoms, a LAMA can be added.

```
graph LR
    LABA_LAMA_IC[LABA + LABA + ICS] --> LABA_LAMA_IC_IC[LABA + LABA + LABA + ICS]
    LABA_LAMA_IC_IC ==> PT[Preferred treatment]
```

© 2017 Global Initiative for Asthma Obstructive Lung Disease 126

126

Pharmacologic treatment algorithms

Group D (continued)
 If patients treated with LABA/LAMA/ICS still have exacerbations the following options may be considered:

- ▶ Add roflumilast. This may be considered in patients with an FEV1 < 50% predicted and chronic bronchitis, particularly if they have experienced at least one hospitalization for an exacerbation in the previous year.
- ▶ Add a macrolide. The best available evidence exists for the use of azithromycin. Consideration to the development of resistant organisms should be factored into decision making.
- ▶ Stopping ICS. A reported lack of efficacy, an elevated risk of adverse effects (including pneumonia) and evidence showing no significant harm from withdrawal supports this recommendation

© 2017 Global Initiative for Asthma (GINA) | 2021 Obstructive Lung Disease 127

127

Bronchodilators

- Important pharmacological treatment
 - Short (albuterol) and long acting (formoterol, salmeterol, aformoterol)
 - Improve emptying of lungs, exercise tolerance and reduce hyperinflation

Wright, 2021 128

128

Short Acting Inhaled Beta-2 Agonists

- Albuterol (Proventil HFA, Ventolin HFA, ProAir HFA)
 - 90mcg/puff, 200 puffs
 - 2 puffs q 4-6 hours or 2 puffs 15 minutes before exercise
 - Onset: 5 minutes

Wright, 2021 129

129

Short Acting Anticholinergics

- SAMA
 - Ipratropium bromide (inhaled and nebulized)
- SAMA/SABA
 - Ipratropium bromide/albuterol (inhaled or nebulized)

Wright, 2021 130

130

All Stages...

- SABA or SAMA should be available to individuals with all stages of COPD
- May be used as needed and with exacerbations

Wright, 2021 131

131

Long Acting Muscarinic Antagonists

- LAMAs
 - Umeclidinium inhaled (Incruse Ellipta)
 - Tiotropium inhaled (Spiriva Respimat or Handihaler)
 - Glycopyrrolate inhaled (Lonhala Magnair, Seebri Neohaler)
 - Acridinium bromide inhaled (Tudorza Pressair)
 - Revedfenacin inhaled (Yupelri nebulizer)

Wright, 2021 132

132

Long Acting Beta-2 Agonists

- LABAs
 - Salmeterol (Serevent)
 - Arformoterol inhaled (Brovana, Perforomist)
 - Indacaterol inhaled (Arcapta Neohaler)
 - Olodaterol inhaled (Striverdi Respimat)
 - Formoterol (Foradil Aerolizer)

Wright, 2021 133

133

Long Acting Muscarinic Antagonists/Long-Acting Beta-2 Agonists

- LAMA/LABA combination
 - Umeclidinium/vilanterol (Anoro Ellipta)
 - Glycopyrrolate/formoterol (Bevespi Aerosphere)
 - Tiotropium/olodaterol inhaled (Stiolto Respimat)
 - Indacaterol/glycopyrrolate inhaled (Utibron Neohaler)

Wright, 2021 134

134

Inhaled Corticosteroids

- ICSs
 - Beclomethasone (QVAR and QVAR Redihaler)
 - Budesonide (Pulmicort Flexhaler and Respules)
 - Flunisolide (AeroBid, Aerospan)
 - Fluticasone (Flovent, Arnuity Ellipta, ArmonAir)
 - Mometasone (Asmanex HFA and Twisthaler)
 - Ciclesonide (Alvesco)

Wright, 2021 135

135

Triple Drug Inhaler

- Fluticasone furoate/umeclidinium/vilanterol inhaled (Trelegy Ellipta)

Wright, 2021 136

136

Methylxanthines

- Theophylline
 - Theo-24, Theo-Dur, Uni-Dur, Slo-Bid
 - Bronchodilates and increases the force with which the diaphragm contracts
 - 6 years and older
 - Difficult to manage and as a result has not really gained wide spread acceptance
 - Indicated for individuals with moderate to severe asthma
 - Numerous drug interactions

137

137

Phosphodiesterase-4 Inhibitors

- PDE-4s
 - Roflumilast (Daliresp)
 - 250 mcg once daily x 4 weeks then...
 - 500 mcg po once daily
 - Caution: liver disease, mood changes
 - Decreases acute exacerbations by approximately 20% - 25%

Wright, 2021 138

138

Antimicrobials

- Macrolide antimicrobial
 - Nonsmokers
 - Best evidence exists with azithromycin 250 mg daily
 - Macrolides have anti-inflammatory and immunoregulatory effects
 - Potential QT prolongation and temporary and permanent hearing deficits

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4203601/> accessed 02-24-2019
Wright, 2021

139

Long-term oxygen therapy

- Goal
 - To ensure adequate oxygen delivery to the vital organs by increasing the baseline PaO₂ at rest to => 60 mm Hg at sea level and/ or producing a SaO₂ => 90%.

Utilized with permission from Fitzgerald Health Education Associates, 2008
Wright, 2021

140

Long-term oxygen therapy

- Indications to initiate long-term (> 15 hours/day) oxygen therapy
 - PaO₂ < 55 mmHg or SaO₂ < 88%
 - OR... PaO₂ > 55 but < 60 mmHg with right heart failure or erythrocytosis
 - Goal: SaO₂ ≥ 90%

• Source- www.goldcopd.org

141

141

Pulmonary Rehab

- Exercise training
- Nutrition counseling
- Education
- Conducted over 6 weeks
- Improves exercise performance and reduces dyspnea (no improvement on FEV1)

Wright, 2021 142

142

Surgery

- Bullectomy
- Lung Volume Reduction Surgery
- Lung transplant surgery

Wright, 2021 143

143

Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Exacerbations

An exacerbation of COPD is:

“an acute event characterized by a worsening of the patient’s respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication.”

Wright, 2021 144

144



Management of Exacerbations

OVERALL KEY POINTS (1 of 3):

- ▶ An exacerbation of COPD is defined as an acute worsening of respiratory symptoms that results in additional therapy.
- ▶ Exacerbations of COPD can be precipitated by several factors. The most common causes are respiratory tract infections.
- ▶ The goal for treatment of COPD exacerbations is to minimize the negative impact of the current exacerbation and to prevent subsequent events.
- ▶ Short-acting inhaled beta₂-agonists, with or without short-acting anticholinergics, are recommended as the initial bronchodilators to treat an acute exacerbation.

© 2017 Global Initiative for Chronic Obstructive Lung Disease 145

145



Management of Exacerbations

OVERALL KEY POINTS (2 of 3):

- ▶ Maintenance therapy with long-acting bronchodilators should be initiated as soon as possible before hospital discharge.
- ▶ Systemic corticosteroids can improve lung function (FEV₁), oxygenation and shorten recovery time and hospitalization duration. Duration of therapy should not be more than 5-7 days.
- ▶ Antibiotics, when indicated, can shorten recovery time, reduce the risk of early relapse, treatment failure, and hospitalization duration. Duration of therapy should be 5-7 days.
- ▶ Methylxanthines are not recommended due to increased side effect profiles.

© 2017 Global Initiative for Chronic Obstructive Lung Disease 146

146



Management of Exacerbations

OVERALL KEY POINTS (3 of 3):

- ▶ Non-invasive mechanical ventilation should be the first mode of ventilation used in COPD patients with acute respiratory failure who have no absolute contraindication because it improves gas exchange, reduces work of breathing and the need for intubation, decreases hospitalization duration and improves survival.
- ▶ Following an exacerbation, appropriate measures for exacerbation prevention should be initiated

© 2017 Global Initiative for Chronic Obstructive Lung Disease 147

147



Management of Exacerbations

COPD exacerbations are defined as an acute worsening of respiratory symptoms that result in additional therapy.

► They are classified as:

- Mild (treated with short acting bronchodilators only, SABDs)
- Moderate (treated with SABDs plus antibiotics and/or oral corticosteroids) or
- Severe (patient requires hospitalization or visits the emergency room). Severe exacerbations may also be associated with acute respiratory failure.

© 2017 Global Initiative for Chronic Obstructive Lung Disease 148

148

Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Exacerbations: Key Points

- The most common causes of COPD exacerbations are viral upper respiratory tract infections and infection of the tracheobronchial tree.
- Diagnosis relies exclusively on the clinical presentation of the patient complaining of an acute change of symptoms that is beyond normal day-to-day variation.
- The goal of treatment is to minimize the impact of the current exacerbation and to prevent the development of subsequent exacerbations.

Wright, 2021 149

149

Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Exacerbations: Key Points

- Short-acting inhaled beta₂-agonists with or without short-acting anticholinergics are usually the preferred bronchodilators for treatment of an exacerbation.
- Systemic corticosteroids and antibiotics can shorten recovery time, improve lung function (FEV₁) and arterial hypoxemia (PaO₂), and reduce the risk of early relapse, treatment failure, and length of hospital stay.
- COPD exacerbations can often be prevented.

Wright, 2021 150

150

Global Strategy for Diagnosis, Management and Prevention of COPD
Manage Exacerbations: Treatment Options

Oxygen: titrate to improve the patient's hypoxemia with a target saturation of 88-92%.

Bronchodilators: Short-acting inhaled beta₂-agonists with or without short-acting anticholinergics are preferred.

Systemic Corticosteroids: Shorten recovery time, improve lung function (FEV₁) and arterial hypoxemia (PaO₂), and reduce the risk of early relapse, treatment failure, and length of hospital stay. A dose of 30-40 mg prednisolone per day for 5 – 7 days is recommended.

Wright, 2021 151

151

New Information Emerging...

- 40 mg daily x 5 days may be all that is necessary for exacerbation of COPD
- Equal outcomes

Wright, 2021 152

152

Global Strategy for Diagnosis, Management and Prevention of COPD
Manage Exacerbations: Treatment Options

Antibiotics should be considered and/or prescribed with moderate – severe exacerbations:

- Three cardinal symptoms: increased dyspnea, increased sputum volume, and increased sputum purulence.
- Who require mechanical ventilation or hospitalization.

Wright, 2021 153

153

Antimicrobial Therapy	
<p>Mild to Moderate Exacerbations Antimicrobial therapy may not be indicated. If prescribed, consider spectrum of antimicrobial activity and side effects)</p>	<p>If prescribed, use one of the following:</p> <ol style="list-style-type: none"> 1. Amoxicillin 875 mg 1 pill bid x 5 – 7 days 2. TMP-SMX DS 1 pill bid x 5 – 7 days 3. Doxycycline 100 mg 1 pill bid x 5 – 7 days 4. Cephalosporin (cefдинир, cefpodoxime, cefuroxime)
<p>More Moderate - Severe Exacerbations</p> <p>Severe: hospital admission</p>	<p>Use one of the following:</p> <ol style="list-style-type: none"> 1. Amoxicillin-clavulanate 875 mg 1 pill bid x 5 – 7 days 2. Cephalosporin: 2nd – 3rd generation 3. Azithromycin or clarithromycin 4. Respiratory fluoroquinolone (moxifloxacin or levofloxacin)
<p><small>Source: Gilbert, D., Chambers, H., Saag, M., Pavia, A. (2017) The Sanford Guide to Antimicrobial Therapy (47th ed.). Sperryville, VA: Antimicrobial Therapy, Inc. 154</small></p>	

154

FDA Warning
<ul style="list-style-type: none"> • Fluoroquinolones: <ul style="list-style-type: none"> – Spontaneous tendon rupture – Tendonitis – Peripheral neuropathy – Aortic dissection – Significant hypoglycemia <p><small>https://www.forbes.com/sites/brucelee/2018/12/21/fda-warns-about-what-fluoroquinolone-antibiotics-may-do-to-your-aorta/#121315605e7e</small></p> <p style="text-align: center;"><small>Wright, 2021 155</small></p>

155

Global Strategy for Diagnosis, Management and Prevention of COPD
<p>Manage Exacerbations:</p> <p>Indications for Hospital Admission</p> <hr/> <ul style="list-style-type: none"> ▪ Marked increase in intensity of symptoms ▪ Severe underlying COPD ▪ Onset of new physical signs ▪ Failure of an exacerbation to respond to initial medical management ▪ Presence of serious comorbidities ▪ Frequent exacerbations ▪ Older age ▪ Insufficient home support <p style="text-align: center;"><small>Wright, 2021 156</small></p>

156

Emerging Infectious Diseases

Wright, 2021 157

157

WHO in 2019:
What's Driving Infectious Diseases

- Antibiotic overuse and antimicrobial resistance
 - Resistant *C. difficile*
 - Resistant *candida* strains
 - Resistant gram negative pathogens
- Vaccine hesitancy and refusals
 - Measles
 - Influenza

Wright, 2021 158

158

Antibiotic overuse and antimicrobial resistance

Wright, 2021 159

159

Neisseria gonorrhoeae

- 2018 statistics
 - 580,000 cases; up 5% from 2017
 - Highest number reported since 1991
- Increasing antimicrobial resistance
 - 5,093 isolates
 - 25.3% resistant to tetracycline
 - 19.2% to ciprofloxacin
 - 16.2% to penicillin

www.cdc.gov accessed 01-19-2021

Wright, 2021 160

160

*Updated 2020:
Neisseria gonorrhoeae*

- Treatment:
 - Single 500 mg IM dose of ceftriaxone for treatment of uncomplicated urogenital, anorectal, and pharyngeal gonorrhea.
 - If over 300 pounds (150kg or more) – 1 gram of ceftriaxone is recommended.
 - If chlamydial infection has not been excluded, concurrent treatment with doxycycline (100 mg orally twice a day for 7 days) is recommended.
- Changes are due to increased antimicrobial resistance to azithromycin

https://www.cdc.gov/mmwr/volumes/69/wr/mm6950a6.htm?s_cid=mm6950a6_w accessed 12-30-2020

Wright, 2021 161

161

*Updated 2020:
Alternatives for N. Gonorrhea Treatment*

- When ceftriaxone cannot be used for treating urogenital or rectal gonorrhea because of cephalosporin allergy, a single 240 mg IM dose of gentamicin plus a single 2 g oral dose of azithromycin is an option.

https://www.cdc.gov/mmwr/volumes/69/wr/mm6950a6.htm?s_cid=mm6950a6_w accessed 12-30-2020

Wright, 2021 162

162

Test of Cure?

- A test-of-cure is unnecessary for persons with uncomplicated urogenital or rectal gonorrhea who are treated with any of the recommended or alternative regimens

https://www.cdc.gov/mmwr/volumes/69/wr/mm6950a6.htm?s_cid=mm6950a6_w accessed 12-30-2020

Wright, 2021

163

163

COVID – 19 Elephant in the Room







Wright, 2021

164

164

Information

-  SARS-CoV-2
-  Disease Called: COVID-19
-  The SARS-CoV-2 virus is a betacoronavirus, like MERS-CoV and SARS-CoV
-  All three of these viruses have their origin in bats; believed to be mix of virus from bats and pangolin from a wet market in Wuhan, China. How it made its way to the people remains a topic of controversy

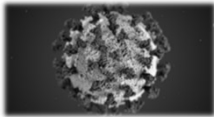
Wright, 2021

165

165

What is a Coronavirus?

- **Common human coronaviruses**
- 1. 229E (alpha coronavirus)
- 2. NL63 (alpha coronavirus)
- 3. OC43 (beta coronavirus)
- 4. HKU1 (beta coronavirus)
- **Other human coronaviruses**
- 5. MERS-CoV (the beta coronavirus that causes Middle East Respiratory Syndrome, or MERS)
- 6. SARS-CoV (the beta coronavirus that causes severe acute respiratory syndrome, or SARS)
- 7. SARS-CoV-2 (the novel coronavirus that causes coronavirus disease 2019, or COVID-19)



DOI: 10.1016/j.cmi.2020.05.004. Retrieved November 26, 2020. From <https://doi.org/10.1016/j.cmi.2020.05.004>

Wright, 2021 166

166

What Happens When Exposed?

Guan, A., Niham, M. Y., Song, K., Lee, H., Wang, S., Shen, T. S., & Feinberg, D. C. (2020). Pathophysiological mechanisms of COVID-19. *Nature Reviews Microbiology*, 18(11), 591-601.

Wright, 2021 167

167

Symptoms

- 2-14 days after exposure
 - Cough
 - Fever
 - Shortness of breath
 - Loss of smell/taste
 - Headaches
 - Nasal congestion
- Some individuals can begin with nausea, vomiting, diarrhea

Wright, 2021 168

168

Extrapulmonary Side Effects

Neurologic
Headaches
Dizziness
Encephalopathy
Guillain-Barre
Aphasia
Myopia
Anemia
Stroke

Renal
Acute kidney injury
Proteinuria
Hematuria
Hypertension

Hepatic
Elevated aminotransferases
Elevated bilirubin

Gastrointestinal
Diarrhea
Nausea/vomiting
Abdominal pain
Anorexia

Thromboembolism
Deep vein thrombosis
Pulmonary embolism
Catheter-related thrombosis
Hemorrhagic stroke

Cardiac
Tachycardia/arrhythmia
Myocardial injury/myocarditis
Cardiac arrhythmias
Cardiogenic shock
Myocardial ischemia
Aortic aneurysm/dissection

Endocrine
Hypoglycemia
Diabetic ketoacidosis

Dermatological
Rash
Livedo reticularis
Erythematous rash
Urticaria
Vasculitis
Purpura-like lesions

Gupta, A., Madhavan, M. V., Sehgal, K., Nair, N., Mahajan, S., Sehrawat, T. S., ... & Freedberg, D. E. (2020). Extrapulmonary manifestations of COVID-19. *Nature medicine*, 26(7), 1017-1032.

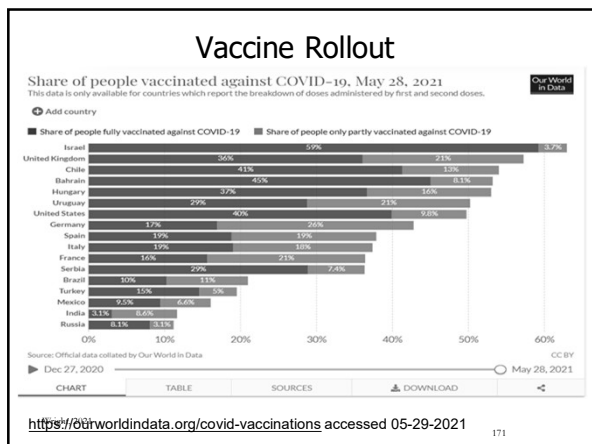
Wright, 2021 169

169

COVID 19 Vaccines

Wright, 2021170

170



171

mRNA Technology

COVID-19 mRNA vaccines are given in the upper arm muscle. Once the instructions (mRNA) are inside the immune cells, the cells use them to make the protein piece. After the protein piece is made, the cell breaks down the instructions and gets rid of them.

Next, the cell displays the protein piece on its surface. Our immune systems recognize that the protein doesn't belong there and begin building an immune response and making antibodies, like what happens in natural infection against COVID-19.

At the end of the process, our bodies have learned how to protect against future infection. The benefit of mRNA vaccines, like all vaccines, is those vaccinated gain this protection without ever having to risk the serious consequences of getting sick with COVID-19.

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/mRNA.html?s_cid=10532:%2Bcovid%20%2Bvaccine%20%2Bchange%20%2Byour%20%2Bdna;sem.b:p:RG:GM:gen:PTN:FY21
 accessed 02-01-2021

172

mRNA Vaccines

<ul style="list-style-type: none"> • Pfizer <ul style="list-style-type: none"> – Two dose series – Separated by 21 days – 52% efficacy 12 days after dose 1 – 95% efficacy 7 days after dose 2 	<ul style="list-style-type: none"> • Moderna <ul style="list-style-type: none"> – Two dose series – Separated by 28 days – 80.2% efficacy after 1 dose – 95.6% efficacy after dose 2 (18-65 years) – 86.4% for those over 65 years
--	---

www.bbc.com/future/article/20211014-covid-19 accessed 01-19-2021
Wright, 2021

173

Approved 2/27/2021

- Johnson & Johnson Vaccine
 - Adenovirus-based vaccine; uses weakened live adenovirus as the delivery method for transporting recombinant vaccine for COVID-19
 - Recombinant vaccines contain a small piece of genetic material from the virus to trigger an immune response
 - Examples of this type: pneumococcal
 - This type of vaccine is generally easy to make
 - Can be used in large number of people; including those who are immunocompromised
 - Single dose

<https://whdh.com/news/johnson-johnsons-covid-19-vaccine-how-it-works-and-why-it-matters/> accessed 02-01-2021
Wright, 2021

174

Johnson & Johnson Vaccine

- 66% effective in preventing moderate and severe disease
- 85% effective overall at preventing hospitalization and death
- Efficacy against moderate and severe disease in the United States: 72%
- South African Variant B.1.351 efficacy against moderate to severe disease: 57%

<https://whdh.com/news/johnson-johnsons-covid-19-vaccine-how-it-works-and-why-it-matters/> accessed 02-01-2021

Wright, 2021175

175

Overview of Vaccines Currently Available or in Late-Stage Development

Vaccine	Pfizer	Moderna	Janssen	AstraZeneca-Oxford	Novavax
Type	mRNA	mRNA	Viral Vector DNA	Viral Vector DNA	Subunit Protein-Based
Doses	2x doses 21d apart	2x doses 28d apart	1 dose	2x doses ~4-12w apart	2x doses 21d apart
Storage	Refrigeration 2-8 °C ≤ 5d Ultra-Frozen -80 to -60 °C ≤ 6m	Refrigeration 2-8 °C ≤ 30d Frozen -25 to -15 °C ≤ 6m	Refrigeration 2-8 °C ≤ 3m Frozen ≤ -20 °C ≤ 2y	Refrigeration 2-8 °C ≤ 6m	Refrigeration 2-8 °C no time limit given
Availability	EUA for ≥16YO EUA in 12-15YO filed 4/9/21	EUA for ≥18YO	EUA for ≥18YO*	EUA filing ~Q1 2021	EUA filing ~Q1 2021

*Distribution resumed 4/23 following CVST concerns; Women < 50 YO should be informed of rare risk of blood clots with low platelets after vaccination

<https://www.ashp.org/-/media/assets/pharmacy-practice/resource-centers/Coronavirus/docs/Vaccine-candidate-tracking-table.ashx>, Feb 8, 2021;
<https://www.idocociety.org/covid-19-real-time-learning-network/vaccines/Pfizer-BioNTech-COVID-19-Vaccine/>, Feb 4, 2021; <https://www.idocociety.org/covid-19-real-time-learning-network/vaccines/moderna-covid-19-vaccine/>, Feb 4, 2021; <https://www.idocociety.org/covid-19-real-time-learning-network/vaccines/janssen/>, Feb 9, 2021; <https://www.biopace.com/article/comparing-covid-19-vaccines-pfizer-biotech-moderna-astrazeneca-oxford-j-and-j-russia-s-sputnik-v/>

176

Vaccines Currently Available or in Late-Stage Development: Efficacy Outcomes

Vaccine	Pfizer	Moderna	Janssen	AstraZeneca-Oxford	Novavax
Efficacy: Symptomatic COVID-19 (Primary Outcome), n	46,307	~30,000	43,783	32,449	~30,000
1 st dose	52%	80%	66% (72% US trials)	76%	NR
2 nd dose	91.3% (up to 6 months)	94%	Pending	76% (±15d after 2 doses 4w apart) 85% (≥65YO)	96.4% 89.7% (incl variants)
Secondary Efficacy Outcomes					
Severe Disease	100% (CDC definition) 95.3% (FDA definition)	100%	85%	100%	100%
Hospitalization/Death	100%	100%	100%	100%	100%

<https://www.ashp.org/-/media/assets/pharmacy-practice/resource-centers/Coronavirus/docs/Vaccine-candidate-tracking-table.ashx>, Feb 8, 2021;
<https://www.idocociety.org/covid-19-real-time-learning-network/vaccines/Pfizer-BioNTech-COVID-19-Vaccine/>, Feb 4, 2021; <https://www.idocociety.org/covid-19-real-time-learning-network/vaccines/moderna-covid-19-vaccine/>, Feb 4, 2021; <https://www.idocociety.org/covid-19-real-time-learning-network/vaccines/janssen/>, Feb 9, 2021; <https://www.biopace.com/article/comparing-covid-19-vaccines-pfizer-biotech-moderna-astrazeneca-oxford-j-and-j-russia-s-sputnik-v/>, Voysey M, et al. Lancet. Feb 1, 2021; <https://www.nejm.org/articles/straZeneca-vaccine-effective-against-u-k-covid-19-variant-in-study-11612530912>, Feb 5, 2021.

177

Vaccines Currently Available or in Late-Stage Development: Efficacy Against Variants

Vaccine	Pfizer	Moderna	Janssen	AstraZeneca-Oxford	Novavax
Efficacy Against Variants	<i>In vitro neutralization potency (direct efficacy remains unknown)</i>				
UK (B.1.1.7)			Data not available	70.4%	86.3%
South Africa (20H/501Y.V2 or B.1.351)	Similar against B.1.1.7 & P.1, but lower against B.1.351	Not significantly changed for B.1.1.7, but reduced by 6-fold for B.1.351 & 2.8 fold for P.1	57%	10.4% (all severity)	48.6% (Overall) 55.4% (HN-negative)
Brazil (P.1)			66% overall (Latin America; incl variant)	Data not available	No trial in Brazil

*Against mild to moderate infections only.
<https://www.aahp.org/media/assets/pharmacy-practice/resource-centers/Coronavirus/docs/Vaccine-candidate-tracking-table.aahp>, Feb 8, 2021.
<https://www.abcociety.org/covid-19-real-time-learning-network/vaccines/moderna-covid-19-vaccine/>, Feb 4, 2021. <https://www.abcociety.org/covid-19-real-time-learning-network/vaccines/vaccines/#Phase3>, Feb 9, 2021. <https://www.biopac.com/articles/comparing-covid-19-vaccines-pfizer-biotech-moderna-astrazeneca-oxford-janssen-janssen-oxford/>, Woysey M, et al. Lancet. Feb 1 2021. <https://www.wsj.com/articles/astrazeneca-vaccine-effective-against-u-k-covid-19-variant-in-study-11612530912>, Feb 5, 2021.

178

May Now Give Other Vaccines Concomitantly

Wright, 2021179

179

CDC Meeting: Week of January 24, 2021

- AstraZeneca:
 - Enrollment has been completed in US
 - 32,459 people enrolled; as of January 21 – 26,327 have received 2nd dose
- V-safe data:
 - 2.08 million people participating (out of 21.8 million vaccinated)
 - 15,131 pregnancies reported to V-safe (they will be monitored for 3 months after babies born)

<https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-01/06-COVID-Shimabukuro.pdf> Wright, 2021180

180

CDC Meeting: Week of January 24, 2021

- V-safe data:
 - Anaphylaxis:
 - Pfizer: 50 people out of 9.943 million doses
 - Moderna: 21 out of 7.581 million doses
 - 90% occurred within 30 minutes
 - 80 and 86% of these individuals (Pfizer/Moderna) had history of allergies
 - VAERS
 - 196 deaths reported after the vaccinations
 - None have been associated with the vaccine (monitoring and adjudication continues)

https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-01/06-COVID-Shimabukuro.pdf Wright, 2021181

181

V-safe: No Surprises

Reactogenicity reported to v-safe

Local and systemic reactions, day 0-7 ^{1,2}	All vaccines %	Pfizer-BioNTech dose 1 %	Pfizer-BioNTech dose 2 %	Moderna dose 1 %
Pain	70.7	67.7	74.8	70.1
Fatigue	33.4	28.6	50.0	29.7
Headache	29.4	25.6	41.9	26.0
Myalgia	22.8	17.2	41.6	19.6
Chills	11.5	7.0	26.7	9.3
Fever	11.4	7.4	25.2	9.1
Swelling	11.0	6.8	26.7	13.4
Joint pain	10.4	7.1	21.2	8.6
Nausea	8.9	7.0	13.9	7.7

¹v-safe data lock point 1/14/2021, 5:00 AM ET
²Reported on at least one health check-in completed on days 0-7 after receipt of vaccine

https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-01/06-COVID-Shimabukuro.pdf Wright, 2021182

182

VAERS: Reports of Deaths

Reports of deaths (due to any cause) following COVID-19 vaccination to VAERS¹ (N = 196)

Characteristics	Reports of death (N = 196)
Median age, years (range)	79 (25–104)
Age <65 years (%)	43 (22)
Female (%)	91 (46)
Long-term care facility (LTCF) resident (%)	129 (66)
Pfizer-BioNTech vaccine	113
Moderna vaccine	83

¹ These reports of death to VAERS involve temporally associated deaths following vaccination due to any cause; adverse event reports to VAERS, including deaths, should not be assumed to be causally related to vaccination
² Data through January 18, 2021

https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-01/06-COVID-Shimabukuro.pdf Wright, 2021183

183

Measles

Wright, 2021 187

187

Measles

- Measles was declared eliminated (absence of continuous disease transmission for greater than 12 months) from the United States in 2000.

What happened?

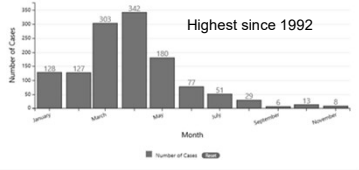
Wright, 2021 188

188

Record Number: 2019

Measles Cases in 2019
From January 1 to December 5, 2019, 1,276* individual cases of measles have been confirmed in 31 states. CDC will now be updating these data monthly.

Measles Cases Reported by Month in 2019*



Month	Number of Cases
January	120
February	132
March	108
April	142
May	100
June	77
July	51
August	29
September	12
October	11
November	8

Highest since 1992

Worldwide 2019:
 -869,770 Cases (556% increase from 2016)
 -207K deaths (50% increase from 2016)
 Highest number in 23 years

<https://www.cdc.gov/measles/cases-outbreaks.html> accessed 12-15-2020 189

189

Why is this occurring?

- In a given year, more measles cases can occur for any of the following reasons:
 - An increase in the number of travelers who get measles abroad and bring it into the U.S., and/or further spread of measles in U.S. communities with pockets of unvaccinated people

Wright, 2021

190

190

CDC Vaccine Recommendations

- All persons aged ≥ 6 months without evidence of measles immunity who travel outside the United States should be vaccinated before travel with 1 dose of MMR vaccine for infants aged 6–11 months and 2 doses for persons aged ≥ 12 months, at least 28 days apart
- Routine MMR vaccination is recommended for all children at age 12–15 months, with a second dose at age 4–6 years.

<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6236a2.htm> accessed 12-27-2013

191

191

Need to Consider: The Three C's


- Cough
- Coryza
- Conjunctivitis
- Fever (up to 105)
- Koplick spots
- Photophobia
- Erythematous, disseminated, coalescing rash

Wright, 2021

192

192

Koplik Spots



http://www.immunize.org/photos/measles/photos.asp 193

193

What about contagion?

- Patients are considered to be contagious from 4 days before to 4 days after the rash appears
- Rash appears about 14 days after the illness begins
- It is the most contagious of all of the infectious diseases
 - 9 out of 10 exposed will develop the disease if not protected
 - Measles remains in the air for 2 hours after person has left the area

https://www.cdc.gov/measles/hcp/index.html 194

194

Complications

- Otitis media, pneumonia, laryngotracheobronchitis, and diarrhea
- One out of every 1,000 measles cases will develop acute encephalitis, which often results in permanent brain damage
- One or two out of every 1,000 children who become infected with measles will die from respiratory and neurologic complications
- Subacute sclerosing panencephalitis (SSPE) is a rare, but fatal degenerative disease of the central nervous system characterized by behavioral and intellectual deterioration and seizures that generally develop 7 to 10 years after measles infection.

https://www.cdc.gov/measles/hcp/index.html 195

195

Diagnosis

- Detection of measles-specific IgM antibody in serum and measles RNA by real-time polymerase chain reaction (RT-PCR) in a respiratory specimen
- Healthcare providers should obtain both a serum sample and a throat swab (or nasopharyngeal swab) from patients suspected to have measles
- Urine samples may also contain virus, and when feasible to do so, collecting both respiratory and urine samples can increase the likelihood of detecting measles virus

<https://www.cdc.gov/measles/hcp/index.html> accessed 12-15-2020

Wright, 2021

196

196

Recommendation

- People who are born during or after 1957 who do not have evidence of immunity against measles should get at least one dose of MMR vaccine.
- Exposed individuals
 - Either administer MMR vaccine within 72 hours of initial measles exposure, **or** immunoglobulin (IG) within six days of exposure. Do **not** administer MMR vaccine and IG simultaneously, as this practice invalidates the vaccine

Wright, 2021

197

197

Polio: September 2019

- Philippines:
 - Two cases of polio – 19 years after it was declared eradicated

Wright, 2021

198

198

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

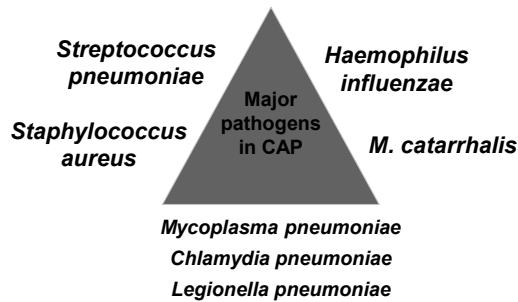
<https://www.atsjournals.org/doi/10.1164/rccm.201908-1581ST>
accessed 10-06-2019

Wright, 2021

199

199

Causative Pathogens in CAP



Wright, 2021

200

200

Microbial Etiology of CAP

- Microbial causes of CAP are changing
- Due in part to the introduction of the pneumococcal conjugate vaccines
- Increased recognition of the role of viral etiology

Wright, 2021

201

201

IDSA/ATS CAP Outpatient Treatment

- For healthy outpatient adults without comorbidities or risk factors for antibiotic resistant pathogens:
 - Amoxicillin 1 g three times daily (strong recommendation) or
 - Doxycycline 100 mg twice daily (conditional recommendation), or
 - A macrolide (azithromycin 500 mg on first day then 250 mg daily or clarithromycin 500 mg twice daily or clarithromycin extended release 1,000 mg daily) only in areas with pneumococcal resistance to macrolides <25% (conditional recommendation)

<https://www.atsjournals.org/doi/10.1164/rccm.201908-1581ST> accessed 10-06-2019

Wright, 2021

202

202

IDSA/ATS CAP classification for outpatient treatment

- For outpatient adults with comorbidities such as chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancy; or asplenia:
 - Combination therapy is now the recommendation

Wright, 2021

203

203

Higher Risk Individuals

- Combination therapy:
 - Amoxicillin/clavulanate 500 mg/125 mg three times daily, or amoxicillin/clavulanate 875 mg/125 mg twice daily, or 2,000 mg/125 mg twice daily, or a cephalosporin (cefepime 200 mg twice daily or cefuroxime 500 mg twice daily);
 - AND
 - Macrolide (azithromycin 500 mg on first day then 250 mg daily, clarithromycin [500 mg twice daily or extended release 1,000 mg once daily]) (strong recommendation),
 - OR doxycycline 100 mg twice daily (conditional recommendation); OR
- Monotherapy:
 - Respiratory fluoroquinolone (levofloxacin 750 mg daily, moxifloxacin 400 mg daily, or gemifloxacin 320 mg daily) (strong recommendation).

Wright, 2021

204

204

What Agent to Use?

- Recent therapy or a repeated course of therapy with beta-lactams, macrolides, or fluoroquinolones are risk factors for pneumococcal resistance to the same class of antibiotic.
- An antimicrobial agent from an alternative class is preferred for a patient who has recently received one of these agents

Wright, 2021

205

205

Opioid epidemic

Wright, 2021

206

206

Hepatitis B

Wright, 2021
207

207

Hepatitis B Vaccination

- Hepatitis B vaccination should be administered to:
 - Unvaccinated adults with diabetes mellitus who are aged 19 through 59 years
 - Hepatitis B vaccination may be administered at the discretion of the treating clinician to unvaccinated adults with diabetes mellitus who are aged ≥ 60 years
 - Administration of the hepatitis B vaccine series should be completed as soon as feasible after diabetes is diagnosed

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6050a4.htm?s_cid=mm6050a4_w accessed 12-20-2012

Wright, 2021
208

208

Hepatitis B Vaccination

- Reasons for vaccination:
 - Risk posed by an increased need for assisted blood-glucose monitoring in LTC facilities, the likelihood of experiencing chronic sequelae if infected with HBV, and the declining immunologic responses to vaccines that are associated with frailty, a geriatric syndrome characterized by decreased physiologic reserve and increased vulnerability, leading to early mortality in older adults

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6050a4.htm?s_cid=mm6050a4_w accessed 12-20-2012

Wright, 2021
209

209

Additional Recommendations

- Hepatitis B series
 - All individuals with liver disease
 - Including fatty liver, cirrhosis, alcoholic liver disease
 - All individuals with ALT or AST $> 2 \times$ upper limits of normal

<http://www.aafp.org/news/health-of-the-public/20161026acipocmtng.html> accessed 03-01-2017

Wright, 2021

210

210

Hepatitis C

- 2016: 41,200 acute hepatitis C cases
- 2016: 2.4 million people in the United States are living with hepatitis C virus infection
- HCV infection becomes chronic in approximately 75%–85% of cases
 - All individuals born between 1945 – 1965 should be screened
 - All injection drug users or those with history

<https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm#a2> 211

211

Hepatitis C

- All 18 years – 79 years should be screened for hepatitis C

<https://www.hhs.gov/hepatitis/blog/2020/03/04/uspstf-issues-updated-hepatitis-c-screening-recommendation.html> accessed 10-1-2020

Wright, 2021 212

212

Hepatitis A: October 2018

- All persons aged 1 year and older who experience homelessness should be routinely immunized against Hepatitis A

Wright, 2021 213

213

Tick Borne Illnesses

Wright, 2021 214

214

Two Sets of Guidelines

- IDSA
– <https://onlinelibrary.wiley.com/doi/10.1002/art.41562> (Updated 2020)
- ILADS
– http://www.ilads.org/files/ILADS_Guidelines.pdf

Wright, 2021 215

215

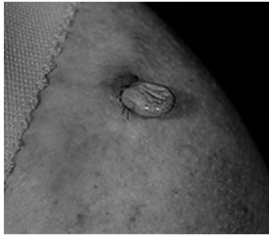
Lyme Disease

- Etiology
 - Caused by a spirochete called *Borrelia burgdorferi*
 - Transmitted by the bite of certain ticks (deer, white-footed mouse)
 - 1st cases were in 1975 in Lyme, Connecticut
 - Affects many systems
 - Children more often affected than adults

Wright, 2021 216

216

This is NOT a Lyme Bearing Tick

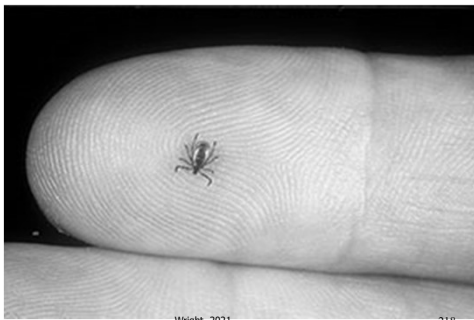


Wright, 2021

217

217

Lyme Bearing Tick



Wright, 2021

218

218

Erythema Chronicum Migrans

• Symptoms

- 3-21 days after bite
- Rash (present in 72-80% of cases)-slightly itchy
- Lasts 3-4 weeks
- Mild flu like symptoms (50% of time)
- Migratory joint pain
- Neurological and cardiac symptoms
- Arthritis, chronic neurological symptoms

Wright, 2021

219

219


Erythema Chronicum Migrans

- **Signs**
 - **Rash:**
 - Begins as a papule at the site of the bite
 - Flat, blanches with pressure
 - Expands to form a ring of central clearing
 - No scaling
 - Slightly tender
 - **Arthralgias:**
 - Asymmetric joint erythema, warmth, edema
 - Knee is most common location

Wright, 2021 220

220


Erythema Migrans



Wright, 2021 221

221

Disseminated Erythema Migrans



© Bernard Cohen, Dermatlas: <http://www.dermatlas.org>
Wright, 2021 222

222

Erythema Chronicum Migrans

- **Signs**
 - Systemic symptoms
 - Facial palsy
 - Meningitis
 - Carditis

Wright, 2021 223

223

Erythema Chronicum Migrans

- **Plan**
 - Diagnostic:
 - CDC and IDSA
 - EIA or immunofluorescence assay — followed by a supplemental immunoblot assay if the first test resulted in a positive or equivocal result.
 - Lyme Western Blot

Wright, 2021 224

224

Per ILADS

- “Diagnosis of Lyme disease by two-tier confirmation fails to detect up to 90% of cases and does not distinguish between acute, chronic, or resolved infection”
- “The Centers for Disease Control and Prevention (CDC) considers a western blot positive if at least 5 of 10 immunoglobulin G (IgG) bands or 2 of 3 immunoglobulin M (IgM) bands are positive. However, other definitions for western blot confirmation have been proposed to improve the test sensitivity. In fact, several studies showed that sensitivity and specificity for both the IgM and IgG western blot range from 92 to 96% when only two specific bands are positive”
 - Lyme specific bands: 31, 34, and 39

http://www.ilads.org/lyme_disease/treatment_guidelines_clearing_ilads.html
Accessed 12-20-2013

Wright, 2021 225

225

Erythema Migrans: IDSA 2020

- 10 days of doxycycline is sufficient
- For children or those unable to tolerate doxycycline, 14 days of amoxicillin or cefuroxime is recommended

<https://www.healio.com/news/infectious-disease/20201204/qa-lyme-disease-guidelines-updated-for-first-time-in-14-years> accessed 01-19-2021

Wright, 2021

226

226

Prophylactic Treatment

- Prophylactic antibiotic therapy should be given only to adults and children within 72 hours of removal of an identified high-risk tick bite
 - If a tick bite cannot be classified with a high level of certainty as a high-risk bite, a wait-and-watch approach is recommended.
 - A tick bite is considered to be high-risk only if it meets the following 3 criteria: the tick bite was from (a) an identified *Ixodes* spp. vector species, (b) it occurred in a highly endemic area, and (c) the tick was attached for ≥ 36 hours

<https://onlinelibrary.wiley.com/doi/10.1002/art.41562>

Wright, 2021

227

227

Erythema Chronicum Migrans

- Plan
 - Prophylactic: Doxycycline 200 mg single dose
 - Therapeutic: IDSA
 - Doxycycline 100 mg bid x 10 days
 - Amoxicillin 500 mg three times daily x 14 days
 - Cefuroxime 500 mg bid x 14 days
 - Alternative Azithromycin 500 mg once daily x 7 days

Wright, 2021

228

228

ILADS

- Believe in Chronic Lyme Disease
- Treatment may be continued as long as needed to treat symptoms
- Alternative recommendations are made:
 - Doxycycline 100-200 mg bid or TCN 500 mg 1 bid
 - Clarithromycin 500 mg 1 po bid along with hydroxychloroquine 200 mg 1 two times daily
 - Azithromycin 500 mg once daily

Wright, 2021 229

229

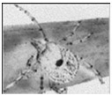

Additional Tick Borne Illnesses

Wright, 2021 230

230

Anaplasmosis

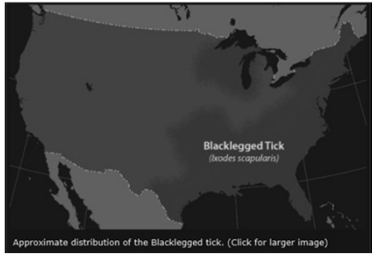
- Formerly referred to as ehrlichiosis
- Transmitted by blacklegged tick or LoneStar tick



Wright, 2021 231

231

Locations of Blacklegged Tick



http://www.cdc.gov/ticks/geographic_distribution.html#blacklegged

232

232

Anaplasmosis (Ehrlichiosis)

• Clinical picture

- Fever, chills, headaches, muscle aches
- Occurs 1-2 weeks after a tick bite
- Additional clues: thrombocytopenia, leukopenia, or elevated liver enzyme levels are helpful predictors of anaplasmosis, but may not be present in all patients
- Testing: may be negative for first 7-10 days; PCR assay test
- Treatment: doxycycline 100 mg 1 pill two times daily x 7-14 days (continue for minimum of 3 days after fever subsides)
 - Alternative: rifampin

<http://www.cdc.gov/anaplasmosis/symptoms/index.html> accessed

Wright, 2021

233

233

Babesiosis

• Babesiosis

- Parasite which invades, infects, and kills the red blood cells (***Babesia microti***)
- *Babesia microti* is spread in nature by *Ixodes scapularis* ticks (also called blacklegged ticks)
- Symptoms: flu-like symptoms, such as fever, chills, sweats, headache, body aches, loss of appetite, nausea, or fatigue. Babesiosis can cause hemolytic anemia (from destruction of red blood cells)

Wright, 2021

234

234

Babesiosis

- **Babesiosis**

- Treatment:

- atovaquone (Mepron) PLUS azithromycin; OR
 - clindamycin PLUS quinine (this combination is the standard of care for severely ill patients)

- Length: 7-10 days

Wright, 2021

235

235

CDC: Babesiosis

Age Category	Drug	Dosage	Maximum	Duration (Days)	
Adults	Prescribe together	Atovaquone	750 mg orally every 12 hours	N/A	7-10
		Azithromycin	On the first day, give a total dose in the range of 500-1000 mg orally; on subsequent days, give a total daily dose in the range of 250-1000 mg*	1000 mg per day	7-10
	OR				
	Prescribe together	Clindamycin**	300-600 mg IV every 6 hours OR 600 mg orally every 8 hours**	N/A	7-10
Quinine**		650 mg orally every 6-8 hours	N/A	7-10	

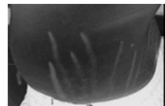
<https://www.cdc.gov/ticks/tickbornediseases/babesiosis.html#:~:text=Babesiosis%20Treatment%20Regimen%20%20%20Age%20Category.%20%20N/A%20%20%20more%20rows> accessed 01-19-2021

Wright, 2021

236

236

Bartonella



- **Bartonella** (cat-scratch)

- Explanation: Bartonella spp. Bacterium
 - Diagnosis: *B. henselae* DNA may be detected by PCR
 - Symptoms: Fever, chills, headache, lymphadenopathy, and severe pain in the tibia, weight loss, sore throat, rash
 - Treatment:
 - Azithromycin:
 - For adults and children > 45.5 kg: 500 mg on day 1, followed by 250 mg for 4 days
 - For children ≤ 45.5 kg: 10 mg/kg on day 1, followed by 5 mg/kg for 4 days
 - ILADS – consider Levofloxacin

<http://www.lymedisease.org/lyme101/coinfections/bartonella.html> accessed 12-20-2013

Wright, 2021

237

237

STARI

- A rash similar to the rash of Lyme disease has been described in humans following bites of the lone star tick, *Amblyomma americanum*
 - Transmitted via the lone-star tick
- The rash may be accompanied by fatigue, fever, headache, muscle and joint pains.
- This condition has been named southern tick-associated rash illness (STARI)
- Treated with doxycycline

Wright, 2021

238

238

Alpha-Gal Meat Allergy

- May be linked to the lone star tick
 - Significant evidence that the lone star tick can inject the alpha-gal carbohydrate molecule into the human upon tick bite, thereby leading to an excessive production of IgE antibodies
- Alpha-gal allergy is a syndrome that was first described in 2009 as a delayed anaphylaxis to red meat
- Occurs about three to eight hours after eating red meat
 - Can resolve over 1 – 5 years

<https://www.columbia-lyme.org/alpha-gal-meat-allergy>

239

239

Rocky Mountain Spotted Fever

- Rapidly progressing disease
- Can be fatal within days if not diagnosed
- Generally within 1-5 days after tick bite
- Symptoms:
 - Early: fever, headache, n/v, abdominal pain, hand edema
 - Later symptoms – pink macular rash which spreads and can involve palms/soles, confusion, organ failure, petechial rash

Wright, 2021

240

240

Rocky Mountain Spotted Fever

- **Diagnosis:**
 - IFA for immunoglobulin IgG R. rickettsia antigen; acute and convalescent sample separated by 2-4 weeks
- **Treatment:**
 - Begin treatment immediately, even if no testing able to be completed
 - Doxycycline: AAP says able to use this in children of all ages for RMSF
 - 100 mg bid for adults until 3 days after fever subsides
 - Children < 45 kg – 2.2 mg/kg to a max of 100 mg bid
 - Pregnant women: must discuss benefits and risks

Wright, 2021

241

241

Enterovirus D-68

- **Enterovirus:**
 - Associated with common cold
 - Common in summer and fall
 - Started appearing August 2014 when children presented with more severe respiratory infections, many of whom were hospitalized
 - Not a new virus, but seems to be more common and more severe

www.cdc.gov accessed 10-13-2014

242

242

Enterovirus – D68

- From mid-August to October 10, 2014, CDC or state public health laboratories have confirmed a total of 691 people in 46 states and the District of Columbia with respiratory illness caused by EV-D68
- **Testing:**
 - nasopharyngeal and oropharyngeal swabs are preferred
- **Treatment: aggressive asthma treatment**
 - Prednisone and albuterol

www.cdc.gov accessed 10-13-2014

243

243

Acute Flaccid Myelitis

Wright, 2021 244

244

Acute Flaccid Myelitis

- Since 2014, most patients with AFM (more than 90%) had a mild respiratory illness or fever consistent with a viral infection before they developed AFM (CDC started tracking in 2014)
- Coxsackievirus A16, EV-A71, and EV-D68 found in the spinal fluid of four of 542 confirmed cases
- In 2014, 120 children in the US developed flaccid myelitis

Wright, 2021 245

245

Acute Flaccid Myelitis

- Incubation period: 6 – 20 days
- Paralysis: 11 – 17 days; but depending upon etiology can be as soon as 2 days and as long as 12 weeks
- Diagnosis: MRI – spinal cord lesions in the gray matter; pleocytosis of 5 cells/mm³
- Treatment: admission, antivirals and supportive care
 - Corticosteroids, IVIG – little evidence to support

Wright, 2021 246

246

Enterovirus D68

- Recent increase in Netherlands (June – July 2016)
 - 8 adults and 17 children
 - Severe respiratory symptoms
 - 13 children required ICU management
 - 1 acute flaccid myelitis
 - No specific treatment

https://wwwnc.cdc.gov/eid/article/23/1/16-1313_article accessed 12/17/2016

Wright, 2021

247

247

Rotavirus Vaccine

- **Rotavirus vaccine**
 - Linked to lower rates of type 1 diabetes
 - 33% less likely to develop type 1 diabetes later in life than those who weren't vaccinated
 - Studied looked at 1.5 million infants in the US between 2001 and 2017

<https://www.nature.com/articles/s41598-019-44193-4> accessed 06-29-2019

Wright, 2021

248

248

Necrotizing Fasciitis

- Severe, deep, necrotizing infection
- Involves subcutaneous tissue down into the muscles
- Spreads rapidly
- Caused by Group A Beta Hemolytic Strep, Staph, Pseudomonas, E Coli
- Mortality: 8-70% depending upon organism and rapidity of treatment
- Disfigurement common

▪ Bologna, Jean, Joseph L. Jorizzo, and Ronald P. Rapini. *Dermatology*. 2nd ed. St. Louis, Mo.: Mosby/Elsevier, 2008. Print.
▪ Habif, Thomas P.,... *Skin disease: diagnosis and treatment*. 2nd ed. Philadelphia: Elsevier Mosby, 2005. Print.
▪ Hunter, J. A. A., John Savin, and Mark V. Dahl. *Clinical dermatology*. 3rd ed. Malden, Mass.: Blackwell Science, 2008. Print.

249

Necrotizing Fasciitis

- Symptoms
 - Usually occurs after surgery, traumatic wounds, injection sites, cutaneous sores
 - Generalized body aches, fever, irritability
 - Key: Red area of skin that is severely painful (It is out of proportion to findings)
 - Leg is most common location
- Physical Examination Findings
 - 1st appears as local area of redness that looks like cellulitis

■ Bologna, Jean, Joseph L. Jorizzo, and Ronald P. Rapini. *Dermatology*. 2nd ed. St. Louis, Mo.: Mosby/Elsevier, 2008. Print.
■ Habif, Thomas P. *Skin disease: diagnosis and treatment*. 2nd ed. Philadelphia: Elsevier Mosby, 2005. Print.
■ Hunter, J. A. A., John Savin, and Mark V. Dahl. *Clinical dermatology*. 3rd ed. Malden, Mass.: Blackwell Science, 2002. Print.

250

Necrotizing Fasciitis

- Physical Examination Findings
 - Tender
 - Bullae with purulent center which ruptures quickly
 - Black eschar appears and the pain decreases
 - Systemic symptoms begin

■ Bologna, Jean, Joseph L. Jorizzo, and Ronald P. Rapini. *Dermatology*. 2nd ed. St. Louis, Mo.: Mosby/Elsevier, 2008. Print.
■ Habif, Thomas P. *Skin disease: diagnosis and treatment*. 2nd ed. Philadelphia: Elsevier Mosby, 2005. Print.
■ Hunter, J. A. A., John Savin, and Mark V. Dahl. *Clinical dermatology*. 3rd ed. Malden, Mass.: Blackwell Science, 2002. Print.

251

Necrotizing Fasciitis



Bullae: Below these lesions is necrotic tissue Wright, 2021⁵²

252

Necrotizing Fasciitis

- Plan
 - Diagnosis: Culture of wounds, blood cultures, biopsy of area, CBC with differential, urinalysis
 - Therapeutic: HOSPITAL ADMISSION
 - Educational: Good wound hygiene

■ Bologna, Jean, Joseph L. Jorizzo, and Ronald P. Rapini. *Dermatology*. 2nd ed. St. Louis, Mo.: Mosby/Elsevier, 2008. Print.
■ Habif, Thomas P.,. *Skin disease: diagnosis and treatment*. 2nd ed. Philadelphia: Elsevier Mosby, 2005. Print.
■ Hunter, J. A. A., John Savin, and Mark V. Dahl. *Clinical dermatology*. 3rd ed. Malden, Mass.: Blackwell Science, 2003. Print.

253

Fifth's Disease (Erythema Infectiosum)

- Human Parvovirus B19
 - Occurs in epidemics
 - Occurs year round: Peak incidence is late winter and early spring
- Most common in individuals between 5-15years of age
 - Period of communicability believed to be from exposure to outbreak of rash
 - Incubation period: 5-10 days
 - Can cause harm to pregnant women and individuals who are immunocompromised

Wright, 2021⁵⁴

254

Fifth's Disease (Erythema Infectiosum)

- Low grade temp, malaise, sore throat
 - May occur but are less common
- 3 distinct phases
 - Facial redness for up to 4 days
 - Fishnet like rash within 2 days after facial redness
 - Fever, itching, and petechiae
- Petechiae stop abruptly at the wrists and ankles
 - Hands and feet only

Wright, 2021⁵⁵

255

Fifth's Disease (Erythema Infectiosum)

- Physical Examination Findings
 - Low grade temperature
 - Erythematous cheeks
 - Nontender and well-defined borders
 - Netlike rash
 - Erythematous lesions with peripheral white rims
 - Rash-remits and recurs over 2 week period
 - Petechiae on hands and feet

Wright, 2021^{F56}

256

Fifth's Disease



Wright, 2021^{F57}

257

Classic

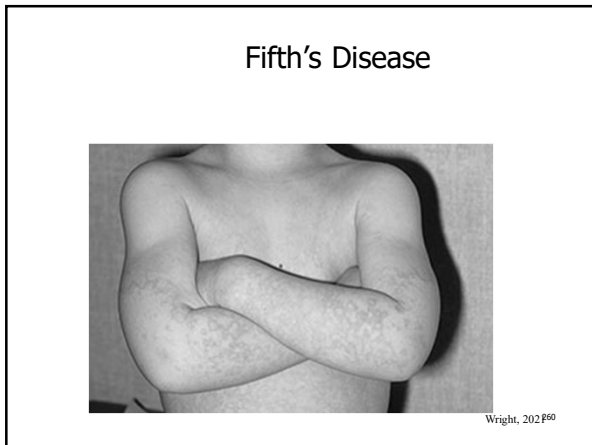


Wright, 2021^{F58}

258



259



260

Fifth's Disease
(Erythema Infectiosum)

- Diagnosis/Plan
 - Parvovirus IgM and IgG
 - IgM=Miserable and is present in the blood from the onset up to 6 months
 - IgG=Gone and is present beginning at day 8 of infection and lasts for a lifetime
 - CBC-May show a decreased wbc count

Wright, 2021⁶¹

261

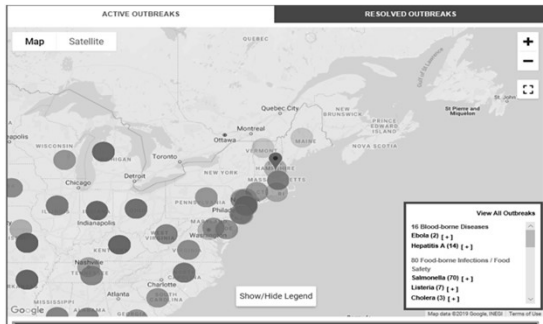
Fifth's Disease (Erythema Infectiosum)

- Diagnosis/Plan
 - Was contagious before rash appeared therefore, no isolation needed
 - Spread via respiratory droplets
 - Symptomatic treatment
 - Patient education-I.e. contagion, handwashing
 - Can cause aplastic crisis in individuals with hemolytic anemias
 - Concern regarding: miscarriage, fetal hydrops
 - Adults: arthralgias

Wright, 2021⁶²

262

Great Resource



<https://www.contagionlive.com/outbreak-monitor>

263

263

Great Resource

Category	Disease	Outbreak Name	Location	Total Cases	Total Deaths	Source
Skin & Soft Tissue Diseases	Acute Flaccid Myelitis	Acute Flaccid Myelitis 2019	Tennessee	2	0	Enterovirus A71 and Acute Flaccid Myelitis
Skin & Soft Tissue Diseases	Measles	Illinois Measles Outbreak	Illinois	4	0	More Exemptions and Less Vaccination: The 2 Factors Driving US Measles Outbreaks
Skin & Soft Tissue Diseases	Measles	Texas Measles Outbreak	Texas	8	0	More Exemptions and Less Vaccination: The 2 Factors Driving US Measles Outbreaks
Skin & Soft Tissue Diseases	Measles	Washington State Measles Outbreak	Multnomah County, Oregon	4	0	Travel-Associated Measles Outbreaks On the Rise in US
Skin & Soft Tissue Diseases	Measles	Rockland County, NY Measles Outbreak	Rockland County, NY	138	0	More Exemptions and Less Vaccination: The 2 Factors Driving US Measles Outbreaks
Zoonotic & Vector-borne	Salmonella	Hedgehog Salmonella	Massachusetts	4	0	CDC Announces Salmonella Outbreak

<https://www.contagionlive.com/outbreak-monitor>

Wright, 2021

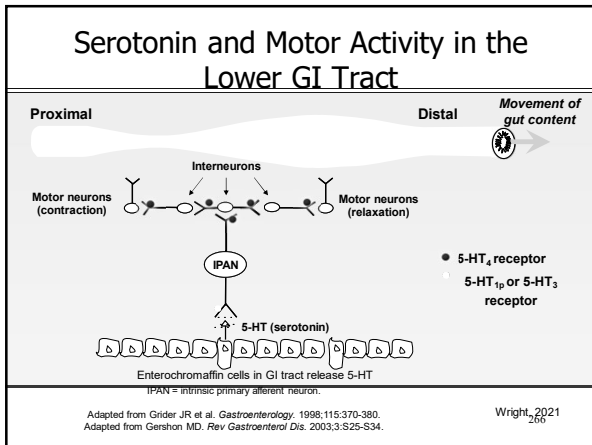
264

264

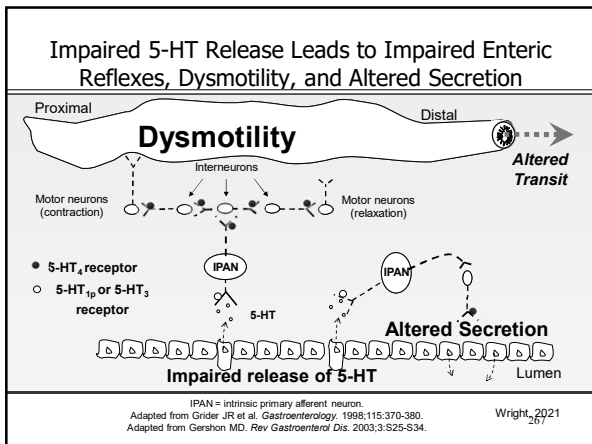
GI Disorders

Wright, 2021 265

265



266



267

5-HT (5 Hydroxytryptamine)
What Role Does Serotonin Play in Functional Bowel Disorders?

Wright, 2021
268

268

**Role of 5-HT
(5-hydroxytryptamine)**

- 5-HT is a neurotransmitter within the enteric nervous system
- Gut contains 95% of all 5-HT in the body
- 14 sub-types of 5-HT
 - 5-HT(3) and 5-HT (4) receptors are proving to be very important in the patient with IBS

An Evidence Based Approach to the Management of Chronic Constipation In North America. *American J of Gastroenterology* 2005;100:S1.
Wright, 2021
269

269

**Role of 5-HT(3) Receptors
(5-hydroxytryptamine)**

- 5-HT(3) receptors are extensively distributed within the gastrointestinal tract
- These receptors have been implicated in the mechanisms controlling colonic motility/transit time, gastrointestinal secretions and pain.

An Evidence Based Approach to the Management of Chronic Constipation In North America. *American J of Gastroenterology* 2005;100:S1.
Wright, 2021
270

270

**Role of 5-HT(3) Receptors
(5-hydroxytryptamine)**

- Blockade of these receptors has been shown to reduce intestinal distension, reduce bowel frequency, slows colonic transit/motility, and increases jejunal water and sodium absorption.
- Alosetron - works on the 5-HT (3) receptors
 - Is now available

An Evidence Based Approach to the Management of Chronic Constipation
In North America. *American J of Gastroenterology* 2005;100;S1.
Wright, 2021

271

**Role of 5-HT(4) Receptors
(5-hydroxytryptamine)**

- Blockade of these receptors has been shown to increase motility.
- New medication approved in 2018
 - Prucalopride (Motegrity)

An Evidence Based Approach to the Management of Chronic Constipation
In North America. *American J of Gastroenterology* 2005;100;S1.
Wright, 2021

272

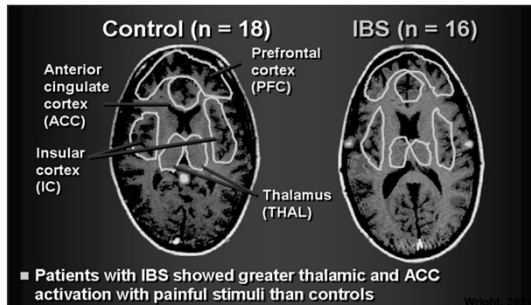
Pathophysiology

- Diarrhea and constipation are explained by the alteration in motor function.
- Abnormal pain experienced by patients with IBS is believed to be caused by excessive sensitivity to colonic distension.
 - Smaller amounts of distension causes more abdominal distress

Mertz H, Morgan V, Tanner G, et al. Regional cerebral activation in irritable bowel syndrome and control subjects with painful and nonpainful rectal distention. *Gastroenterology*. 2000;118:842-848.
Wright, 2021

273

fMRI Imaging with Rectal Distension in IBS



*Adapted from Mertz, GUT 2002 51, Suppl I29

274

The Role of Stress in IBS

- Stress is widely believed to play a significant role in the pathophysiology and clinical presentation of IBS.
- Genetically predisposed individual.
- Sustained stress can result in a permanent increased stress response in the central stress circuits/pathways.

Drossman DA. Do psychosocial factors define symptom severity and patient status in irritable bowel syndrome? *Am J Med* 1999;107:41S-50S.

Drossman DA. Irritable bowel syndrome and sexual/physical abuse history. *Eur J Gastroenterol Hepatol* 1997;9:327-30.

Wright, 2021

275

Irritable Bowel Syndrome (PI-IBS) Four Years After The Outbreak Of Waterborne Gastroenteritis (GE)

- Purpose: Determine the incidence and natural history of Post Infectious-IBS (PI-IBS) in a population exposed to a municipal water contamination in Canada in 2000
- Methods/ Results:
 - Bowel Disease Questionnaire employed to identify IBS via Rome I criteria (n=1587)
 - 1,012 (63.8%) reported GE in '00, and of those, 273 (17.2%) fulfilled Rome I IBS criteria in '04

• Marshall J et al, DDW 2006 abstract 344

Wright, 2021

276

Irritable Bowel Syndrome (PI-IBS) Four Years After The Outbreak Of Waterborne Gastroenteritis (GE)

- **Conclusions:**
 - The prognosis of PI-IBS appears favorable, with spontaneous resolution in half of patients.
 - Independent predictors of IBS in '04 were: female gender, weight loss, abdominal pain, and duration of diarrhea at outbreak

• Marshall J et al, DDW 2006 abstract 344 Wright, 2021

277

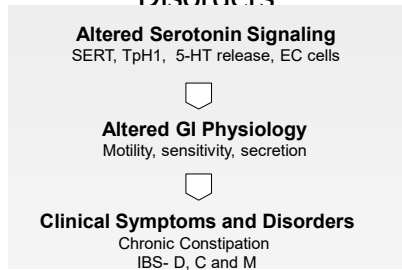
What About SIBO? (Small Intestinal Bacterial Overgrowth)

- Increasing attention to the role of small intestinal bacterial overgrowth in IBS
 - 84% of patients diagnosed with IBS had SIBO compared with 20% of control group
 - 35% of IBS group treated with neomycin had improvement in symptoms vs. 11.4% of placebo group
 - Further research is clearly needed
 - Now available: hydrogen breath test

Pimentel, M, Chow, EJ, Lin HC. Eradication of small intestinal bacterial Overgrowth reduces symptoms of irritable bowel syndrome: a double-blind, randomized controlled study. Am J Gastroenterol. 2003;98:412-19. Wright, 2021

278

Pathophysiology of Functional Bowel Disorders



Coates MD et al. *Gastroenterology*. 2004;126:1657-1664.
Crowell M et al. *Curr Opin Investig Drugs*. 2004;5:55-60.
Baig MK et al. *Colorectal Dis*. 2002;4:348-354.

Wright, 2021

279

Diagnosis of Functional Bowel Disorders

Wright, 2021

280

Rome III Diagnostic Criteria for Irritable Bowel Syndrome (all subtypes)

- At least 3 months, with onset at least 6 months previously of recurrent abdominal pain or discomfort (uncomfortable sensation not described as pain) associated with 2 or more of the following:
 - Improvement with defecation; and/or
 - Onset associated with a change in frequency or stool; and/or
 - Onset associated with a change in form (appearance) of stool

ROME III *Gastroenterology* 2006;130:1377-1390.

Wright, 2021

281

Diagnostic Criteria: Chronic Constipation

- Characterized by unsatisfactory defecation that results from:
 - Infrequent stools or
 - Difficult stool passage
 - Characterized by: straining, sense of difficulty passing stool, incomplete evacuation, hard/lumpy stools, prolonged time to stool, or need for manual maneuvers to pass stool
 - Or, a combination of both

An Evidence Based Approach to the Management of Chronic Constipation In North America. *American J of Gastroenterology* 2005;100:911-921

282

Chronic Constipation and IBS-C Share GI Dysmotility Symptoms

Symptoms >3 months	Chronic Constipation	IBS-C
Straining	+++	+++
Hard/lumpy stools	+++	+++
<3 BM/wk	+++	+++
Feeling of incomplete evacuation	+++	+++
Bloating/abdominal distension	++	+++
Abdominal pain/discomfort	+	+++

IBS-C = irritable bowel syndrome with constipation.
 Thompson WG et al. *Gut*. 1999;45(suppl 2):II43-II47.
 Drossman DA et al. *Gastroenterology*. 1997;112:2120-2137. Wright, 2021

283

Red Flags

- Evaluate for alarm features
 - Reported weight loss
 - Nocturnal symptoms
 - Recent travel history
 - Family history of colon cancer or inflammatory bowel disease
 - Family history of Celiac disease
 - Onset in older patients (> 50)
 - Fevers
 - Oral ulcers
 - **Bloody stools**

Wright, 2021

284

Red Flags

- Evaluate for alarm features
 - Abnormal exam (weight loss, arthritis, rashes)
 - Fever, oral ulcers
 - Anemia
 - Leukocytosis
 - Abnormal chemistry – abnormal LFT's, Creatinine
 - Elevated sed rate
 - Abnormal TSH
 - Positive fecal occult blood test

Wright, 2021

285

ACG Evidence-Based Guideline: Diagnostic Testing

Chronic Constipation

- Among CC patient without alarm features, there are inadequate data to make a recommendation about the *routine* use of diagnostic tests

Irritable Bowel Syndrome

- Among IBS patients without alarm features, the *routine* use of colonoscopy (<50 years old), flexible sigmoidoscopy, thyroid function tests, etc is not recommended.
- Routine testing for celiac disease may be considered.
- Individuals \geq 50 years should undergo colorectal cancer screening

Wright, 2021
ACG Functional GI Disorder Task Force. *Am J Gastroenterol.* 2005;100:S1-S21. 286
ACG Functional GI Disorder Task Force. *Am J Gastroenterol.* 2002;97:S1-S5.

286

Biochemical Assays for IBS

- Anti-Cdtb
- Anti-Vinculin
 - Antibodies in serum; present in IBS
 - Approximately 90% accuracy
 - Trial performed in 3000 individuals

Wright, 2021

287

287

Laboratory Evaluation

- Fecal wbc's
- Fecal lactoferrin¹
 - During intestinal inflammation, activated leukocytes infiltrate the mucosa and lumen, increasing the level of fecal lactoferrin¹
 - Lactoferrin is a glycoprotein secreted by mucosal membranes
 - Fecal lactoferrin is elevated in patients suffering from active inflammatory bowel disease (IBD) but not in those with irritable bowel syndrome (IBS)

¹<http://www.techlabinc.com/presentations/lactoferrin.pps> Accessed September 13, 2006

288

Possible Additional Tests

- Celiac Disease Testing
 - 4.6% of individuals with IBS are likely to have this present; Compared with 0.25-0.5% of general population
 - Celiac Panel: Immunoglobulin A (IgA), anti-tissue transglutaminase (tTGA), and IgA anti-endomysial antibodies (AEA)
- Sigmoidoscopy vs. Colonoscopy
 - Positive occult blood test
 - Nocturnal awakenings
 - Colon cancer

Wright, 2021

289

Consider Pelvic Floor Dysfunction and Colonic Inertia

- Rectal manometry
 - Catheter inserted into rectum to assess muscle pressure and nerve function
- Defecography
 - Done on individuals who have had an inconclusive result on rectal manometry or individuals suspected of a structural abnormality of the rectum
 - Barium is instilled into rectum. Patient then sits on radiolucent commode and pictures are taken as the patient defecates
- Sitz Marker Study
 - Procedure to assess colonic motility
 - Ingest Sitz Marker capsule; brought back in for abdominal x-ray on day 1, day 3 and day 5
 - Normal: complete evacuation by day 5

http://www.medscape.com/viewarticle/501075_4
Accessed on September 13, 2006.

Wright, 2021

290

Case Study

- **45 year old woman presents with a 30+ year history of straining, hard/lumpy stools, and a sense of incomplete evacuation. She passes stool approximately 2 times per week.**
- **Upon further questioning, she also notes frequent bloating, minimal abdominal discomfort, and partial relief with defecation.**

What is her diagnosis?

Wright, 2021

291

Treatment Options for Functional Bowel Disorders

Wright, 2021

292

Non-pharmacologic Treatments

- Dietary modification
 - Given high incidence of concomitant lactose intolerance, dairy avoidance may be helpful
 - 2 week trial of a lactose free diet can be helpful
 - Lactaid or similar as an adjunct to dairy products

ROME III *Gastroenterology* 2006:130:1377-1390.

Wright, 2021

293

Non-pharmacologic Treatments

- Dietary modification
 - Avoid potential triggers: caffeine, alcohol, sorbitol, citrus fruits, high fiber foods, high fructose corn syrup
 - Gas producing foods (beer, cauliflower, grapes, onions, beans, brussel sprouts, plums, raisins, red wine)
 - High fiber foods may occasionally help some individuals but need to tailor to individual patient

ROME III *Gastroenterology* 2006:130:1377-1390.

Wright, 2021

294

Pharmacologic Options

Wright, 2021

295

Bulking Agents

- Bulking agents
 - Psyllium (Metamucil): 15-25 grams per day
 - 1 teaspoon or packet 1 – 3 times/day
 - Methylcellulose (Citrucel): 19 – 57 grams per day
 - 1 heaping tablespoon 1 – 3 times/day
 - Polycarbophil (Fibercon)
 - 625 mg tablet
 - 2 tablets 1 – 4 times daily
- Bijerk CJ, Muris JWM, Knottnerus JA et al. Systematic review: the role of different types of fiber in the treatment of irritable bowel syndrome. *Aliment Pharmacol Ther* 2004;19:245-251.

Wright, 2021

296

Bulking Agents

- Begin these agents very slowly
 - Bloating, flatulence and abdominal pain are the side effects frequently encountered
- Advance dosage every 2 – 4 weeks
- Each patient will respond differently to each agent
 - Try various products

Bijerk CJ, Muris JWM, Knottnerus JA et al. Systematic review: the role of different types of fiber in the treatment of irritable bowel syndrome. *Aliment Pharmacol Ther* 2004;19:245-251. Wright, 2021

297

Summary of Trials on Bulking Agents

- 13 trials; 7 met high quality criteria
 - 3 trials showed a statistically significant benefit
- Supplemental fiber
 - Accelerates colonic and oro-anal transit
 - Improves constipation with sufficient supplementation (20-30g per day)
 - May worsen some IBS symptoms
 - Bloating and pain
 - Limited data suggest equivocal benefits in IBS

Muller-Lissner, *BMJ* 1988;296:615
Cann et al, *Gut* 1984; 25:168
Coot et al, *Gastroenterology* 1990; 99:866
Lucey et al, *Gut* 1987;28:221

Wright, 2021

298

Polyethylene Glycol

- Polyethylene glycol (Miralax)
 - Osmotic agent
- Indication: Constipation
- Adult dosage: 17 g in 8 ounces of water
 - FDA indication: once daily for up to 2 weeks
- Precautions
 - Nausea and vomiting
- Contraindications
 - Bowel obstruction

Am J Gastroenterol 2002;97: Suppl Nov. S18-25.

Wright, 2021

299

Anticholinergic Agents

- Anticholinergic agents (Antispasmodic)
 - Reduce sigmoid motility in response to fat
 - Decrease postprandial pain and distension by inhibiting postprandial colonic contractions

ROME III *Gastroenterology* 2006;130:1377-1390.

Wright, 2021

300

Anticholinergic Agents

- Dicyclomine (Bentyl)
–20mg-40mg ac
- Hyoscyamine sulfate (Levsin)
–0.125mg 1-2 tabs po q 4 hours prn
–Levsin SL, LevBid (0.375mg 1 – 2 tablets po bid)

ROME III *Gastroenterology* 2006;130:1377-1390.

Wright, 2021

301

Prescribing Information

- Precautions:
– Cardiovascular disease, Hypertension, Elders
- Side Effects
– Drowsiness
– Anticholinergic side effects
- Contraindications
– Glaucoma
– Unstable CV status

Hyoscyamine Product Insert

302

Lactulose

- Lactulose:
– Constulose; Enulose; Generla; Kristalose
- Dosage:
– 10-20 g/day; increased to bid as needed
- Indication: Chronic Constipation
- Mechanism of Action: Osmotic (draws fluid into colon)
- Precautions: use with caution in those with diabetes; monitor electrolytes
- Adverse Reactions: flatulence, diarrhea, abdominal discomfort, nausea, vomiting

Product insert

Wright, 2021

303

Lubiprostone

- **Amitiza (lubiprostone)**
- **Class:**
 - Locally acting chloride channel activator
- **Indications:**
 - IBS-C in women 18 years of age and older
 - Chronic idiopathic constipation in the adult population
 - Men and women
 - All adults, including 65 and older

Gastroenterology 2006;130:5
Amitiza Product Insert

Wright, 2021
304

304

Lubiprostone

- **Dosage:**
 - 8 mcg bid with food
 - 24 mcg bid with food
- **Mechanism of Action:**
 - Activates CIC-2 (found in the human intestine)
 - By increasing intestinal fluid secretion and increases motility in the intestine
- **Efficacy**
 - Increases BM's by 3 per week on average
 - Significant increase over placebo of spontaneous bowel movements within first 24 hours after taking medication

Gastroenterology 2006;130:5
Amitiza Product Insert

Wright, 2021
305

305

Lubiprostone

- **Side effects:**
 - Nausea - 30%
 - Diarrhea – 13%
- **Contraindications**
 - History of mechanical GI obstruction
 - Diarrhea
- **Precautions:**
 - Not studied in individuals with moderate - severe hepatic or renal impairment
 - Pregnancy – C

Gastroenterology 2006;130:5
Amitiza Product Insert

Wright, 2021
306

306

New Approval

- Lubiprostone
 - Opioid-induced constipation
 - Not effective for those on diphenylheptane opioids (e.g., methadone) has not been established
 - 24 mcg two times daily with food

Wright, 2021
307

307

Linaclotide

- Brand name: Linzess
- Class:
 - Guanylate cyclase-C agonist
 - Activation of the GC-C – results in an increased in intra and extracellular concentrations of cGMP.
 - This stimulates secretion of chloride and bicarbonate into the intestinal lumen; resulting in increased intestinal fluid and accelerated transit
 - Also reduces intestinal visceral pain
- Indications:
 - Irritable bowel syndrome with constipation (IBS-C)
 - Chronic idiopathic constipation (CIC)
- Dosage:
 - IBS –C: 290 mcg once daily
 - CIC: 145 mcg once daily
 - Take on empty stomach; 30 minutes before first meal of the day
 - Taking it WITH foods – increases risk of loose stools/diarrhea
 - *** NOW available in 72 mcg dosage

http://www.frx.com/pi/linzess_pi.pdf accessed 12-20-2012

Wright, 2021
308

308

Linaclotide

- Boxed warning:
 - Contraindicated in pediatric patients up to 6 years of age
 - Avoid use in children 6 – 17 years of age
 - Linaclotide caused deaths in young juvenile mice
 - Another contraindication: suspected or known mechanical gastrointestinal obstruction

http://www.frx.com/pi/linzess_pi.pdf accessed 12-20-2012

Wright, 2021
309

309

Linaclootide

- Precautions:
 - Pregnancy category C
 - Nursing mothers (unknown if excreted in breast milk)
- Adverse reactions:
 - Diarrhea: 16% - 20% (depending upon indication)
 - Abdominal pain: 7%
 - Approximately 8% - 9% of patients treated with linaclotide and 3%-4% with placebo discontinued due to adverse reactions
- Drug/drug interactions:
 - NONE; does not use P450 system; nor is it an inhibitor or substrate of the P-gp (P-glycoprotein)

http://www.frx.com/pi/linzess_pi.pdf accessed 12-20-2012 Wright, 2021
310

310

Plecanatide (Trulance)

- Class:
 - Guanylate cyclase-C agonist
- Indication:
 - Adults for treatment of chronic idiopathic constipation
- Dosage:
 - 3 mg taken orally once daily
 - With or without food; may be crushed and put in applesauce but not cut in 1/2

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208745lbl.pdf
Accessed 12-30-2017 Wright, 2021
311

311

Other options

- Methylnatrexone bromide (Relistor)
 - Indicated for the treatment of opioid-induced constipation when other therapies are ineffective
 - Subcutaneous injection
 - Used a lot in individuals receiving palliative care
 - One dose every other day
 - Dosage is weight based

Wright, 2021

312

Prucalopride (Motegrity)

- Indication:
 - Treatment of chronic idiopathic constipation (CIC) in adults
- Class:
 - Serotonin-4 (5-HT₄) receptor agonist
 - Gastrointestinal prokinetic agent that stimulates colonic peristalsis and increases bowel motility

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210166s000lbl.pdf
Accessed 01-04-2019 Wright, 2021 313

313

Prucalopride

- Dosage:
 - 2 mg once daily
 - With or without food
- Warnings and precautions:
 - Renal dosing (CrCl < 30 mL/min) : 1 mg once daily
 - Monitor patients for persistent worsening of depression and emergence of suicidal thoughts and behavior
 - Pregnancy, Lactation, and Children
- Contraindications:
 - Intestinal perforation or obstruction due to structural or functional disorder of the gut wall, obstructive ileus, severe inflammatory conditions of the intestinal tract such as Crohn's disease, ulcerative colitis, and toxic megacolon/megarectum

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210166s000lbl.pdf
Accessed 01-04-2019 Wright, 2021 314

314

Prucalopride

- Efficacy:
 - 2530 patients enrolled in clinical trials
 - 1251 received drug/1279 placebo
 - Responder was defined as a patient with an average of 3 or more CSBMs per week, over the 12-week treatment period
 - 33% vs. 10% and 38% vs. 18% (5 of 6 studies stat. significant)
- Drug – Drug Interactions:
 - No significant drug-drug interactions

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210166s000lbl.pdf
Accessed 01-04-2019 Wright, 2021 315

315

Prucalopride

- Side effects (Drug/placebo):
 - Headache (19% vs. 9%)
 - Abdominal pain (16% vs. 11%)
 - Nausea (14% vs. 7%)
 - Diarrhea (13% vs. 5%)
 - Dizziness (4% vs. 2%)
 - Vomiting (3% vs. 2%)
- Advantages:
 - Another option to the market
 - No QT prolongation

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210166s000lbl.pdf
 Accessed 01-04-2019 Wright, 2021 316

316

Prucalopride

- Competition:
 - No direct competition
 - Tegaserod (Zelnorm) – 5-HT4 receptor agonist withdrawn from the market in 2007
 - Cisapride (also withdrawn from the market)

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210166s000lbl.pdf
 Accessed 01-04-2019 Wright, 2021 317

317

Summary: Traditional Treatment Options for IBS-D

Agent	GI Indication
Anti Diarrheal	IBS-D
Bile Acid Sequestrant	IBS-D
Selective 5 HT3 Receptor Antagonist	IBS -D
Discussion of possible psychological factors. Symptom resolution and reassurance	

Gastroenterology 2006;130:5. Wright, 2021

318

IBS - D

- Loperamide HCl (Imodium)
 - Initially: 4 mg followed by 2 mg, as needed
 - Maximum: 16 mg daily
 - Mechanism of action: slows colonic motility
 - Side effects: abdominal pain, dry mouth, nausea

Loperamide HCL Product Insert Wright, 2021

319

IBS-D

- Diphenoxylate hydrochloride and atropine (Lomotil)
 - Initially: 2.5mg
 - 1-2 pills up to 4x/day until control achieved
 - Maximum: 8 mg daily
 - Mechanism of Action: inhibits excessive GI motility and decreases GI propulsion
 - Side Effects: tachycardia, dry mouth, nausea

Lomotil Product Insert Wright, 2021

320

IBS - D

- Cholestyramine (Questran); Colesevelam (Welchol); Colestipol (Colestid)
 - Off-label usage
 - Bile acid sequestrant
 - Cholestyramine - Dosage: 1 packet or scoop in fluid bid
 - Maximum: 6 scoops daily
 - Colesevelam: 4 – 7 capsules daily; titrate as needed
 - Side effects:
 - Constipation
 - Impaction
 - Inhibits absorption of other medications
Gastroenterology 2006;130:5.

Product Inserts Wright, 2021

321

Alosetron

- Alosetron (Lotronex)
 - Withdrawn from the market in December of 2000
- Reintroduced in 2002
- Available under promethius prescribing program
- Indication: IBS – D
- Dosage: 0.5 – 2 mg daily

An Evidence Based Approach to the Management of Chronic Constipation
In North America. *American J of Gastroenterology* 2005;100:S1.
Alosetron Product Insert Wright, 2021

322

Alosetron Post-Marketing Information

- Ischemic colitis
 - Of 275,000 patients given alosetron, ischemic colitis occurred in 80 patients
 - 74% of the cases occurred in the 1st month of alosetron use
 - Of the 80 cases, 48 hospitalizations, 6 surgeries, no deaths

An Evidence Based Approach to the Management of Chronic Constipation
In North America. *American J of Gastroenterology* 2005;100:S1.
Alosetron Product Insert Wright, 2021

323

Eluxadoline (Viberzi)

- Eluxadoline
- Class: mu-opioid receptor agonist
- Indications: IBS-diarrhea predominant
- Dosage: 100 mg two times daily with food
 - Start lower dosage (75 mg two time daily) in the following individuals
 - Concomitant OATP1B1 inhibitor (Organic Anion Transporting Polypeptide1B1) inhibitor
 - Mild-moderate hepatic impairment

www.viberzi.com accessed 01-02-2016

324

324

Eluxadoline Efficacy

- 1700 patients with IBS-D have been exposed to eluxadoline
- Length of exposure: 3 months – 12 months
- ROME III criteria for IBS-D
- Efficacy in Study 1 (improvement in worst abdominal pain by 30% AND reduction in the BSS to < 5 on at least 50% of days):
 - 12 weeks: 24% – 25% vs. 17% placebo
 - 26 weeks: 23% – 29% vs. 19%
 - Abdominal pain improvement \geq 30%: 42% – 43% vs. 40%

www.viberzi.com accessed 01-02-2021

325

325

Eluxadoline Efficacy

- Study 2:
 - Same criteria as study 1
 - Response over 12 weeks:
 - 29% - 30% vs. 16%
 - Response over 26 weeks:
 - 30% - 33% vs. 20%
 - Abdominal pain response improved by \geq 30% over 12 weeks
 - 48% - 51% vs. 45%

www.viberzi.com accessed 01-02-2016

326

326

Eluxadoline

- Contraindications:
 - Biliary duct obstruction
 - Alcoholism or individuals drinking more than 3 drinks per day
 - History of pancreatitis
 - Severe hepatic impairment
 - Severe constipation

www.viberzi.com accessed 01-02-2016

327

327

Eluxadoline Precautions

- NOW contraindicated in individuals without a gallbladder

www.viberzi.com accessed 01-02-2016
Wright, 2021
328

328

Eluxadoline

- Side effects:
 - Constipation (8% vs. 2%)
 - Nausea (7% vs. 5%)
 - Abdominal pain (7% vs. 4%)
 - Vomiting (4% vs. 1%)
- Drug/drug interactions
 - OATP1B1 Inhibitors: cyclosporine, gemfibrozil, antiretrovirals, rifampin
 - Use 75 mg two times daily

www.viberzi.com accessed 01-02-2016
Wright, 2021
329

329

Additional drug/drug interactions

- Strong CYP inhibitors
 - Ciprofloxacin, gemfibrozil, fluconazole, clarithromycin, paroxetine and bupropion
 - Use 75 mg two times daily
- Rosuvastatin
 - Increase exposure to rosuvastatin
 - Use lowest dosages of rosuvastatin
- Caution in drugs with narrow therapeutic index
 - www.viberzi.com accessed 01-02-2016

Wright, 2021
330

330

Eluxadoline

- Avoid in pregnancy and lactation
- Do not use in children < 18 years of age
- Do not take other medications such as alosetron (Lotronex) or loperamide (Imodium) on a regular basis while using this medication

www.viberzi.com accessed 01-02-2016

331

331

Rifaximin (Xifaxan)

- Indication: IBS-D; targeting SIBO
- Dosage: 550 mg three times daily x 2 weeks
 - May repeat dose up to 2 times if helpful or patient has recurrent symptoms
- With or without food

www.xifaxan.com accessed 01-03-2016

332

332

Rifaximin (Xifaxan)

- Precautions/Contraindications:
 - Avoid use in 1st trimester (increased risk of congenital abnormalities based upon animal data)
- Side effects:
 - Diarrhea
 - Peripheral edema
 - Nausea
 - Risks of *C. difficile*
- Drug/drug interactions:
 - P-glycoprotein inhibitors (cyclosporine): increased rifaximin exposure

www.xifaxan.com accessed 01-03-2016

333

333

TCA's

- Numerous products:
 - Examples: Amitriptyline and nortriptyline
- Mechanism of action
 - Low dose at bedtime may reduce abdominal pain
 - May decrease diarrhea, therefore helping those with IBS-D
 - May worsen IBS-C
- Side effects:
 - Sedation
 - Anticholinergic effects

Wright, 2021
334

334

SSRI's

- Although no conclusive evidence exists to document efficacy...
 - SSRI's work on the 5-HT (2) receptors in the body
 - Majority are in the brain but some are in the bowels
 - Some patients report significant improvement in anxiety, frequency, and urgency of stools

Gastroenterology 2006;130:5.

Wright, 2021
335

335

Studies to Date on SSRI's

- Broekaert and colleagues reported that Citalopram (Celexa) reduced the number of abdominal pain days as well as the severity of the pain
 - Also reduced bloating and severity
 - Only 14 patients studied
- Paroxetine (Paxil) has also been looked at in patients with ibs
 - 257 patients; 78% women; randomized to 1 or 3 treatment arms: routine care by GI provider; 8 weeks of psychotherapy or 20 mg of paroxetine
 - Paroxetine: lower number of pain days at 3 months; not statistically significant at 1 year

Gastroenterology 2006;130:5.

Wright, 2021
336

336

Probiotics

- Bifidobacterium infantis
 - Only one shown in multiple clinical trials to be effective
 - Has been shown to reduce gas, bloating, abdominal pain
 - ? May help to reduce inflammatory cytokines in IBD
 - Decreased straining and hard stools
 - Note: symptoms may worsen before better

Wright, 2021

337

Case Study



Wright, 2021

338

Case Study

- 45-year old woman presents with a 30+-year history of straining, hard/lumpy stools, and a sense of incomplete evacuation. She passes stool approximately 3 times per week
- **Previously, she tried bulking agents and anticholinergic agents with minimal improvement in her symptoms, and she experienced bloating with lactulose**

What treatment would you consider?

Wright, 2021

339

What Would You Recommend?

- Nonpharmacologic therapies??
- Pharmacologic therapies??

Wright, 2021
340

340

GERD

Wright, 2021
341

341

EE

- 52 year old female presents with anterior chest pain; non-radiating and not associated with any exertion. Occurs daily unless she avoids most foods. Has tried OTC antacids without much effect.
- Aggravating factors:
 - Foods – fatty meals, spicy meals
- Alleviating factors:
 - None
- Medications:
 - Lexapro 5 mg one daily

Wright, 2021

342

EE (Continued)

- PMH
 - Anxiety disorder
 - Postmenopausal
 - Overweight
 - L5-S1 disc surgery
- No previous work-up for symptoms
- Physical Examination
 - Unremarkable except for 1+ tenderness epigastric region
 - 12-lead ECG: No abnormalities
 - Hemocult: negative

Wright, 2021

343

What is GERD?

- Heartburn is one symptom of GERD
- This is characterized by:
 - Reflux of food and acid from stomach into esophagus
 - Often associated with esophageal inflammation
 - May be associated with mucosal injury or even cancer
 - Erosive esophagitis and/or Barrett's

Wright, 2021

344

Symptoms of GERD

- Burning, substernal pain
- Radiates up into the throat
- Acid taste in mouth
- Chest pain
- Nausea
- Hoarseness of voice
- Wheezing
- Cough
- Dysphagia

Wright, 2021

345

Frequency of Heartburn

- Frequency and severity of heartburn does not necessarily correlate with development of esophageal damage or erosions
- Individuals with severe and frequent heartburn may have no esophageal damage whereas individuals with little heartburn may have significant damage
- Therefore...response to standard OTC medications by the patient is likely to be a predictor of more serious or less serious pathology

Wright, 2021
346

346

EE (Continued)

- Most likely diagnosis is:
 - GERD
 - Consider cardiac etiology given age; Negative nuclear stress test

Wright, 2021
347

347

Etiology of Heartburn and GERD

- Heartburn and GERD occurs when:
 - The lower esophageal sphincter (LES) temporarily relaxes
 - Allows reflux of stomach acid into the esophagus
 - Normally, gravity and peristalsis clear material from the esophagus and the saliva that we swallow neutralizes the remaining esophageal acid
 - Heartburn occurs when any one of these mechanisms are impaired

Wright, 2021
348

348

Cause of Lower Esophageal Sphincter Relaxation

- Relaxation or weakening of the LES can be caused by:
 - Eating certain foods
 - Onions, garlic, black pepper
 - Pressure on the stomach because of an individual's weight
 - Frequent bending and lifting, particularly after eating
 - Vigorous exercise

Wright, 2021

349

Cause of Lower Esophageal Sphincter Relaxation

- Relaxation or weakening of the LES can be caused by:
 - Pregnancy
 - Progesterone relaxes LES; slows peristalsis and increases retention of partially digested food and acid
 - Medications also can decrease LES pressure
 - CCB's, hormone replacement therapy, muscle relaxants, beta blockers
 - Alpha-blockers
 - Nitrates
 - Pathophysiologic mechanisms
 - Hiatal hernia and gastric acid hypersecretion
 - Zenker's diverticulum

Wright, 2021

350

Etiology

- Several other defects thought to contribute to heartburn and GERD
 - Abnormal esophageal epithelial resistance
 - Abnormalities of gastric emptying
 - Gastric distention
 - Abnormal acid production

Wright, 2021

351

Diagnosis of Heartburn and GERD

- Diagnosis of heartburn is usually made with history and physical examination
 - Usually, this is all that is needed
- Many clinicians will try routine treatments first and assess for response prior to ordering a variety of tests
- EGD – is not needed to make diagnosis

Wright, 2021

352

Diagnosis

- Multiple tests available to make this diagnosis
 - Often times, patient is treated with medication 1st to see how he/she responds
 - If inadequate response, testing performed or...if any worrisome signs present
 - UGI: easiest, least expensive test
 - Hiatal hernia: present in 40-60% of population
 - Mild reflux seen in 30% of general population
 - Looking for esophageal irregularities, ulcers
 - Normal barium swallow may be seen in 40-60% of all individuals with GERD

Wright, 2021

353

Endoscopy

- Endoscopy (Esophagoscopy)
 - Best study for the evaluation and treatment of GERD
 - Allows for direct visualization of the mucosa of the esophagus and the lining of the stomach
 - Essential when suspecting Barrett's esophagitis
 - If abnormalities are seen, biopsy is conducted

Wright, 2021

354

Intraesophageal Acid Perfusion

- Also called Bernstein test
- This is a test where the patients symptoms are reproduced or eliminated with this procedure
- NG tube placed 30-35 cm from the tip of the nares into the esophagus
 - Saline is infused followed by HCL
 - Looking for reproduction of symptoms with HCL and relief of symptoms with saline infusion

Wright, 2021
355

355

24-hour pH Monitoring

- 2 mm flexible probe is placed transnasally to about 5 cm above the LES
- Probe is connected to a box similar to a Holter monitor
- Wireless: transmits signals to box regarding pH
- Monitoring of pH is conducted in addition to the patients symptoms

Wright, 2021
356

356

Esophageal Motility Studies

- Conducted to measure the pressure of the LES
- Thin, pressure sensitive tube is passed through mouth or nose and into stomach
- Once in place, the tube is pulled back slowly into the esophagus while the patient is asked to swallow
- The pressure of the muscle contractions is then measured along several sections of the tube

Wright, 2021
357

357

H. Pylori

- Role of *H. pylori* in heartburn is subject of frequent debate
- *H. pylori* – water supplies
- First identified in countries where water supply is poor
- Transmitted via saliva
- Bacteria may help erode protective layer of esophagus
- *H. pylori* breath test or stool tests – most accurate tests to be performed in primary care
 - Biopsy – gold standard

Wright₃₅₈, 2021

358

H. Pylori

- ***H. pylori*** is associated with significant morbidity
- Causes more than 90% of duodenal ulcers and up to 80% of gastric ulcers
- Linked to 60% of gastric cancer (adenocarcinoma and primary β -cell lymphoma [MALT lymphoma]) cases
 - The World Health Organization has classified *H. pylori* as a Group 1 carcinogen

Wright₃₅₉, 2021

359

H. Pylori Breath Test or Stool Test

Sensitivity and Specificity of Tests for *H. pylori* Infection¹²

	Sensitivity	Specificity
UBT	95% ^a	96% ^a
Stool (antigen test)	93% ^a	93% ^a
Serology (ELISA)	N/A ^a	N/A ^a
Endoscopic biopsy (Routine histology)	93% ^b	90% ^b

- Used to detect urease
- By measuring the ratio of CO₂ to CO₂ in the patient's breath samples, UBT accurately detects active *H. pylori*-associated urease
- No PPI's x 2 weeks, No peptobismol; no food x 1 hour
- Okay to use H2RA's

Wright₃₆₀, 2021

360

ACG

- Routine testing for *H. Pylori* is not necessary for GERD

Wright, 2021 361

361

Barrett's Esophagitis

- Occurs in < 1% of heartburn sufferers
- Occurs when the esophageal lining is replaced by tissue normally found in the intestines (metaplasia)
- Increased risk of adenocarcinoma of the esophagus
 - 30 – 125 times higher in the patient with Barrett's
- Treatment:
 - PPI
 - Halo procedure: thermal ablation of tissue

Wright, 2021 362

362

The Good News IS...

- 53 – 71% of all heartburn sufferers have endoscopically normal esophageal mucosa

Wright, 2021 363

363

Treatments

- Lifestyle Modification
- Elimination of medications
- PPI (Proton pump inhibitors)
 - Have become first line therapy
- Surgery
 - For recalcitrant cases

Wright, 2021
364

364

EE

- History and physical examination were consistent with GERD
- No additional testing performed
- Cardiac pathology ruled-out
- No additional red flags
- Patient started on lifestyle modification and a proton pump inhibitor given frequency and severity of symptoms

Wright, 2021
365

365

**Treatment
Options**

Wright, 2021
366

366

AGA Guidelines

- PPI therapy is now first line
- No role for H. pylori
- No diagnostic testing needed
- No need for repeat endoscopy

Wright, 2021 367

367

Nonpharmacologic Treatment Options

- Dietary Modification
 - Bland diet
 - Smaller meals
 - Less acidic foods
 - Avoidance of chocolate/mint

Wright, 2021 368

368

Nonpharmacologic Treatment Options

- Dietary Modification
 - Avoidance of alcohol
 - Decrease fat in diet
 - Weight loss
 - Lifestyle changes
 - Elevate head of bed

Wright, 2021 369

369

Medications

Wright, 2021
370

370

ACG

- It is appropriate to start with PPI for patients with GERD
- Two week trial may be all that is needed
- 8 weeks necessary to heal erosive esophagitis unless patient has Barrett's

Wright, 2021 371

371

Antacids

Wright, 2021

372

Antacids

- Examples:
 - Maalox
 - Aluminum hydroxide, magnesium hydroxide
 - Mylanta
 - Same as above
 - Rolaids
 - Calcium carbonate, magnesium hydroxide
 - Surpass
 - Calcium carbonate
 - Tums
 - Calcium carbonate

Wright, 2021

373

Antacids

- Although antacids have long been thought to work in the gastric lumen to decrease gastric acidity, they actually work in the esophageal lumen
- Rapidly increase esophageal pH
- Neutralize esophageal acid for 90 minutes after dosing
- Little change in gastric pH
- Indication: intermittent or episodic heartburn

Wright, 2021

374

Antacids

- Advantages
 - Multiple products available
 - Many different preparations: liquid, swallowable tablets, chewable tablets, effervescent solutions and gum
 - Gum and chewed tablet antacids seem to be more effective (per patients) than liquid products
 - Fast onset of action
 - Ease of dosing – take when patient has symptoms

Wright, 2021

375

Disadvantages of Antacids

- Frequent dosing required
 - Short duration of action
- Few studies done with antacids
- No role with prevention

Wright, 2021
376

376

H2RA's

Wright, 2021
377

377

H2RA's

- Axid
 - 75 mg nizatidine
- Pepcid AC
 - 10 mg famotidine
- Maximum Strength Pepcid AC
 - 20 mg famotidine
- Pepcid Complete
 - 10 mg famotidine, 800 mg of CaCO₃ (Tums) and 165 mg of MG (OH)₂
- Tagamet HB
 - 200 mg cimetidine
- Zantac 75/150
 - 75 mg ranitidine

Wright, 2021
378

378

Mechanism of Action

- Drugs bind to histamine-2 receptors on parietal cells to decrease gastric acid secretion
- Begin to work by decreasing gastric acid secretion within 1 – 2 hours of dosing
- Seem to work best on nocturnal acid secretion vs. daytime (i.e. after meal secretion)
- Antacids vs. H2RA
 - Antacids: Onset: 30 minutes, Last: 60 minutes
 - H2RA: Onset: 90 minutes, Last: 9 hours

Wright, 2021

379

H2RA's

- Numerous studies conducted at both OTC and prescription strength dosages
- Clearly surpass placebo in onset of action and sustained efficacy

Wright, 2021

380

H2RA's

- Indication: episodic heartburn
- All products can be taken daily
- Not indicated for frequent heartburn

Wright, 2021

381

Combination of Antacid and H2RA

Wright, 2021
382

382

Low Dose H2RA and Antacid

- H2RA and antacid combination
- Speed of an antacid + duration of H2RA
- Indication: intermittent or episodic heartburn
 - Not cost effective or indicated for individuals with frequent heartburn

Wright, 2021
383

383

Proton Pump Inhibitors

Wright, 2021
384

384

Mechanism of Action

- PPIs
 - Suppress gastric acid production by blocking parietal cell hydrogen/potassium ion adenosine triphosphatase
 - Known as the proton pump
 - This is the final pathway involved in acid secretion
 - Remember...PPI's affect only those pumps which are active
 - Not all pumps are active at the same time
 - 25% of new proton pumps are synthesized daily

Wright, 2021
385

385

Proton Pump Inhibitors

- Omeprazole (Prilosec)
- Lansoprazole (Prevacid)
- Esomeprazole (Nexium)
- Rabeprazole (AciphHex)
- Pantoprazole (Protonix)
- Deslansoprazole (Dexilant)

Wright, 2021
386

386

Proton Pump Inhibitors

- Recent studies have shown an increased risk of:
 - Osteoporosis
 - Should take calcium citrate NOT carbonate
 - Carbonate – i.e. Tums needs an acidic environment
 - Pneumonia
 - Diminished acid protection
 - B12 deficiency
 - C. difficile related infections
 - ? Link with dementia

Wright, 2021

387

Combination Therapy

- Omeprazole/sodium bicarbonate (Zegerid)
 - Indications
 - Gastric and duodenal ulcer
 - Erosive esophagitis
 - Symptomatic GERD

Wright, 2021
388

388

Interaction with Clopidigrel

- Interaction is well documented
- Does not necessarily seem to be a class effect
- Most interaction to least interaction
 - Omeprazole (Prilosec), esomeprazole (Nexium), lansoprazole (Prevacid)
 - Lowest interaction: pantoprazole (Protonix) and deslansoprazole (Dexilant)

Wright, 2021
389

389

Surgical Options

- Nissen fundoplication
 - The upper curve of the stomach (the fundus) is wrapped around the esophagus and sewn into place so that the lower portion of the esophagus passes through a small tunnel of stomach muscle
 - This surgery strengthens the LES between the esophagus and stomach
 - In one study, 62% of people who had surgery were still taking medications to control GERD symptoms.
 - However, they were less likely to need to take medications regularly; and, when they did not take medications, their remaining symptoms were likely to be less severe.

Wright, 2021

390

Additional Surgical Option

- EsophyX
 - Transoral Incisionless Fundoplication
 - Treatment of GERD
 - Reconstruction of the antireflux barrier
 - Restores GE junction back to normal anatomy
 - Same concept as the Nissen without incisions
 - Now FDA approved and cleared for US market

Wright, 2021

391

EE

- Patient returns 1 month after initiating treatment with a PPI; no improvement in symptoms
- Referred for endoscopy given lack of response to traditional methods
 - Endoscopy shows mild esophagitis; negative biopsy
- PPI – increased by GI to 2 daily
 - No improvement at 1 month

Wright, 2021

392

What Now??

- 24 hour pH probe
- Esophageal motility studies
- Bernstein test

Wright, 2021

393

EE

- 24 hour probe shows NO significant correlation between pH and symptoms
- Esophageal motility studies showed decreased motility
 - Started on metoclopramide (reglan) 5 mg 1 po tid – 30 minutes prior to meals with significant improvement in symptoms
 - Black box warning re: tardive dyskinesia

Wright, 2021
394

394

Thank You For Your
Time and Attention!!!

Wendyarnp@aol.com

Wright, 2021

395

395
