Indiana Department of Health

CLINICIAN UPDATES

GUY CROWDER, M.D., MPHTM
CHIEF MEDICAL OFFICER

8/23/2024

OUR MISSION:

To promote, protect, and improve the health and safety of all Hoosiers.

OUR VISION:

Every Hoosier reaches optimal health regardless of where they live, learn, work, or play.

Conflict of interest

I have no conflicts of interest to disclose

CMEs

CME credits are available for physicians participating in this webinar.

Once you complete the REDCap survey (link will be added to the chat during the Clinician Update), the IDOH enters your name into the Accreditation Council for Continuing Medical Education (ACCME) Program and Activity Reporting System (PARS). PARS is your entry point into the digitized world of CME.

To access the CME credit from this webinar, please go to PARS - ACCME (This will allow you to monitor CMEs awarded and entered into ACCME's PARS) and/or Homepage (cmepassport.org) (This will allow you to monitor CME credits and find other available opportunities to gain CMEs.)

Thank you!

Today is Dr. Shireesha Vuppalanchi's last day as IDOH medical director.

Indiana Department of Health

Folic Acid Supplementation

Dr. Kaitlyn G. Edwards

Indiana Department of Health

Neural Tube Defects and Folic Acid

What the Primary Care Provider needs to know

Kaitlyn Edwards, MD

Riley Hospital for Children
Indiana University Health

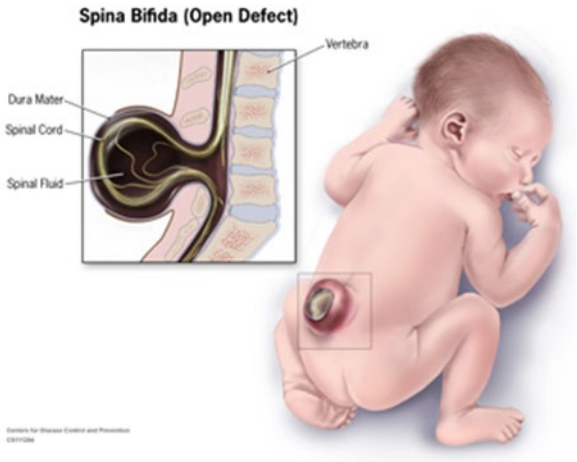
Acknowledgements and objectives

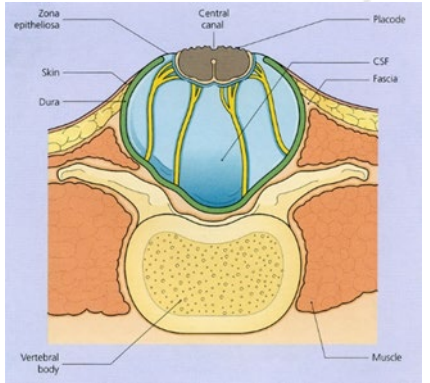
- Special thanks to:
  - Indiana Department of Health
  - Indiana Chapter of American Academy of Pediatrics
  - Riley Hospital for Children, Indiana University Health

- Objectives
  - What is spina bifida and how does it happen?
  - What are some of the known risk factors
  - How does Folic Acid play a role and its impact
  - Recommendations and USPSTF
  - Implementing recommendations

What is Spina Bifida?

- Spina bifida is Greek for “split spine”
- Open spinal dysraphism is a cleft in the vertebral column, with a corresponding defect in the skin so that the meninges and spinal cord are exposed.
- Closed spinal dysraphism is when the neural tissue is covered by skin





Types of Spinal Dysraphism

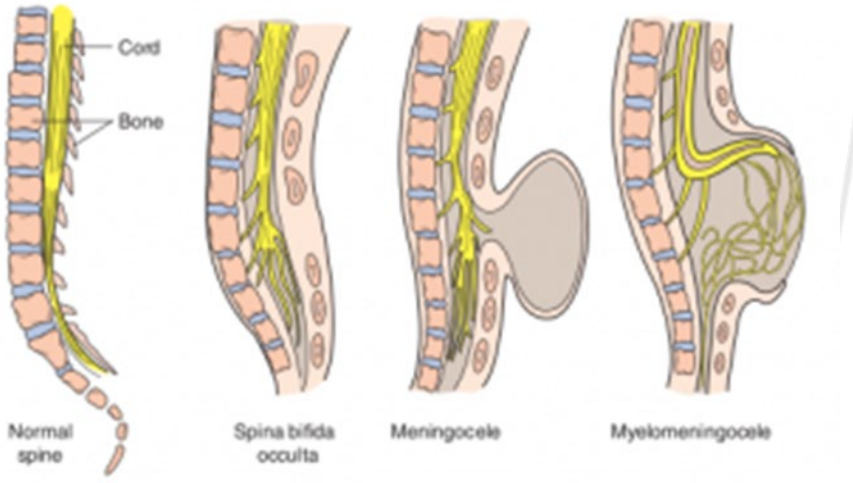
Spina bifida occulta-When one or more vertebrae are malformed and a layer of skin covers the opening in the vertebrae.

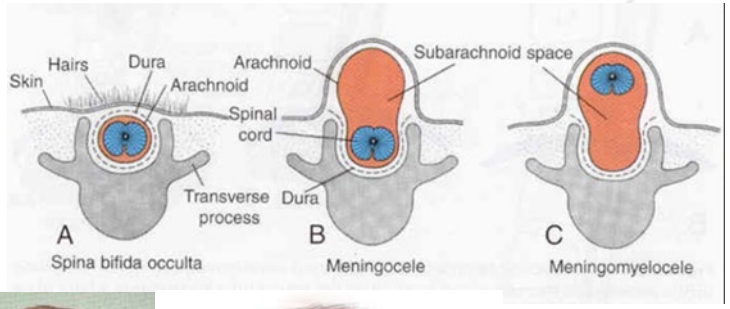
Meningocele- When spinal fluid and meninges come through an opening in the vertebrae, but the malformation does not contain spinal nerves.

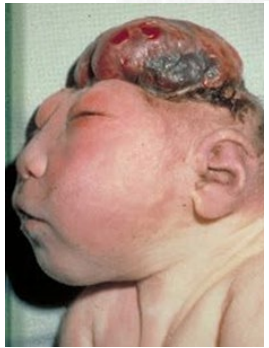
Myelomeningocele- When the spinal cord is exposed through the opening of the spine and contains spinal nerves.

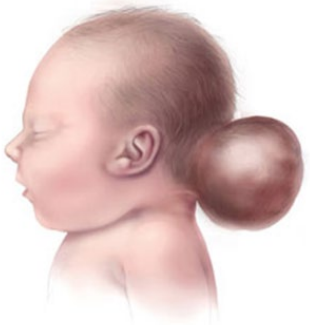
Anencephaly—failure of skull and brain to form

Encephalocele—protrusion of brain and meninges through a defect in the skull









Complications of Spina Bifida

Bladder dysfunction: Most patients with myelomeningocele have some degree of bladder incontinence.

Bowel dysfunction: Myelomeningocele is associated with anal sphincter dysfunction that results in bowel incontinence.

Immobility: Most myelomeningocele patients have significant weakness, which results in severe ambulation deficits or paraplegia.

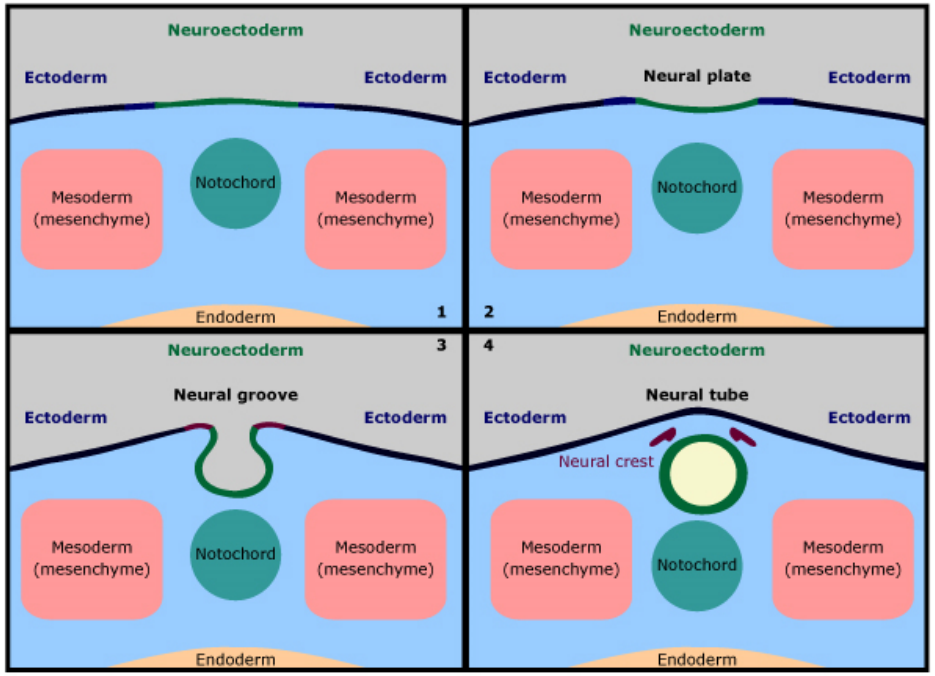
Infections: Due to a neurogenic bladder, many have urine colonization and infections.

Frequent Hospitalizations

Embryology of Spina Bifida

During embryogenesis three layers form: ectoderm, mesoderm and endoderm

Primary Neurulation—day 21-27



The central nervous system initially appears as a plate of thickened ectoderm called the neural plate at the beginning of the third week of embryonic life

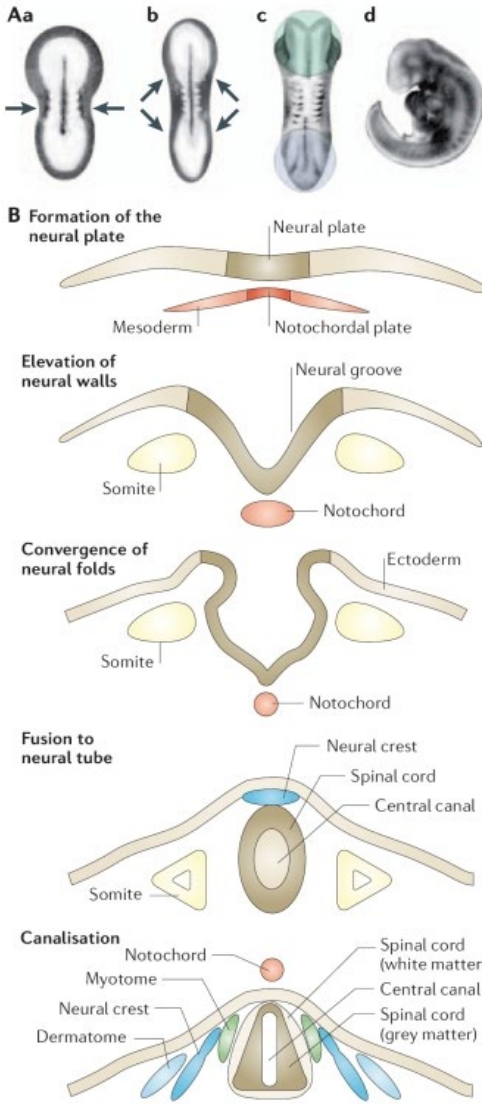
The lateral edges of the neural plate become elevated to form neural folds creating the neural groove

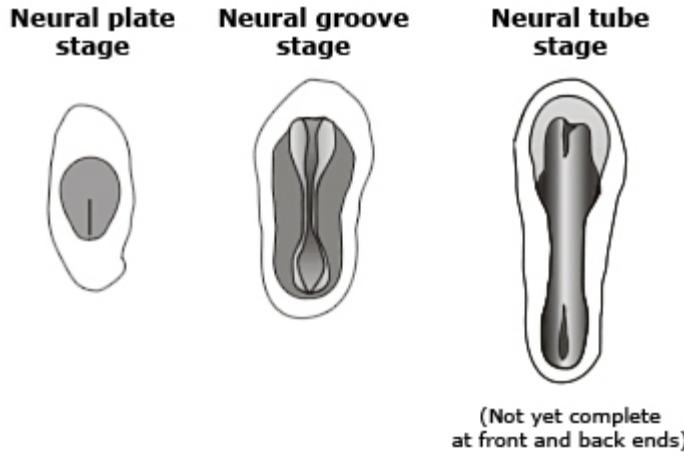
These neural groove subsequently fuse to form the neural tube

Embryology of Spina Bifida-Primary Neurulation

Fusion of the neural tube

- **Forms anterior and posterior neuropores:**
  - Anterior neuropore closes on the 25th day after conception (becomes the brain)
  - Posterior neuropore closes approximately two days later (becomes the spine)
- This process is called primary neurulation and forms all of the functional central nervous system, which extends to the mid-sacral levels of the embryo.
- Spina bifida is caused by a failure of primary neurulation, (ie, failure of the neural tube to close normally by 28 days after conception).





Epidemiology

- In the US, about 1,278 babies are born with spina bifida, or 1 in every 2,875 births (CDC)
  - Indiana averages about 15 to 25 babies born with a NTD annually
  - Currently, there have been 15 babies with SB born this year at RHC
- Hispanic women have the highest rate of having a child affected by spina bifida (CDC)
  - Hispanic: 3.80 per 10,000 live birth
  - Non-Hispanic Black or African-American: 2.73 per 10,000
  - Non-Hispanic White: 3.09 per 10,000 (estimated to be higher in certain nationalities)
- Rate of spina bifida in US estimated to be 3.17 per 10,000 births

Risk Factors

- Neural Tube defects are highly concordant in monozygotic twins compared to dizygotic
- Recurrence risk:
  - One previously affected pregnancy—1/20
  - Two previously affected pregnancies—1/10
- NTD more frequent in females than males
- Methylenetetrahydrofolate reductase (MTHFR) is an enzyme that regulates methylation of DNA. Mutations lead to decreased folate concentrations in the blood

Syndromes associated with Neural Tube defects

- Meckel-Gruber
- Roberts
- Jarcho-Levin
- Trisomy 13 and 18
- Limb-body wall complex
- OEIS (omphalocele, exstrophy of cloaca, imperforate anus, and spine abnormalities)
- HARD (hydrocephalus, agyria, retinal dysplasia)

Other Contributing factors

- Pregestational maternal diabetes
- Maternal obesity
- Maternal B12 status
- Maternal hyperthermia (febrile illness in first trimester of pregnancy)
- Antiepileptics (valproic acid, carbamazepine)
- Folic acid levels (related to lower SDOH?)

Folate

Folate is a general term for Vitamin B9

Folate is an umbrella term used to describe its different forms (both natural and synthetic):

- Food folate
- Folic acid
- Dihydrofolate (DHF)
- Tetrahydrofolate (THF)
- 5-methyltetrahydrofolate (5-MTHF)

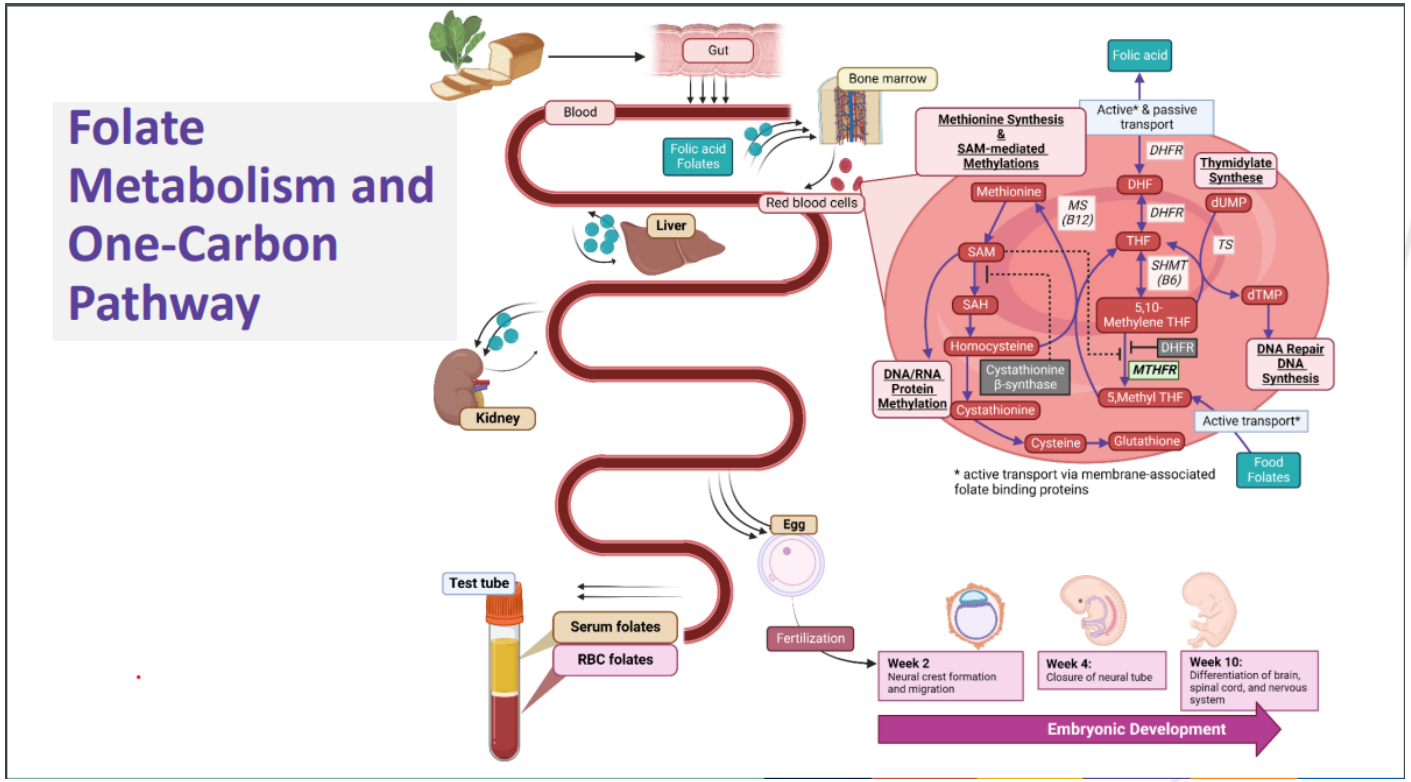
Folate is critical to basic cellular processes

Folic acid is a synthetic form of folate that is heat stable

- Food folate is not as stable to heat or light

Folic acid and role in energy production

Folate-mediated one-carbon metabolism (FOCM) is an interconnected metabolic network that serves to activate and transfer one-carbon units for many biochemical processes all of which support diverse cellular functions such as cell proliferation, protein synthesis, and mitochondrial respiration (Hiroko Watanabe and Tomoko Miyake, INTECH, 2017)



Role of Folic Acid Fortification and Spina Bifida

A study performed from 1995-2002 found the following:

11,078,407 births from 21 states in United States were analyzed

prevalence of spina bifida (per 10,000 births) decreased from 1995-1996 to 1998-2002 from

6.49 to 4.18 in Hispanic patients

5.13 to 3.37 in non-Hispanic White patients

3.57 to 2.9 in non-Hispanic Black patients

prevalence of anencephaly (per 10,000 births) decreased from 1995-1996 to 1998-2002 from

3.85 to 2.84 in Hispanic patients

2.79 to 1.98 in non-Hispanic White patients

1.98 to 1.8 in non-Hispanic Black patients

(Pediatrics 2005 Sep;116(3):580)

Randomized Control Trials (RCTs) Demonstrate Folic Acid Prevents NTDs

1991:

Among women with a previous NTD-affected pregnancy (n=1,817) • 4,000 mcg (µg)/day supplement containing only folic acid

• 72% reduction in NTDs (MRC Vitamin Study Research Group. Lancet. 1991 Jul 20;338(8760):131-7)

1992:

Among women without previous NTD-affected pregnancy (n=4,753) • 800 mcg (µg)/day multivitamin supplement containing folic acid

• 100% reduction in NTDs (Czeizel AE, Dudás I. N Engl J Med. 1992 Dec 24;327(26):1832-5)

Methylenetetrahydrofolate Reductase (MTHFR)

- The MTHFR gene codes for a protein that helps the body process folate
- Common MTHFR variants: MTHFR 677 CT, MTHFR 677 TT, MTHFR A1298C
- Routine screening for the MTHFR C677T variant is not recommended by the American College of Obstetricians and Gynecologists (ACOG)
- Studies show that getting 400 mcg of folic acid daily can increase blood folate levels, regardless of your *MTHFR* genotype.

USPSTF Recommendations for Folic Acid

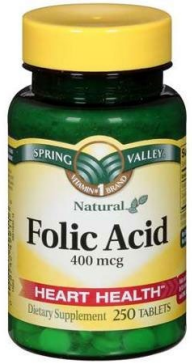
What does the USPSTF recommend?	**Persons who plan to or could become pregnant:** Take a daily supplement containing 0.4 to 0.8 mg (400 to 800 µg) of folic acid. **Grade: A**
To whom does this recommendation apply?	This recommendation applies to all persons who are planning to or could become pregnant. It does not apply to persons who have had a previous pregnancy affected by neural tube defects or who are at very high risk due to other factors such as family history or those taking medication known to block the function of folic acid.
What's new?	This recommendation is consistent with the 2017 USPSTF recommendation.
How to implement this recommendation?	All persons who are planning to or could become pregnant should take a daily supplement or multivitamin containing 0.4 to 0.8 mg (400 to 800 µg) of folic acid.
How often?	• Supplementation should be taken daily. The critical period for folic acid supplementation starts at least 1 month before conception and continues through the first 2 to 3 months of pregnancy. • Nearly half of all pregnancies in the US are unplanned, meaning that many persons may not know they are pregnant during the crucial time. To gain the full benefits of supplementation, clinicians should advise all persons who plan to or who could become pregnant to take a daily folic acid supplement.
Why is this recommendation and topic important?	• Neural tube defects are caused by a failure of closure of the embryonic neural tube, which results in birth defects of the brain, spinal cord, and overlying tissues. The most common forms of neural tube defects are anencephaly, encephalocele, and spina bifida. • Neural tube defects are among the most common congenital malformations in the US, with an estimated 3000 pregnancies affected each year. Neural tube defects can result in death and a range of disabilities affecting children. • Daily supplementation with folic acid is shown to prevent neural tube defects.
What are additional tools and resources?	The Community Preventive Services Task Force recommends community-wide education campaigns to promote the use of folic acid supplements among persons of childbearing age (https://www.thecommunityguide.org/findings/pregnancy-health-community-wide-campaigns-promote-use-folic-acid-supplements.html).
Where to read the full recommendation statement?	Visit the USPSTF website (https://www.uspreventiveservicestaskforce.org/uspstf/) or the JAMA website (https://jamanetwork.com/collections/44068/united-states-preventive-services-task-force) to read the full recommendation statement. This includes more details on the rationale of the recommendation, including benefits and harms; supporting evidence; and recommendations of others.

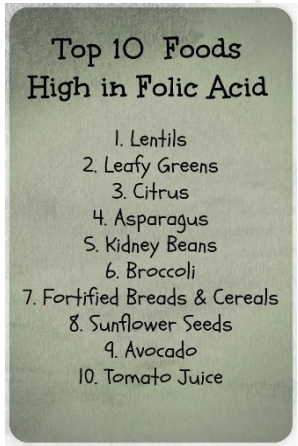
The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision-making to the specific patient or situation.

USPSTF indicates US Preventive Services Task Force.

How much folic acid should a woman take before pregnancy?

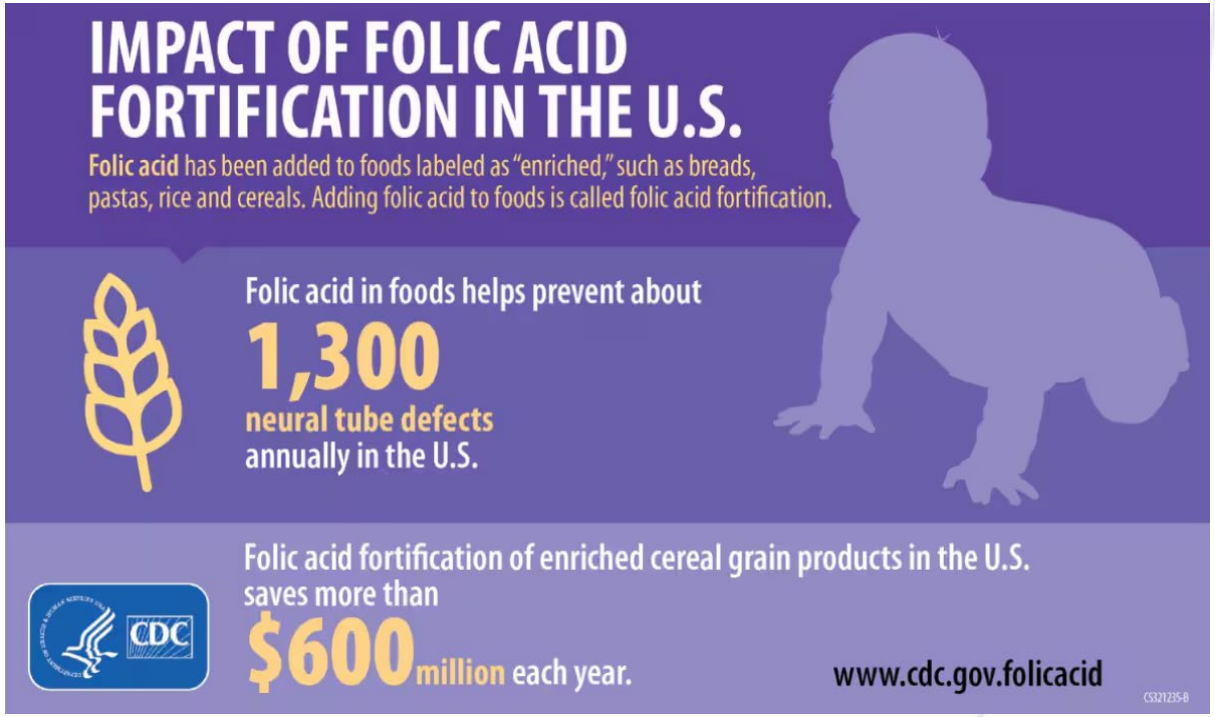
- Women who could become pregnant should take 400 mcg (0.4 mg) of folic acid through a vitamin.
- Women who have a child or had a pregnancy affected by Spina Bifida or have Spina Bifida themselves should take 4000 mcg (4.0 mg) of folic acid for one to three months before pregnancy.





Implementing Recommendations

- Encourage folate-rich diets
  - Legumes, asparagus, eggs, broccoli, leafy greens)
  - “Enriched” foods in the U.S. now contain 140 micrograms folic acid per 100 grams of grain product
- Encourage multivitamins, read the label and make sure it is folic acid (folic acid is the only form of folate shown in randomized control trials to prevent NTDs)



Implementing Recommendations

- Providing information regarding the importance of folic acid to women of childbearing age
  - Discussions during health class in school
  - Well child checks

- Working to make folate-rich foods more available

Folic Acid Safety

Per CDC:

“Folic acid not used by the body is called "unmetabolized folic acid." Folic acid is absorbed by the intestines into the bloodstream and then converted to other forms of folate by the liver. The liver is capable of processing only a certain amount of folic acid at one time. Unused folic acid in the blood goes to the kidneys and leaves the body in urine.

Since the beginning of mandatory folic acid fortification, most people have had some unmetabolized folic acid circulating in their blood.6 Although some people have been concerned about unmetabolized folic acid in the blood, no confirmed health risks have been found.”

Questions/Thoughts?

A big thank you to Dr. Joe O'Neil for his mentorship and support during this presentation!

References

- https://www.massgeneral.org/children/spina-bifida/causes-symptoms
- https://www.ncbi.nlm.nih.gov/books/NBK557722/
- https://www.ncbi.nlm.nih.gov/books/NBK10080/#:~:text=During%20primary%20neurulation%2C%20the%20original,3)%20the%20neural%20crest%20cells.
- https://www.cdc.gov/spina-bifida/data/index.html#:~:text=Spina%20bifida%20occurs%20among%201,the%20risk%20of%20spina%20bifida.
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4151938/
- DynaMedex. Spina Bifida. EBSCO Information Services. Accessed August 22, 2024. https://www.dynamedex.com/condition/spina-bifida
- (Folic Acid). In: Merative Micromedex® DRUGDEX® (electronic version). Merative Healthcare Solutions/EBSCO Information Services, Greenwood Village, Colorado; Cambridge, Massachusetts, USA. Available at: https://www.dynamedex.com (cited: August 22, 2024)
- https://www.cdc.gov/folic-acid/media/pdfs/cdc-presentation-folic-acid-best-tool-prevent-ntds-p.pdf

References

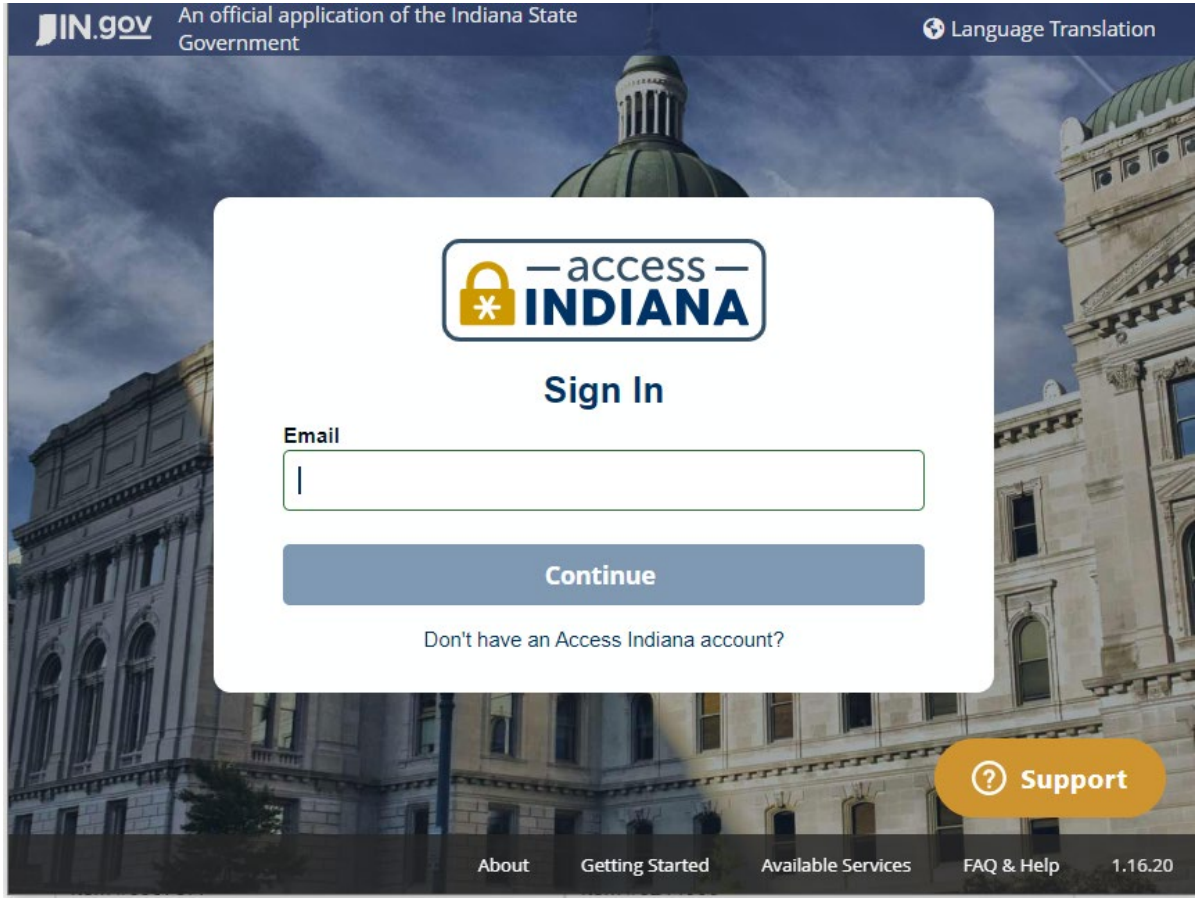
- Watanabe, H., & Miyake, T. (2017). Folic and Folate Acid. InTech. doi: 10.5772/intechopen.69383
- Williams LJ, Rasmussen SA, Flores A, Kirby RS, Edmonds LD. Decline in the prevalence of spina bifida and anencephaly by race/ethnicity: 1995-2002. Pediatrics. 2005 Sep;116(3):580-6. doi: 10.1542/peds.2005-0592. PMID: 16140696.
- https://www.thelancet.com/journals/lancet/article/PII0140-6736(91)90133-A/fulltext
- https://www.nejm.org/doi/full/10.1056/NEJM199212243272602
- US Preventive Services Task Force. Folic Acid Supplementation to Prevent Neural Tube Defects: US Preventive Services Task Force Reaffirmation Recommendation Statement. *JAMA.* 2023;330(5):454–459. doi:10.1001/jama.2023.12876

IDOH Laboratory: LimsNet Reminders

Indiana Department of Health

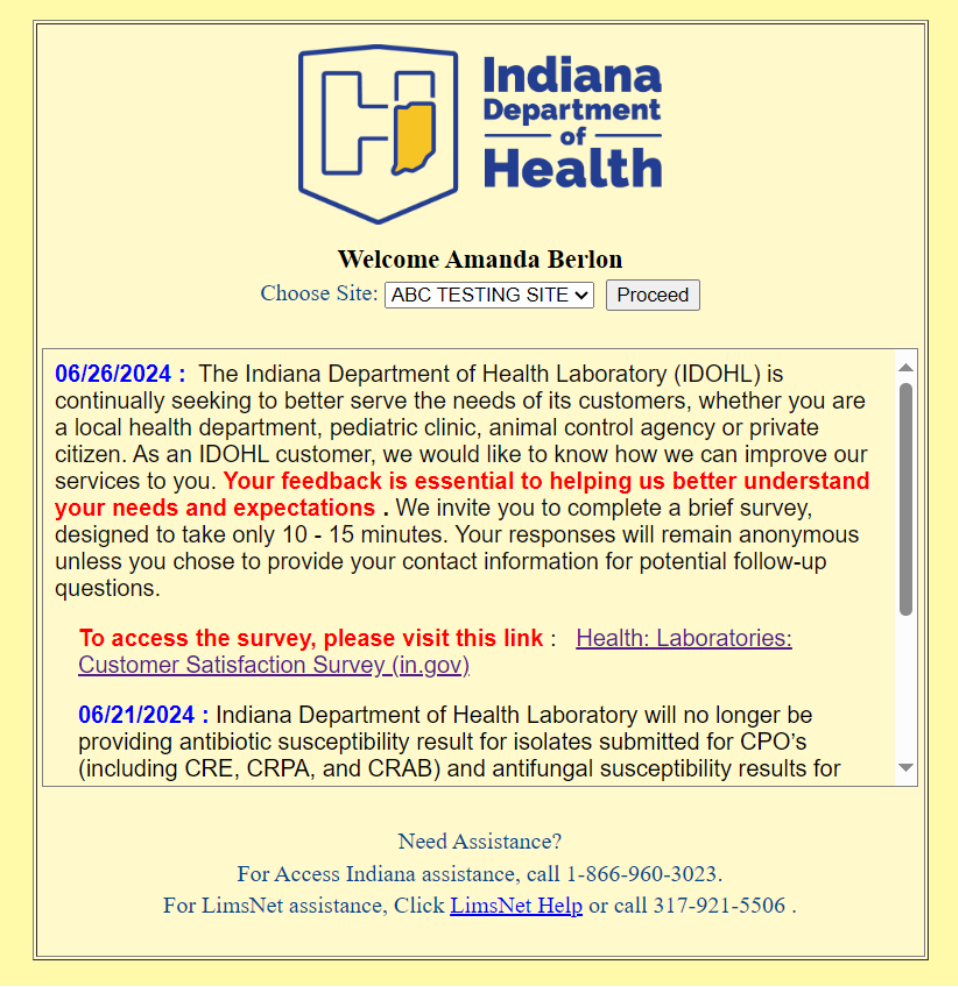
LimsNet Access

Remember, the LimsNet log in portal is now through Access Indiana:



Indiana Department of Health

LimsNet Updates

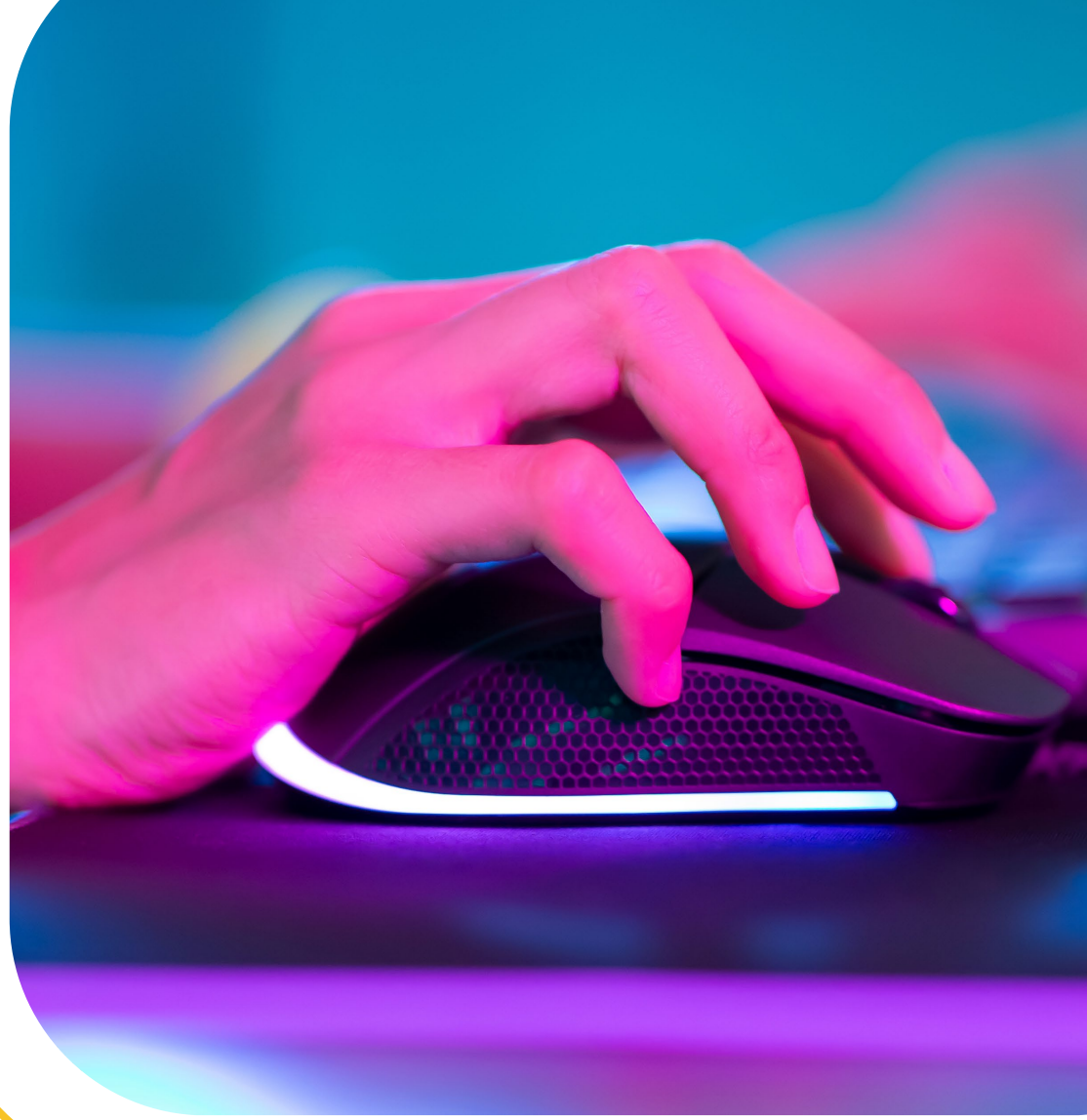


Before selecting your site, please review the **Message of the Day** section to see the most recent LimsNet and/or Laboratory testing updates.

Indiana Department of Health

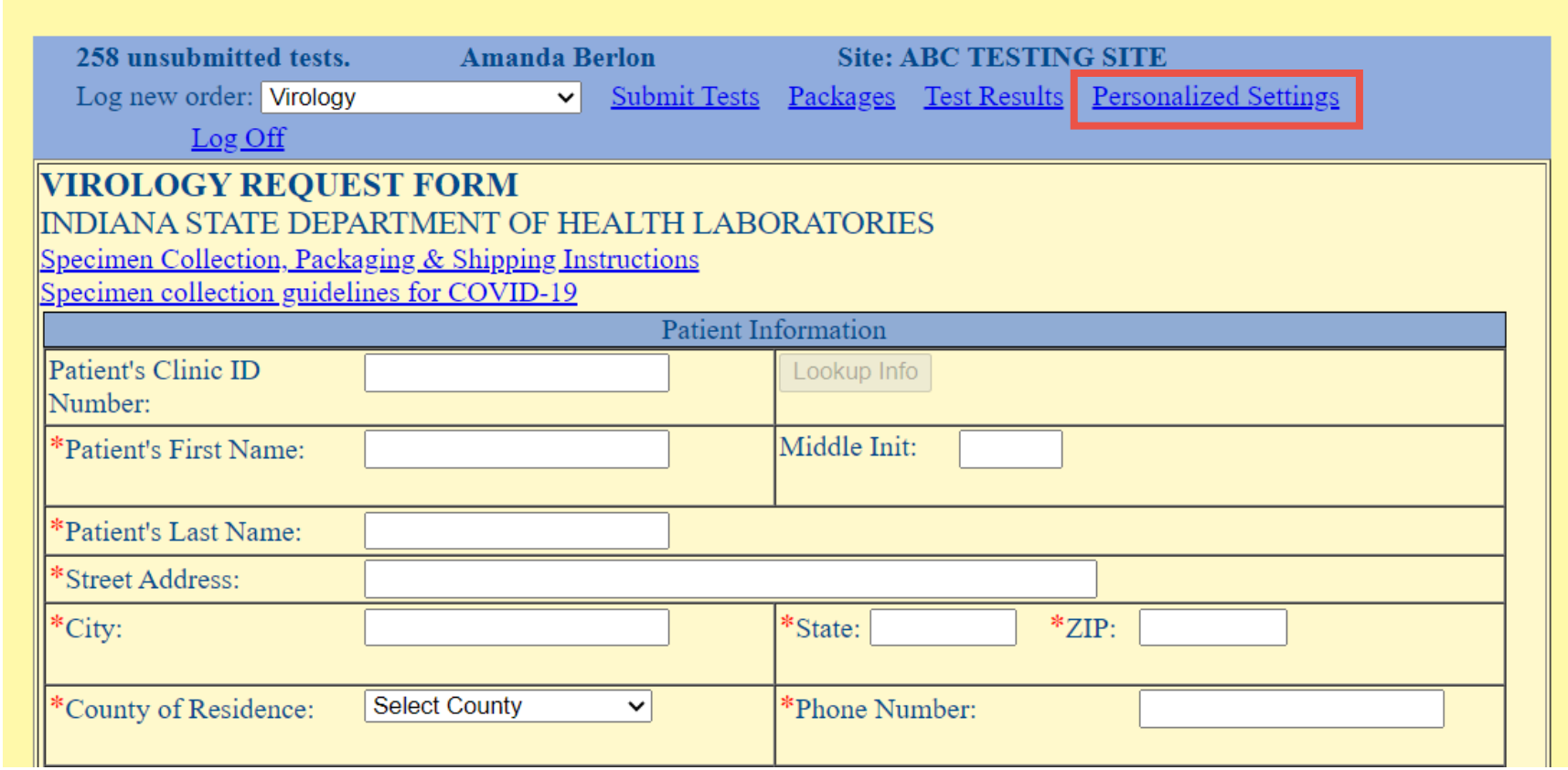
LimsNet Email Notifications

- Setting up email notifications in LimsNet only takes **3 clicks** after choosing your site!
- This is an **OPT IN ONLY** setting.



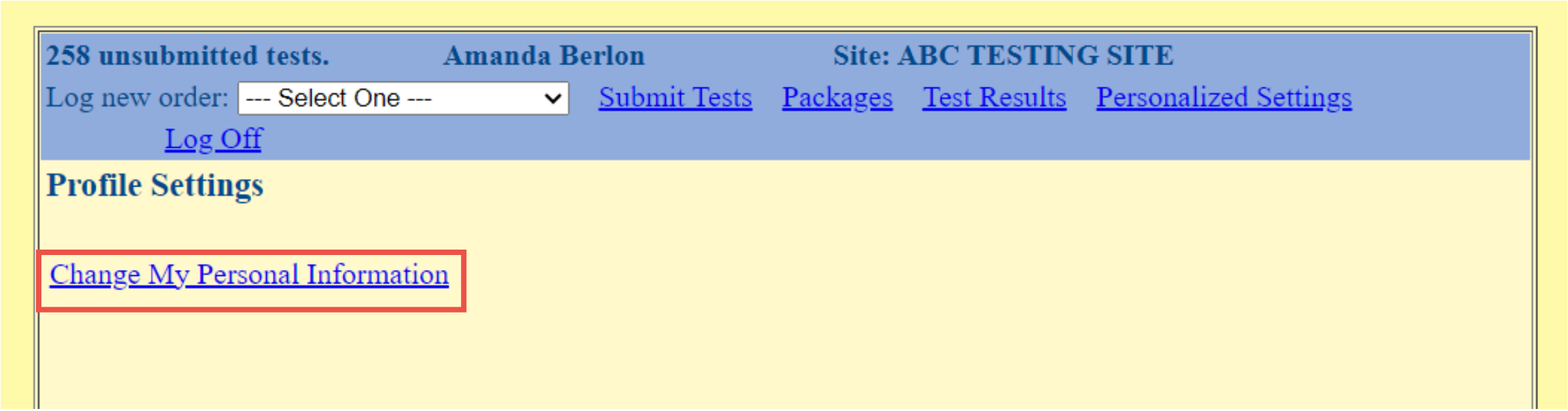
How to OPT IN to email notifications

1. Go to your blue LimsNet header and select "Personalized Settings."



How to OPT IN to email notifications

2. On the Profile Settings page, click on "Change my Personal Information."



How to OPT IN to email notifications

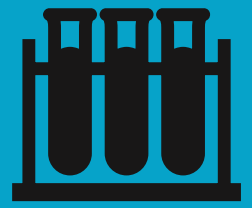
3. On the Profile Settings Page, check the box for "Subscribe to Email Notifications" and click "Update My Information." The system will automatically update to reflect the new setting.

LimsNet Result Reporting Responsibilities

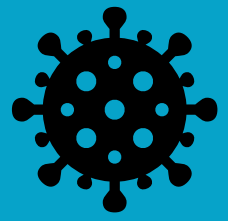
IDOH Laboratory's Responsibility

Testing completed at IDOH Laboratory

Results published on LimsNet



Notification email* sent to the SUBMITTING LimsNet account ONLY**



Submitter's Responsibility

We recommend: LimsNet report receiver uploads results to EHR

Ordering provider reviews results in EHR and decides next clinical steps

*ONLY if the account holder has opted in to LimsNet email notifications (as previously shown).

**This is due to HIPAA and IDOH Confidentiality Policy and cannot be changed (i.e., adding additional email addresses).

Indiana Department of Health

LimsNet Contact Information

Email: LimsAppSupport@health.IN.gov

Help desk: 317-921-5506 (during business hours)

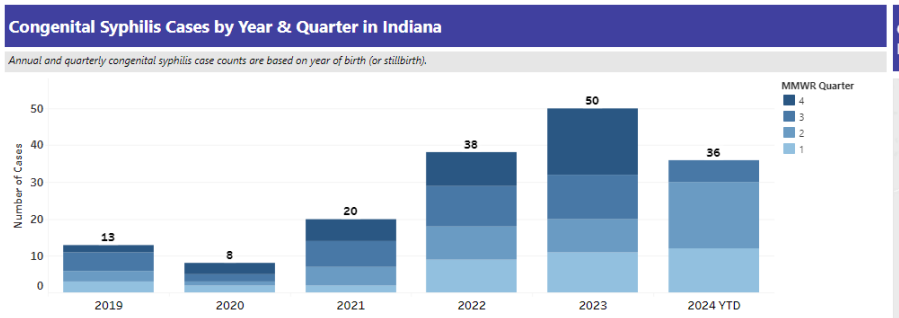
Please do NOT leave a message. Email or call again.

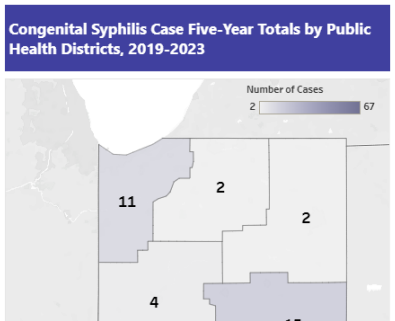
Infectious Diseases of Public Health Importance

Indiana Department of Health

Syphilis

- Currently have 36 cases of congenital syphilis in Indiana this year as of this week (50 last year)
- New at-home testing approved by the FDA on 8/16
  - Per the manufacturer's package insert for healthcare providers:
    - 93.4% PPA, 99.5% NPA
    - Around $30





Congenital Syphilis Cases by Public Health Districts in Indiana

Annual and quarterly congenital syphilis case counts are based on year of birth (or stillbirth). District is based on mother's residence at birth.

	2019				2020				2021				2022				2023				Five-Year Total	2024 YTD		
	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4		1	2	3
District 1		1		1	1					1			1	1				2		3	11		1	
District 2									1								1				2	1		
District 3															1		1				2			
District 4										1	1						1	1			4	1	1	1
District 5			2	1	1	1		1	1	1	6	2	6	4	6	6	6	5	8	10	67	7	12	5
District 6			1				2	1		1		3	1	2		3				1	15			
District 7			1					1						2	2				1		7	1	1	
District 8	1																1		1	2	5	1		
District 9	1	2								1		1							2		7		1	
District 10	1		1										1		2		1	1		2	9	1	2	

FDA NEWS RELEASE

FDA Marketing Authorization Enables Increased Access to First Step of Syphilis Diagnosis

First Home Antibody Test Can Inform Patients of Current or Past Infection and Lead to Confirmatory Testing with Health Care Provider

WHAT YOU NEED TO KNOW ABOUT FALL VACCINES 2024

Immunizations have been shown to lower risk of severe disease. Speak to your health care provider about the best timing for you.

Vaccine	Who	What	When
FLU	People 6 months of age and older	Updated 2024–2025 flu vaccine	During flu season. September and October remain the best times for most people to get vaccinated
COVID	Everyone aged 6 months and older should get 1 updated Moderna, Novavax, or Pfizer COVID-19 vaccine to be up to date.	Updated 2024–2025 COVID-19 vaccine	During fall and winter respiratory disease season
RSV	Adults over 75 and older and adults 60-74 at increased risk of severe RSV	NOT AN ANNUAL VACCINE	Eligible adults can get any time, best time is in late summer and early fall

WHAT YOU NEED TO KNOW ABOUT FALL VACCINES 2024

Immunizations have been shown to lower risk of severe disease. Speak to your health care provider about the best timing for you.

Vaccine	Who	What	When
RSV	Pregnant women at 32-36 weeks	Pfizer Abrysvo is the only RSV vaccine approved for pregnant women	September through January
RSV	Infants 19 months and younger	Monoclonal antibody shot	October through the end of March

Indiana Department of Health

Indiana Department of Health

https://www.in.gov/health/immunization/files/24_FALL-immunizations-004.pdf

RSV maternal vaccine & infant monoclonal antibody recommendations from CDC

Infants and young children

- To prevent severe RSV disease in infants, CDC recommends either maternal RSV vaccination or infant immunization with RSV monoclonal antibodies. **Most infants will not need both.**

Vaccination for pregnant women

• 1 dose of maternal RSV vaccine during weeks 32 through 36 of pregnancy, administered **September through January.** Pfizer Abrysvo is the only RSV vaccine recommended during pregnancy.

Immunization for infants and young children (monoclonal antibodies)

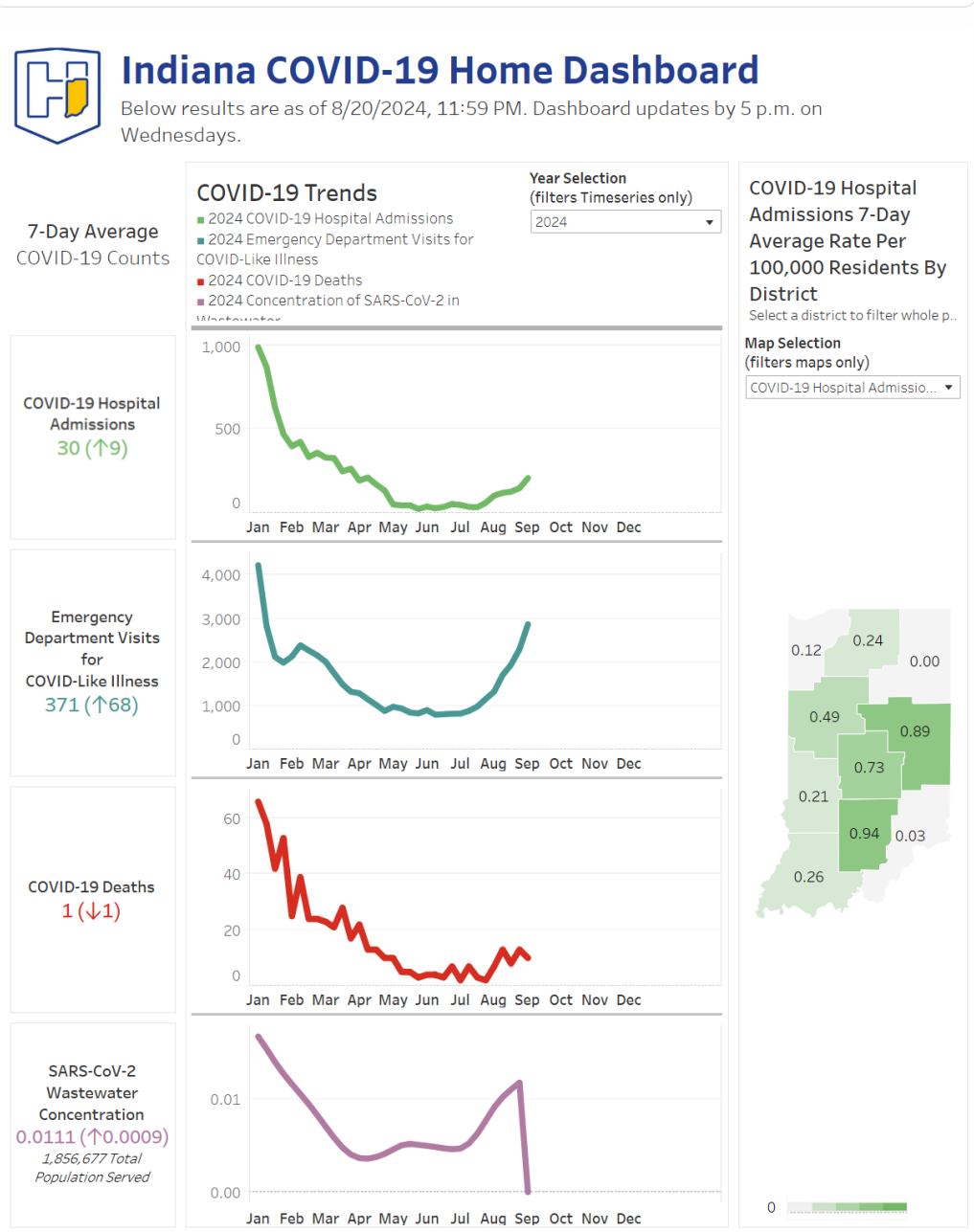
• 1 dose of nirsevimab is recommended for infants younger than 8 months of age who were born shortly before or are entering their first RSV season (typically fall through spring)

• 1 dose of nirsevimab for infants and children aged 8–19 months who are at increased risk for severe RSV disease and entering their second RSV season.

• *Note:* A different monoclonal antibody, palivizumab, is limited to children aged 24 months and younger with certain conditions that place them at high risk for severe RSV disease. It must be given once a month during RSV season.

COVID-19 in Indiana

[Health: Infectious Disease Epidemiology & Prevention Division: Coronavirus]



Indiana Department of Health

COVID-19 Update for the United States

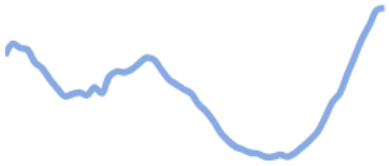
Early Indicators

Test Positivity

% Test Positivity

18.1%

Week ending August 10, 2024
Previous week 17.9%



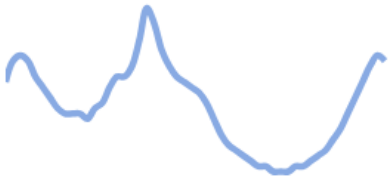
Aug 19, 2023 Aug 10, 2024

Emergency Department Visits

% Diagnosed as COVID-19

2.4%

Week ending August 10, 2024
Previous week 2.5%



Aug 19, 2023 Aug 10, 2024

These early indicators represent a portion of national COVID-19 tests and emergency department visits. Wastewater information also provides early indicators of spread.

Severity Indicators

Hospitalizations

Rate per 100,000 population

3.3

Week ending July 20, 2024
Previous week 3.2

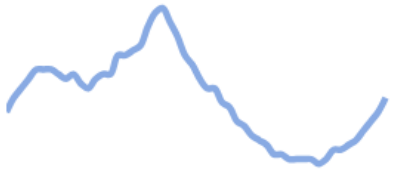
Jul 29, 2023 Jul 20, 2024

Deaths

% of All Deaths in U.S. Due to COVID-19

1.9%

Week ending August 10, 2024
Previous week 1.6%



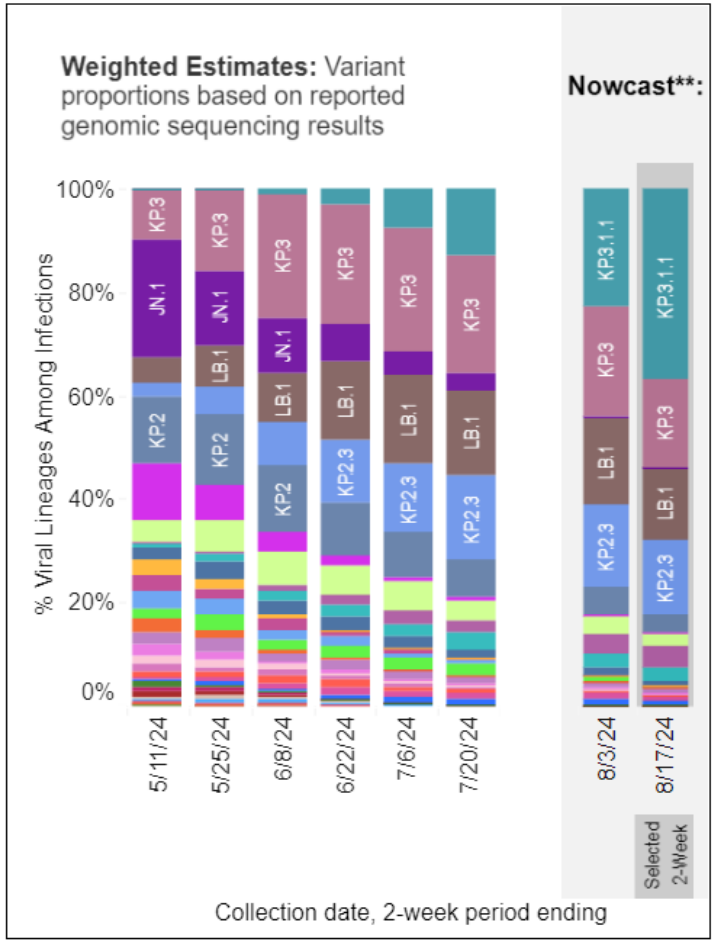
Aug 19, 2023 Aug 10, 2024

CDC | Test Positivity data through: August 10, 2024; Emergency Department Visit data through: August 10, 2024; Hospitalization data through: July 20, 2024; Death data through: August 10, 2024.
Posted: August 19, 2024 3:49 PM ET

Weighted and Nowcast Estimates in United States for 2-Week Periods in 4..

Nowcast Estimates in United States for 8/4/2024 – 8/17/2024

Hover over (or tap in mobile) any lineage of interest to see the amount of uncertainty in that lineage's estimate.



USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	KP.3.1.1	36.8%	31.1-42.7%	
	KP.3	16.8%	14.4-19.6%	
	KP.2.3	14.4%	11.7-17.7%	
	LB.1	14.1%	11.2-17.5%	
	LP.1	4.1%	3.0-5.6%	
	KP.2	3.2%	2.7-3.8%	
	KP.1.1	2.7%	1.9-3.7%	
	KP.1.1.3	2.5%	1.7-3.6%	
	KS.1	1.0%	0.6-1.7%	
	KP.2.15	0.9%	0.4-2.1%	
	LF.3.1	0.9%	0.6-1.4%	
	JN.1.16.1	0.8%	0.5-1.1%	
	JN.1.18	0.4%	0.3-0.7%	
	KP.4.1	0.3%	0.2-0.6%	
	JN.1	0.2%	0.1-0.3%	
	JN.1.11.1	0.2%	0.1-0.3%	
	XDV.1	0.2%	0.1-0.4%	
	KW.1.1	0.1%	0.1-0.2%	
	JN.1.16	0.1%	0.1-0.1%	
	KP.1.2	0.1%	0.0-0.1%	
	JN.1.7	0.1%	0.1-0.1%	
	KQ.1	0.0%	0.0-0.0%	
	JN.1.13.1	0.0%	0.0-0.0%	
	JN.1.4.3	0.0%	0.0-0.0%	
	JN.1.8.1	0.0%	0.0-0.0%	
	XDP	0.0%	0.0-0.0%	
	JN.1.32	0.0%	0.0-0.0%	

Indiana Department of Health

https://covid.cdc.gov/covid-data-tracker/#variant-summary

FDA Approves Updated COVID-19 vaccines

- Based on KP.2 which is of JN.1 lineage
- Monovalent
- FDA recommendations from the release:

FDA NEWS RELEASE

FDA Approves and Authorizes Updated mRNA COVID-19 Vaccines to Better Protect Against Currently Circulating Variants

Unvaccinated individuals 6 months through 4 years of age are eligible to receive three doses of the updated, authorized Pfizer-BioNTech COVID-19 Vaccine or two doses of the updated, authorized Moderna COVID-19 Vaccine.

Individuals 6 months through 4 years of age who have previously been vaccinated against COVID-19 are eligible to receive one or two doses of the updated, authorized Moderna or Pfizer-BioNTech COVID-19 vaccines (timing and number of doses to administer depends on the previous COVID-19 vaccine received).

Individuals 5 years through 11 years of age regardless of previous vaccination are eligible to receive a single dose of the updated, authorized Moderna or Pfizer-BioNTech COVID-19 vaccines; if previously vaccinated, the dose is administered at least 2 months after the last dose of any COVID-19 vaccine.

Individuals 12 years of age and older are eligible to receive a single dose of the updated, approved Comirnaty or the updated, approved Spikevax; if previously vaccinated, the dose is administered at least 2 months since the last dose of any COVID-19 vaccine.

Additional doses are authorized for certain immunocompromised individuals ages 6 months through 11 years of age as described in the Moderna COVID-19 Vaccine and Pfizer-BioNTech COVID-19 Vaccine fact sheets.

https://www.fda.gov/news-events/press-announcements/fda-approves-and-authorizes-updated-mrna-covid-19-vaccines-better-protect-against-currently#:~:text=The%20updated%20mRNA%20COVID%2D19,through%2011%20years%20of%20age.

Increase in *Mycoplasma pneumoniae*

What is Known:

- *M. pneumoniae* usually peaks every 3 to 7 years, with variation of strain types contributing to this pattern.
- During fall 2023, started to see a re-emergence globally and since that time, there has been a relatively intense spike in cases in the U.S.
- *M. pneumoniae* infections are a common bacterial respiratory infections that are most common in young adults and school-aged children.
- In 2024 CDC has seen an increase in *M. pneumoniae* infections, including in young children.

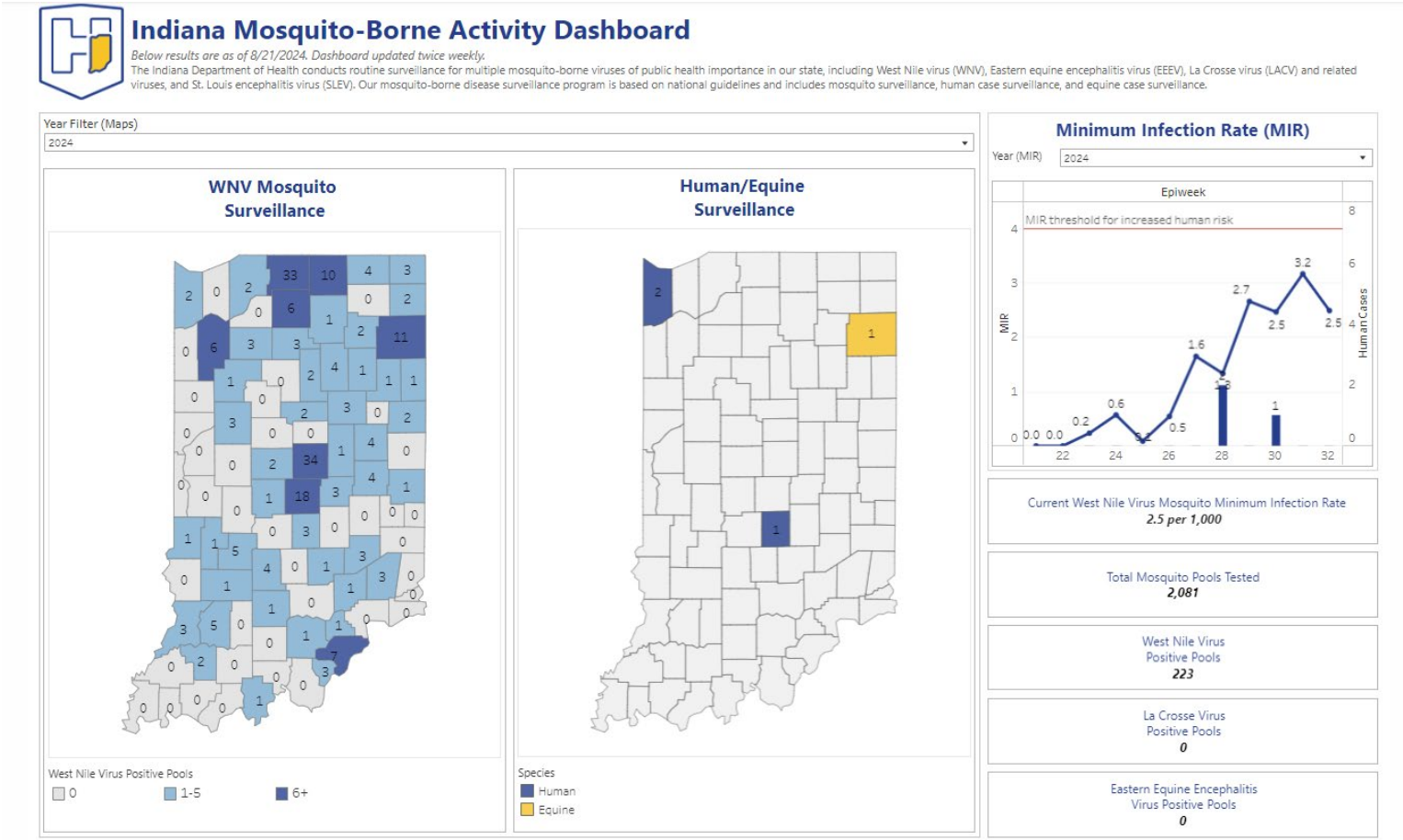
What is Unknown:

- If there is a change in the severity of infections or development of extrapulmonary conditions.
  - This includes tracking if patients are developing *Mycoplasma pneumoniae*-induced rash and mucositis (MIRM) and encephalitis.
  - Resistance to macrolides has remained low in the US

Resources

1. CDC *Mycoplasma pneumoniae* Infection Surveillance and Trends - https://www.cdc.gov/mycoplasma/php/surveillance/index.html
2. Clinical Care of *Mycoplasma pneumoniae* Infection - https://www.cdc.gov/mycoplasma/hcp/clinical-care/index.html
3. Laboratory Testing for *Mycoplasma pneumoniae* - https://www.cdc.gov/mycoplasma/php/laboratories/index.html
4. Submitting Specimens for *Mycoplasma pneumoniae* Testing - https://www.cdc.gov/mycoplasma/php/laboratories/specimen-packing.html
5. MMWR (Notes from the Field): Reemergence of *Mycoplasma pneumoniae* Infections in Children and Adolescents After the COVID-19 Pandemic, United States, 2018-2024 - https://www.cdc.gov/mmwr/volumes/73/wr/mm7307a3.htm?s_cid=mm7307a3_w

Indiana Mosquito-Borne Activity Dashboard



Indiana Department of Health

[Health: Infectious Disease Epidemiology & Prevention Division: Mosquito-Borne Diseases]

Recent Health Alerts from CDC

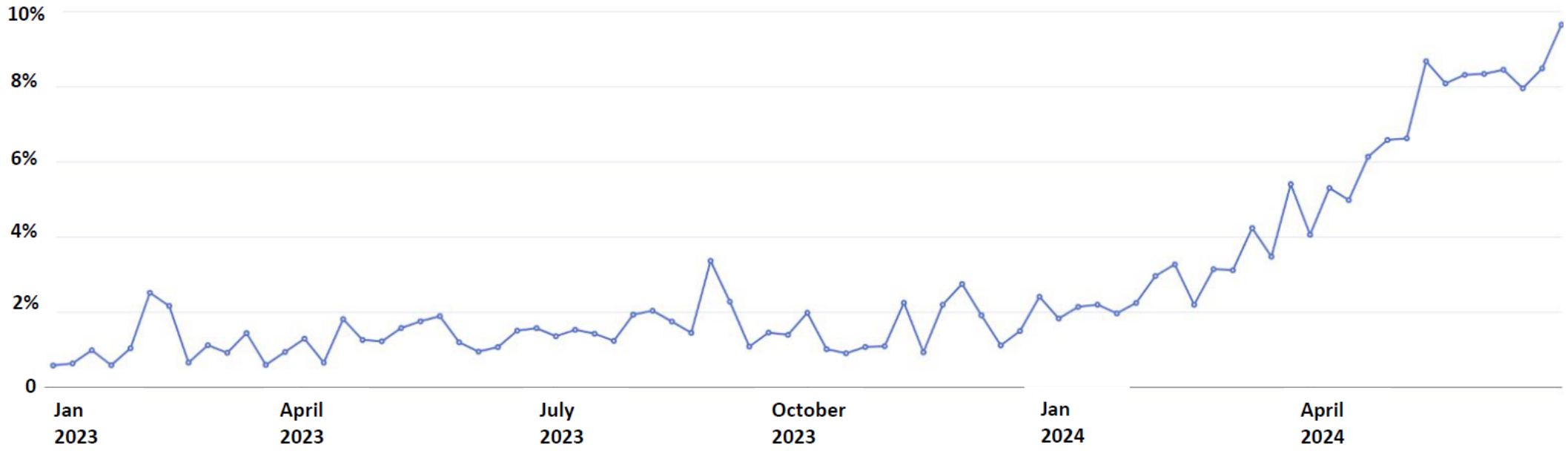
Indiana Department of Health

Increase in Human Parvovirus B19 Activity in the United States

- In the first quarter of 2024, public health authorities in 14 European countries observed unusually high numbers of cases of parvovirus B19.
- In the United States, **there is no routine surveillance for parvovirus B19, and it is not a notifiable condition.** Recently, CDC has received reports indicating increased parvovirus B19 activity in the United States.
    - Data include increased test positivity for parvovirus B19 in clinical specimens and pooled plasma from a large commercial laboratory, and reports of clusters of parvovirus B19-associated complications among pregnant women and people with sickle cell disease.
    - The proportion of people with IgM antibodies, an indicator of recent infection, increased among all ages from <3% during 2022–2024 to 10% in June 2024; the greatest increase was observed among children aged 5–9 years, from 15% during 2022–2024 to 40% in June 2024.
    - Among plasma donors, the prevalence of pooled samples with parvovirus B19 DNA >104 IU/mL increased from 1.5% in December 2023 to 19.9% in June 2024.

A large U.S. commercial laboratory observed increases in test positivity for acute B19 infection in 2024.

Percent positivity of Parvovirus B19 IgM serological testing, Lab A*,
CDC's National Syndromic Surveillance Program, United States Jan 2023 – June 2024

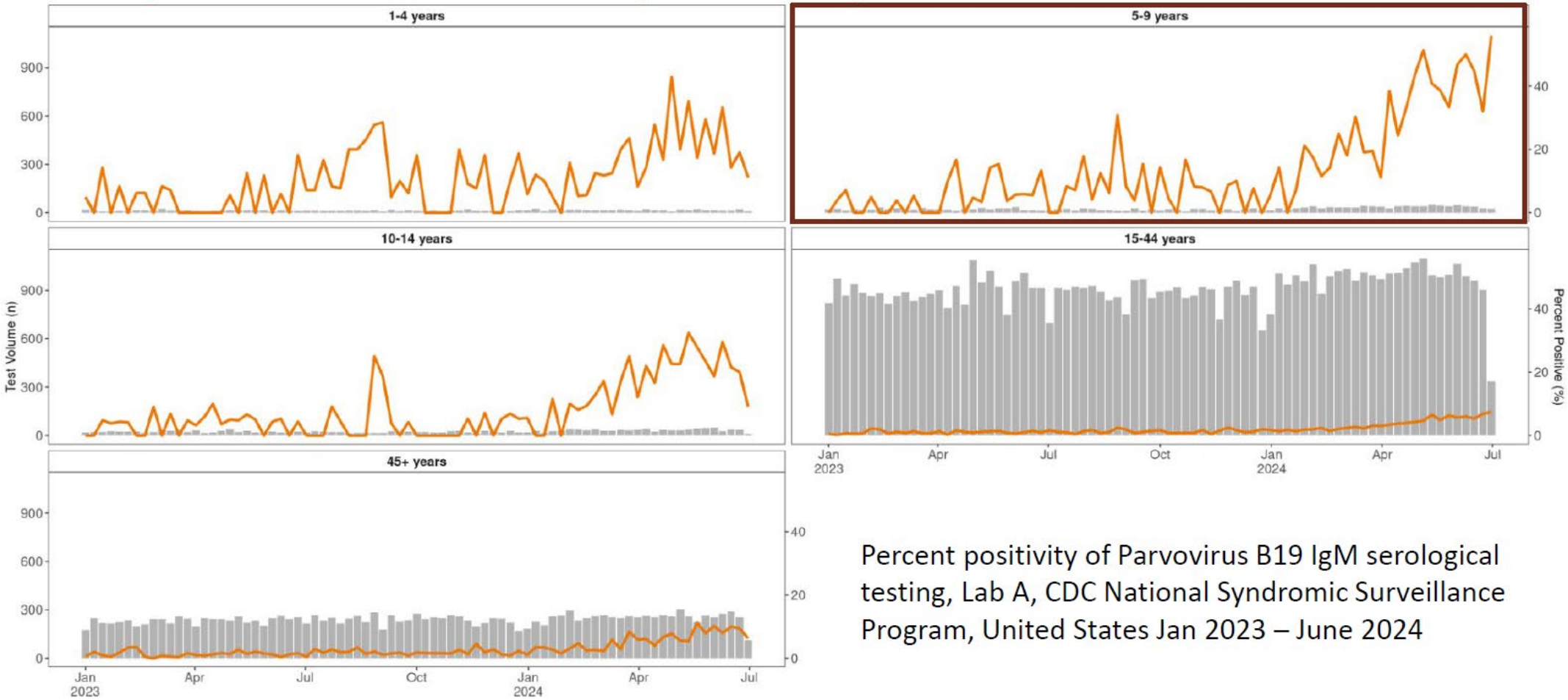


*Lab A conducted between 1,200 – 1,500 B19 IgM tests per week in this period.

Indiana Department of Health

Courtesy: Council of State and Territorial Epidemiologists (CSTE) Meeting August 19, 2024

B19 test positivity increased in all ages and was highest for children aged 5–9 years.



Percent positivity of Parvovirus B19 IgM serological testing, Lab A, CDC National Syndromic Surveillance Program, United States Jan 2023 – June 2024

Indiana Department of Health

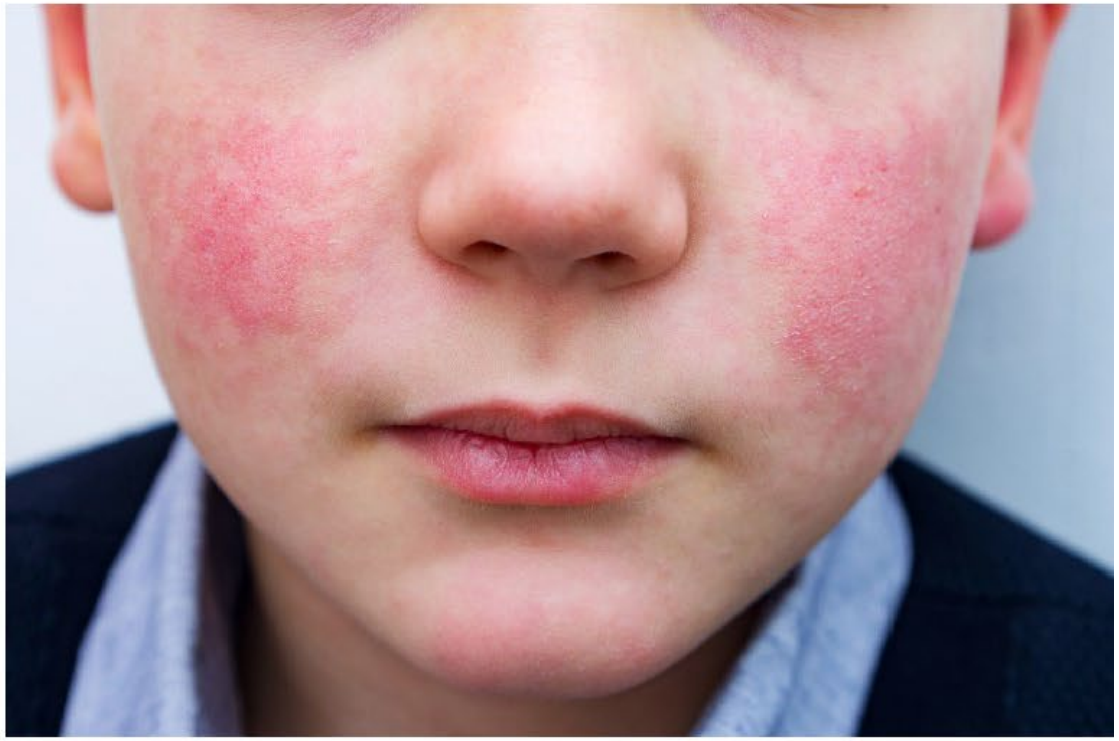
Courtesy: Council of State and Territorial Epidemiologists (CSTE) Meeting August 19, 2024

Clinical Features and Management

- Immunocompetent: Asymptomatic or biphasic illness
- First phase: fever, myalgia, malaise, about 7 days after infection, lasting for about five days. Most contagious. High viral content in respiratory secretions and saliva.
- Second phase:
  - About a week to 10 days later children often present with a characteristic facial rash (erythema infectiosum, or "slapped cheek" appearance), which may be followed by reticulated body rash arthralgia 1–4 days later.
  - In immunocompetent adults, the most common symptoms of parvovirus B19 disease typically occur during the second phase and include a reticular rash on the trunk, arthralgia.
  - Typically, the characteristic facial rash does not appear until after viral loads (a measure of infectiousness) have declined.
- Laboratory tests conducted during acute illness can demonstrate a transient decrease in absolute reticulocyte counts lasting approximately 10 days, mild anemia, thrombocytopenia, or leukopenia.
- Most people require only supportive care during the acute phase of illness and will recover completely.
- Severe outcomes from parvovirus B19 disease, such as myocarditis, hepatitis, or encephalitis, are rare.
- No vaccine or specific treatment is recommended for parvovirus B19 infection.

Parvovirus B19 results in mild respiratory disease for most of the population.

- ~25% of individuals are asymptomatic.
- First phase: Fever, myalgia, and malaise lasting 2-5 days. **Individuals are highly contagious.**
- Second phase: Facial rash ("slapped cheek" in children), body rash, and joint pain. **Individuals are no longer contagious.**



Courtesy: Council of State and Territorial Epidemiologists (CSTE) Meeting August 19, 2024

Possible Complications

Parvovirus B19 infection can lead to adverse health outcomes among patients without pre-existing immunity who are pregnant, immunocompromised, or have chronic hemolytic disorders.

- During pregnancy, most cases of fetal parvovirus B19 infection resolve spontaneously without adverse outcomes.
  - However, the risk of an adverse fetal outcome (e.g., fetal anemia, non-immune hydrops, or fetal loss) is 5–10%, and is highest when acute infection occurs between gestational weeks 9–20.
  - Treatment for acute infection in the pregnant woman is supportive, and management includes monitoring for and treating severe fetal anemia.
- Parvovirus B19 can cause chronic or transient aplastic anemia among people with severely immunocompromising conditions or chronic hemolytic disorders.
  - Red blood cell transfusions and intravenous immunoglobulin are the mainstays of treatment for aplastic anemia.

Recommendations

- Promote core prevention strategies to prevent respiratory illness.
- Have increased suspicion for parvovirus B19 among people presenting with compatible symptoms.
- Provide preventive counseling and have a low threshold to test people who present with compatible signs and symptoms if they are at higher risk of severe parvovirus B19 disease.
- When treating people with suspected or confirmed parvovirus B19, inform them or their caregivers about high-risk groups and advise any exposed contacts in those groups to consult with their healthcare providers.
- Follow standard of care (e.g., professional society guidelines) for testing pregnant women reporting exposure to parvovirus B19 infection or who present with compatible signs and symptoms of maternal or fetal parvovirus B19 disease.
- People at higher risk of severe outcomes or complications who work in settings with higher risk of parvovirus B19 exposure should practice hand hygiene, avoid sharing food or drinks, and consider wearing a respirator or mask while at work if so inclined.
- Follow recommended infection control precautions for patients with parvovirus B19 in healthcare settings.

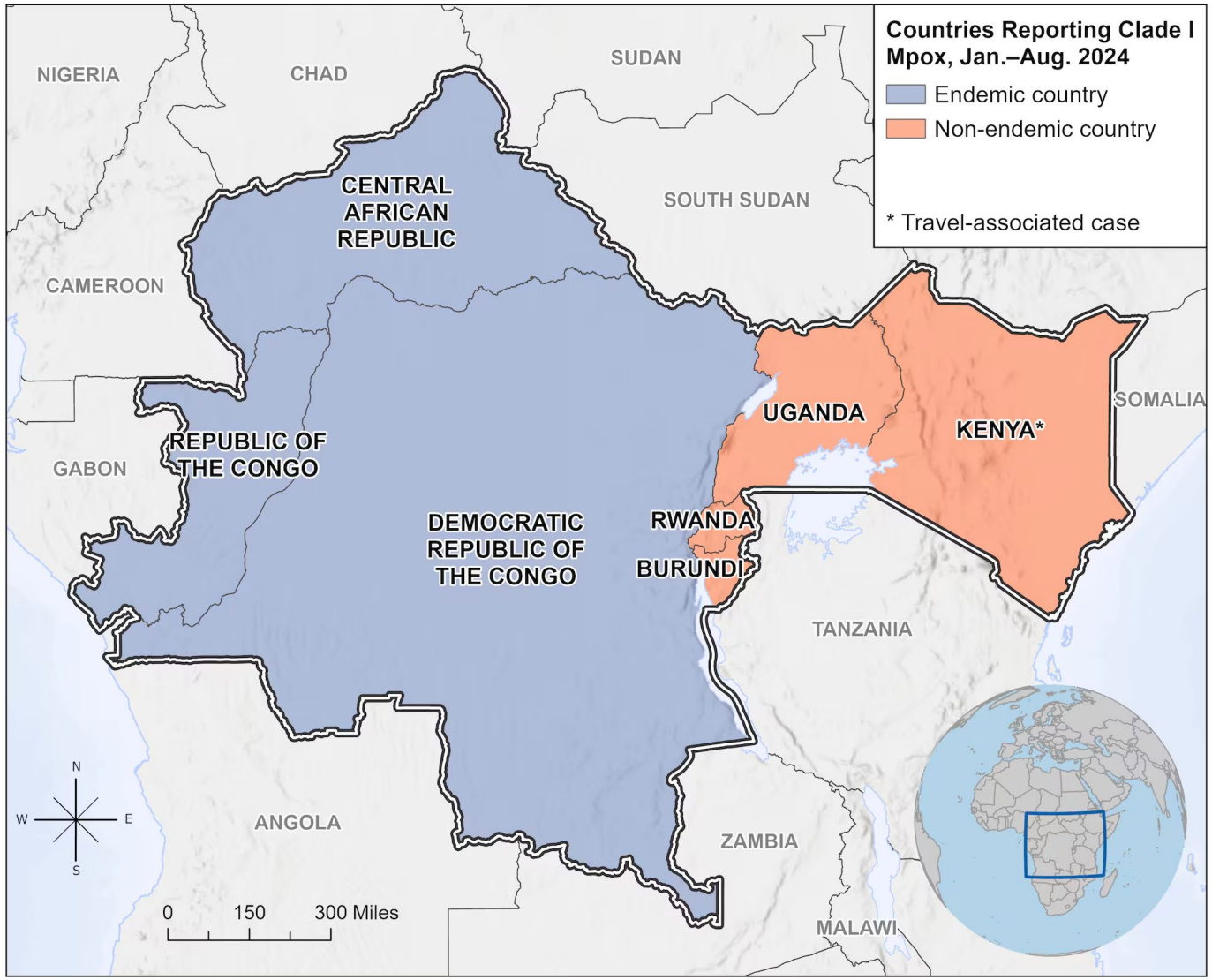
Mpox Clade I detected in countries near DRC: WHO declares mpox outbreak a PHE of International Concern

- In late July 2024, Burundi, Rwanda, and Uganda, which sit on the eastern border of DRC, reported confirmed cases of mpox, with some cases having linkages to DRC. Rwanda and Uganda have confirmed these cases are due to clade I MPXV; in Burundi, clade-specific testing is underway, but cases are presumed to be clade I due to DRC's proximity. Mpox is not known to be endemic in these countries.
- Since January 2023, the DRC has reported the largest number of yearly suspected clade I mpox cases on record.
- While clade I MPXV is endemic, in DRC, the current outbreak is more widespread than any previous DRC outbreak and has resulted in clade I mpox transmission to some neighboring countries.
- The Republic of the Congo (ROC), which borders DRC to the west, declared a clade I mpox outbreak in April 2024, and there have been confirmed cases in the Central African Republic (CAR).
- While clade I mpox is endemic in ROC and CAR, the epidemiologic pattern of recent cases suggests a possible link to DRC.

WHO Director-General declares mpox outbreak a public health emergency of international concern

Health Alert Network (HAN) - 00513 | Mpox Caused by Human-to-Human Transmission of Monkeypox Virus in the Democratic Republic of the Congo with Spread to Neighboring Countries (cdc.gov)

Countries with Confirmed or Presumed Clade I Mpox Cases, Central and Eastern Africa



2023 Outbreak in Democratic Republic of the Congo | Mpox | Poxvirus | CDC

CDC Clinical Recommendations

- Consider the diagnosis of clade I in a patient who develops symptoms suggestive of Mpox with a history of travel to countries in Africa with Clade 1 cases within 21 days:
  - **Consult with IDOH to coordinate testing – 317-508-8490 during business hours (8:15am-4:45pm M-F) or 317-233-1325 after hours or on the weekend**
  - Our lab can send to the CDC for genotyping
- Recommend adding screening questions about travel history if not already included
- Otherwise, treatment and other clinical recommendations are unchanged for now.
- Vaccination continues to be recommended by the CDC for adults who meet the eligibility criteria:

[1]Persons at risk:

- Gay, bisexual, and other men who have sex with men, transgender or nonbinary people who in the past 6 months have had one of the following:
  - A new diagnosis of ≥1 sexually transmitted disease
  - More than one sex partner
  - Sex at a commercial sex venue
  - Sex in association with a large public event in a geographic area where mpox transmission is occurring
- Sexual partners of persons with the risks described in above
- Persons who anticipate experiencing any of the above

Reference the IDOH mpox website, clinical guide for Mpox, and the CDC HAN for more information

Increased Oropouche Virus Activity and Associated Risk to Travelers

- Oropouche virus was first detected in 1955 in Trinidad and Tobago and is endemic in the Amazon basin.
- Between January 1 and August 1, 2024, more than 8,000 cases of Oropouche virus disease were reported, including two deaths and five cases of vertical transmission associated with fetal death or congenital abnormalities. Countries reporting cases include Brazil, Bolivia, Peru, Colombia, and Cuba.
- Sylvatic (enzootic) transmission of Oropouche virus occurs in forested areas between mosquitoes and non-human vertebrate hosts (e.g., sloths, primates, domestic and wild birds, and rodents). Humans can become infected while visiting forested areas and are likely responsible for introducing the virus into urban environments.
- Humans contribute to the transmission cycle in urban environments since infected humans develop sufficient viremia to serve as amplifying hosts.
  - Biting midges (Culicoides paraensis) and possibly certain mosquitoes (Culex quinquefasciatus) are responsible for transmitting the virus from an infected person to an uninfected person in urban areas.

Oropouche Virus

- In the United States and Europe in 2024, travel-associated cases have been identified in travelers returning from Cuba and Brazil. As testing and surveillance for Oropouche virus disease increase in the Americas, reports of cases from additional countries are expected.
  - Although travel-associated cases have been identified in the United States (n=11), no evidence of local transmission currently exists within the United States or its territories.
- Oropouche virus disease is not a nationally notifiable condition. However, CDC encourages jurisdictions to report voluntarily to ArboNET, the national arboviral disease surveillance system

Clinical Presentation

- Approximately 60% of people infected with Oropouche virus become symptomatic.
- The incubation period is typically 3–10 days. Initial clinical presentation is similar to diseases caused by dengue, Zika, and chikungunya viruses, with acute onset of fever, chills, headache, myalgia, and arthralgia. Other symptoms can include retroorbital (eye) pain, photophobia, nausea, vomiting, diarrhea, fatigue, maculopapular rash, conjunctival injection, and abdominal pain. Lab findings: lymphopenia and leukopenia, elevated C-reactive protein (CRP), and slightly elevated liver enzymes.
- Initial symptoms typically resolve after a few days, but a high proportion (about 70%) experience recurrent symptoms days to weeks after resolution of their initial illness.
- Although illness is typically mild, it is estimated less than 5% of patients can develop hemorrhagic manifestations (epistaxis, gingival bleeding, melena, menorrhagia, petechiae) or neuroinvasive disease (meningitis, meningoencephalitis, pleocytosis and elevated protein in CSF.
- Can cause vertical transmission and associated adverse birth outcomes.

Recommendations for Clinicians

- Consider Oropouche virus infection in a patient who has been in an area with documented or suspected Oropouche virus circulation within 2 weeks of initial symptom onset compatible with the clinical picture.
- **If you suspect that your patient may have Oropouche virus infection, you can call our IDOH team:**
  - **During business hours (8:15am-4:45pm M-F) 317-233-7125. After hours and weekends 317-233-1325.**
- Rule out dengue virus infection in travelers with suspect Oropouche virus infection because these viruses often cocirculate and cause similar clinical presentations during acute illness.
- No specific antiviral treatments or vaccines are available for Oropouche virus disease. Manage travelers with suspect Oropouche virus disease with acetaminophen as the preferred first-line treatment for fever and pain. Aspirin and other NSAIDS should not be used to reduce the risk of hemorrhage.
- Monitor pregnancies in women with laboratory evidence of Oropouche virus infection and provide thorough infant evaluations.
- Recommend measures to prevent insect bites in the context of travel.
- Inform pregnant women of the possible risks to the fetus when considering travel to areas with reported Oropouche virus transmission.

Other Public Health Updates

Indiana Department of Health

Federal Respiratory Reporting Changes to NHSN

- From September 2, 2020 to April 30, 2024, acute and critical access hospitals were **required** to report COVID-19 data to the United States Department of Health and Human Services (HHS)/ the Centers for Disease Control and Prevention (CDC) under the Centers for Medicare and Medicaid Services (CMS) Conditions of Participation (CoP) to continue to participate in Medicare and Medicaid services.
- Effective May 1, 2024, COVID-19 hospital reporting became *optional*.
- FY 2025 Hospital Prospective Payment System (IPPS) and Long-Term Care Hospital Prospective Payment System (LTCH PPS) Final Rule[1] (to be published on 8/28/2024), **requires acute care hospitals and critical access hospitals to electronically report information via the National Healthcare Safety Network (NHSN) about COVID-19, influenza, and RSV,** including confirmed infections of respiratory illnesses among hospitalized patients, hospital bed census, and capacity (both overall and by hospital setting and population group [adult or pediatric]), and limited patient demographic information, including age. Reporting changes will go into effect **November 1, 2024**.
- These changes **do not** apply to Long-term Care Facilities, Dialysis Facilities, or Healthcare Personnel (HCP) COVID-19 Vaccination reporting.

[1]Centers for Medicare & Medicaid Services. (2024). *Medicare, Medicaid, and Children's Health Insurance Programs: Hospital Inpatient Prospective Payment Systems for Acute Care Hospitals and the Long Term Care Hospital Prospective Payment System and Policy Changes and Fiscal Year 2025 Rates, etc.* Federal Register. *https://www.federalregister.gov/public-inspection/2024-17021/medicare-medicaid-and-childrens-health-insurance-programs-hospital-inpatient-prospective-payment?ACSTrackingID=USCDC_2134-DM133492&ACSTrackingLabel=New%20CMS%20Requirements%20for%20Reporting%20of%20Hospital%20Respiratory%20Data%20to%20NHSN%20&deliveryName=USCDC_2134-DM133492*

Key Dates

- **September 2, 2020**
  - All hospitals required to report COVID-19 data daily to the Federal Government under the CMS' Conditions of Participation.
- **December 15, 2022**
  - Hospital COVID-19 data collection was transitioned from Teletracking to NHSN
- **May 11, 2023**
  - COVID-19 Public Health Emergency (PHE) initially set to expire, but CMS amended required reporting, extending reporting past the end of PHE
- **November 26, 2023**
  - Optional RSV and flu reporting became available
- **May 1, 2024**
  - COVID-19 reporting for hospitals became optional

Key Dates (Continued)

- **October 1, 2024**
  - Reporting to the NHSN application will continue without changes, with all reporting modalities (webform, API, csv upload) continuing to be available
  - Changes to NHSN application user interface will begin to integrate reporting changes. No action required at this time, as CDC partners will provide communications in future days
- **November 1, 2024**
  - Reporting changes go into effect

Changes to Reporting Cadence

Facility types previously required to report weekly	Facility types previously required to report annually	Facility types not previously required to report
Acute Care Hospitals	Freestanding rehabilitation facilities	CMS-certified rehabilitation units (IRU within a hospital)
Long-term Acute Care Hospitals	Freestanding psychiatric facilities	CMS-certified psychiatric units (IPU within a hospital)
Critical Access Hospitals		Indian Health Services Hospitals (also Tribal Hospitals if they are Medicare participating)
Cancer Hospitals (PPS Exempt Cancer Hospitals)		
Children's Hospitals		

**Under new changes, all facilities listed above will report the same data elements and cadence*

General Reporting Requirements/Elements

- To meet CMS CoP requirements, facilities must report 48 of the 58 elements to include:
  - Prevalent hospitalizations for COVID-19, flu, and RSV+ for pathogen agnostic bed capacity and occupancy
    - Weekly snapshot – Provide data for Wednesday of reporting week
  - New admissions for COVID-19, flu, and RSV+ by age category
    - Weekly total (Sum for Sunday-Saturday for the reporting week)
      - Two pathways/templates for reporting (must choose one or the other):
        - Facility internally totals new admissions for the Sunday through Saturday reporting week, and reports that sum number to NHSN or
        - Facility reports daily new admissions values for each day separately, Sunday through Saturday during the reporting week into NHSN, and the NHSN application will aggregate to provide the total

VFC

Indiana Department of Health

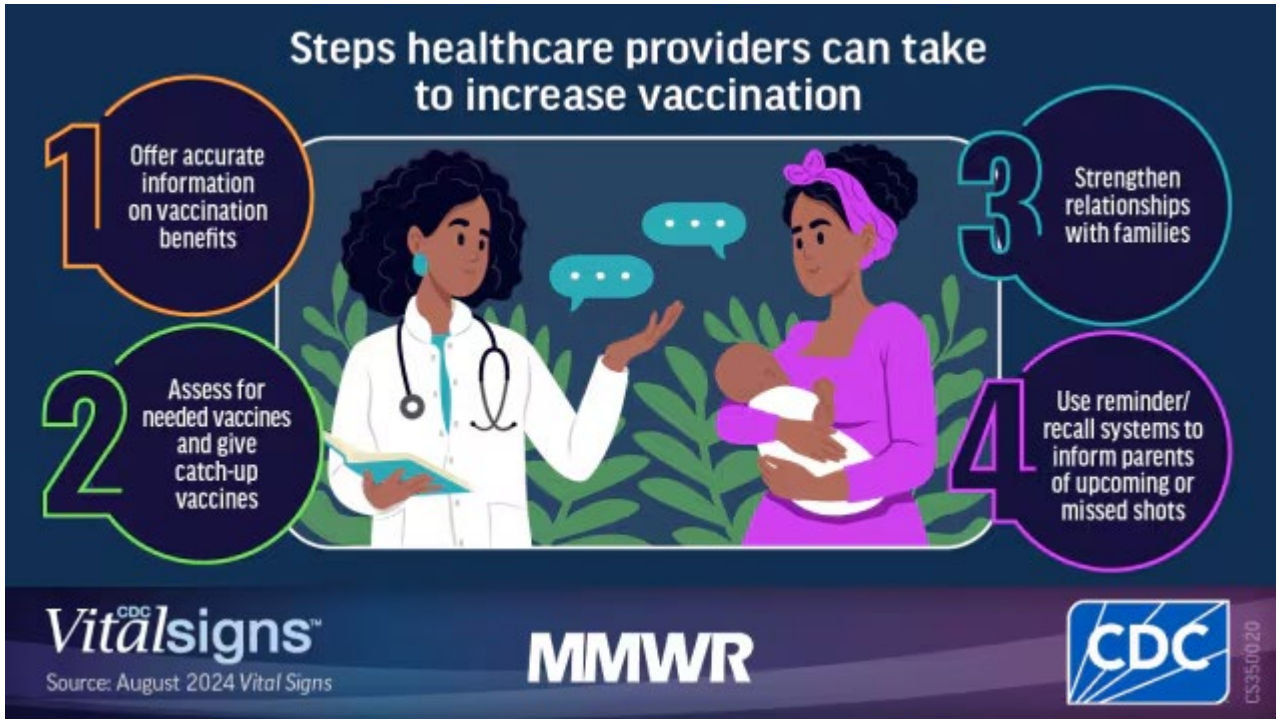
[Health and Economic Benefits of Routine Childhood Immunizations in the Era of the Vaccines for Children Program — United States, 1994–2023 | MMWR (cdc.gov)]

VFC

The Vaccines for Children (VFC) program covers the cost of vaccines for eligible children to help ensure that all U.S. children are protected from life-threatening vaccine-preventable diseases.

Among VFC-eligible children, coverage with measles, mumps, and rubella vaccine was high and stable during 2012 through 2022, but there is room for improvement to increase coverage with other routinely recommended vaccines.

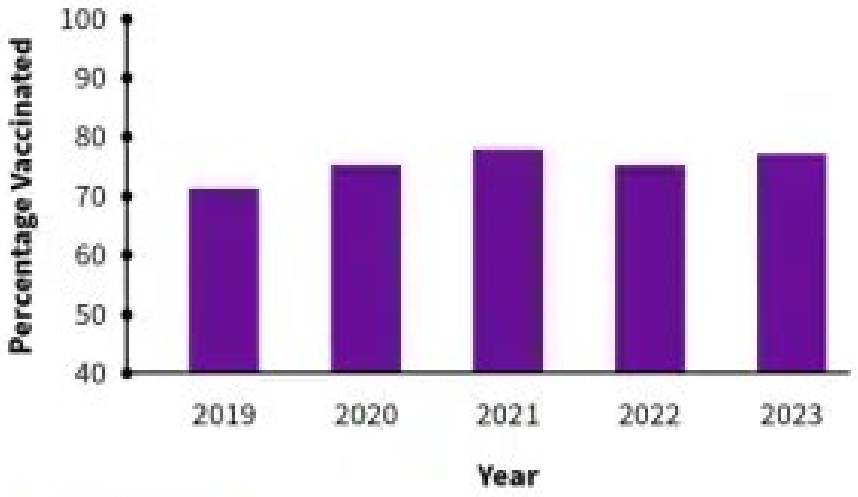
Among children born in 2020, vaccination coverage was 4–14 percentage points lower among children who were eligible versus non-eligible for the VFC program.



Indiana Department of Health

Vital Signs: Trends and Disparities in Childhood Vaccination Coverage by Vaccines for Children Program Eligibility — National Immunization Survey-Child, United States, 2012–2022 | MMWR (cdc.gov)

HPV vaccination coverage has not improved since the pandemic*



*≥1 Dose HPV vaccine coverage, 2019-2023 National Immunization Survey-Teen data

bit.ly/mm7333a1

August 22, 2024

Clinicians:

- Review vaccination records
- Recommend routine HPV vaccination at age 11 or 12 years to prevent HPV-attributable cancers †
- Talk about no-cost vaccination through VFC ‡

†HPV vaccination can be started at age 9

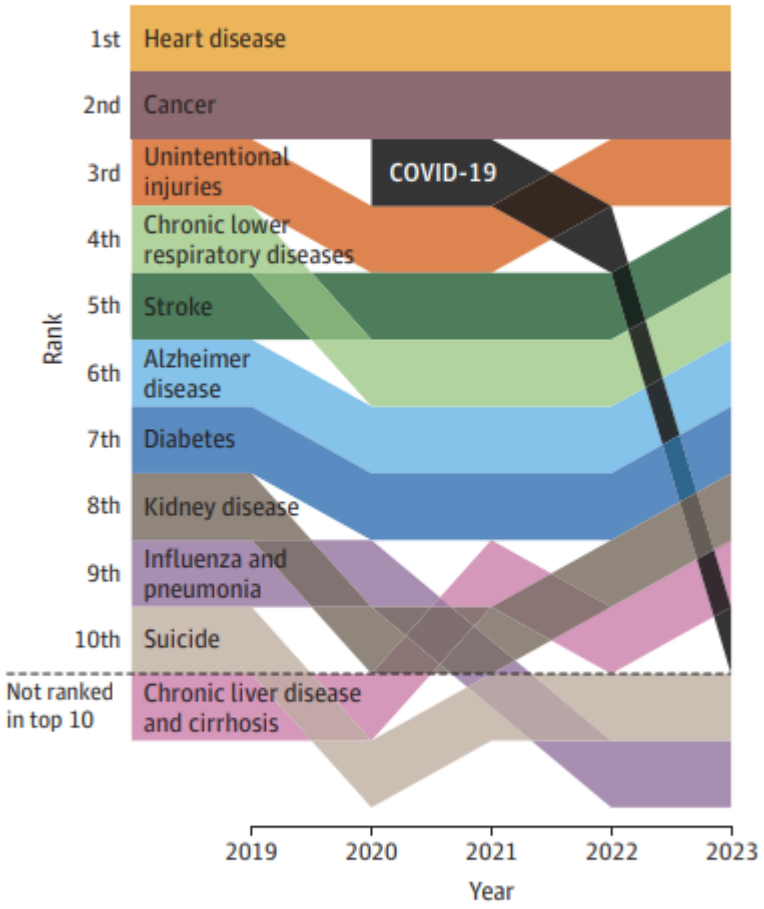
‡Vaccines For Children program

MMWR

Indiana Department of Health

National Vaccination Coverage Among Adolescents Aged 13–17 Years — National Immunization Survey-Teen, United States, 2023 | MMWR (cdc.gov)

Figure. Trends in the Ranking of Leading Causes of Death—US, 2019-2023



Source: National Center for Health Statistics. National Vital Statistics System. Data for 2019-2022 are final. Data for 2023 are provisional.

https://jamanetwork.com/journals/jama/article-abstract/2822207

Ways to connect with us

- Access our webpage with resources for clinicians
- Please let us know what topics you'd like us to cover: Email Gcrowder@health.in.gov
- Sign up for IHAN– Indiana Health Alert Network https://ihan-in.org
- MARK YOUR CALENDARS - Clinician webinars for 2024: Sept. 27, Oct. 25, Nov. 22, Dec. 27

Questions?

CONTACTS:

Guy Crowder, M.D., M.P.H.T.M.
Chief Medical Officer
GCrowder@health.in.gov

Next call: Noon, Sept. 27