

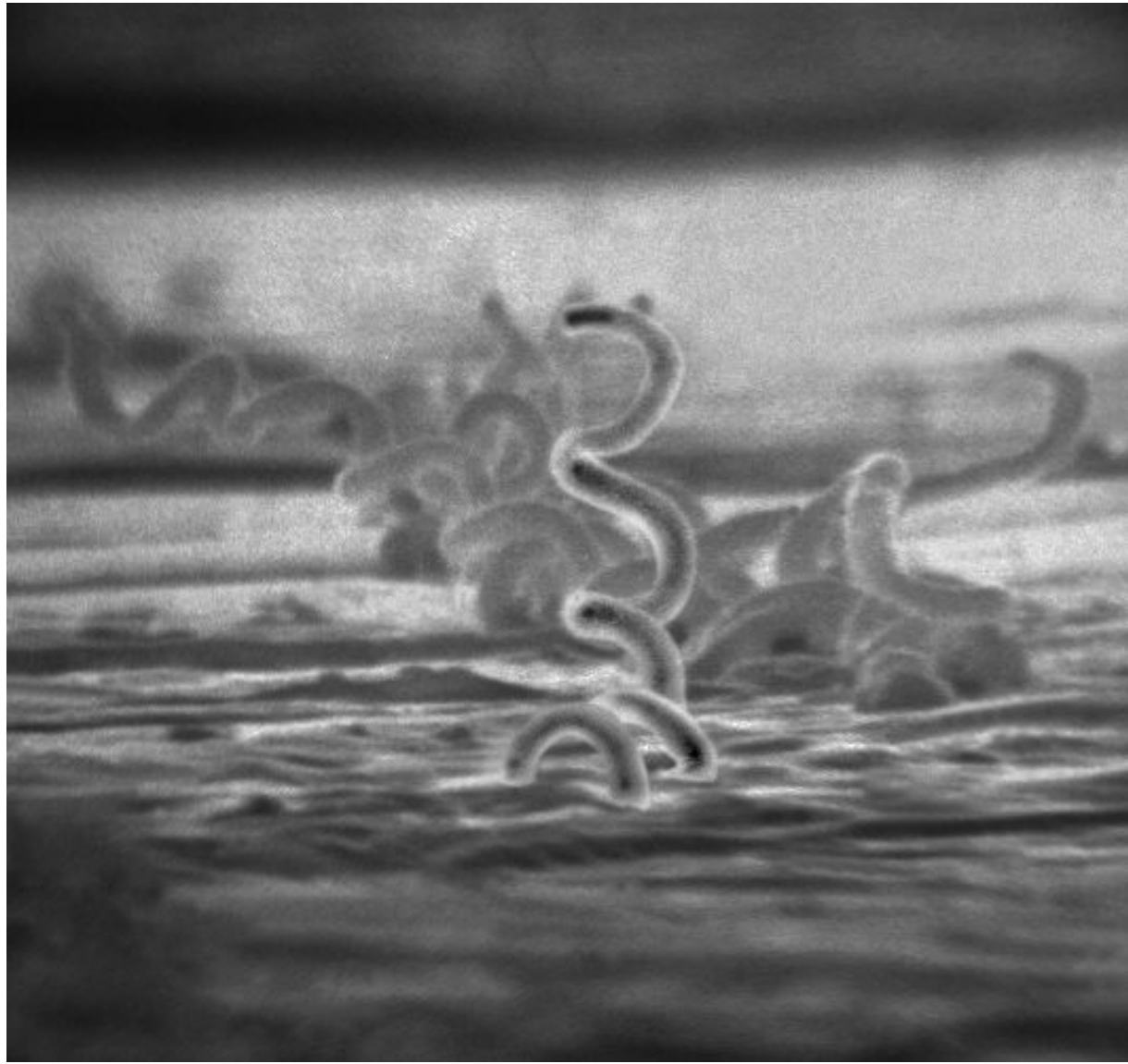
Syphilis

A Brief History

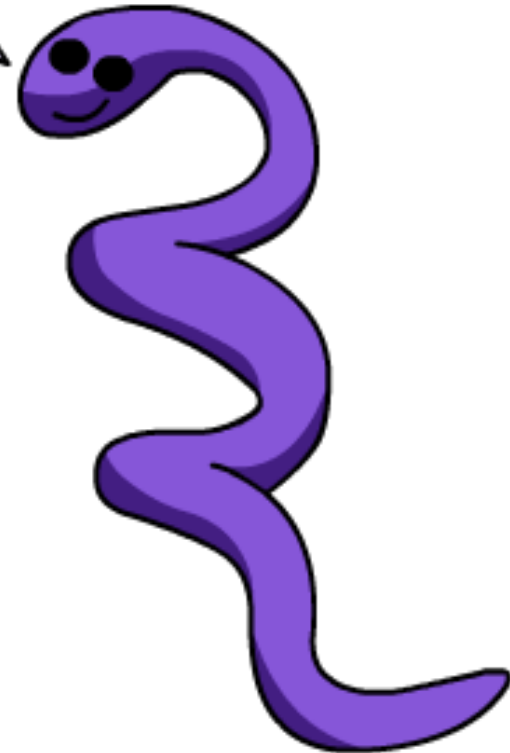
&

Algorithm Review

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Syphilis is a chronic infection
cause by an a motile
spirochete bacterium called
Treponema pallidum



Treponema
pallidum

Transmission

- Sexual contact
- Mucous membranes
- Placental
- Blood products

30-60% exposed will be infected

Incidence

- In 2005 the WHO estimated that 36 million people had syphilis worldwide!
- At risk populations:
 - MSM: 72% of new cases
 - HIV
 - Babies of infected mothers

Manifestation:

- If untreated, progresses through 4 stages:
 - 1.Primary:
 - 2.Secondary
 - 3.Latent
 - 4.Tertiary
- Congenital syphilis: Acquired during fetal development or at birth.

This is normally where gross graphic pictures are shown.....



But not today....

I think we all have seen those before!

Primary: First sign of appears 2 to 10 weeks following exposure. A red, oval sore, called a chancre develops at the site of entry and is often painless.

Secondary: Pathogen spreads throughout body (blood skin, brain). A rash usually appears within 6 weeks to 3 months after chancre heals.

Latent: Asymptomatic , non-infectious stages, the bacteria remain inactive in the lymph nodes and the spleen. Latency can last 3–30 years and may or may not progress to the tertiary stage.

Tertiary: Can begin 3 or more years after infection. 30–40 percent of infected people progress to this stage. The person may no longer be contagious, but the bacteria reactivate, multiply, and spread throughout the body. Tumors may develop on skin, bone, testes, and other tissues; cardiovascular symptoms may develop; degenerative central nervous system disease can produce dementia, tremors, loss of muscle coordination (ataxia), paralysis, and blindness. Damage is irreversible.

Past History of Syphilis:

- Advanced stages can mimic nearly **any** disease...
- Was called “The great imitator”

“He who knows syphilis knows medicine.”

-Sir William Osler ~1900

- Syphilis inspired literature, art, poetry...

Syphilis limerick

There was a young man from Back Bay
Who thought syphilis just went away.
He believed that a chancre
Was only a canker
That healed in a week and a day.

But now he has "acne vulgaris"
(Or whatever they call it in Paris);
On his skin it has spread
From his feet to his head,
And his friends asking
 where his hair is!

There's more to his terrible plight:
His pupils won't close in the light
His heart is cavorting,
His wife is aborting,
And he squints through his gun-barrel sight.

Arthralgia cuts into his slumber;
His aorta's in need of a plumber;
But now he has tabes,
And saber-shinned babies,
While of gummas he has quite a number.

He's been treated in every known way,
But his spirochetes grow day by day;
He's developed paresis,
Has long talks with Jesus,
And thinks he's the Queen of the May.

Emergence of syphilis appears in Europe in the 1490s

- Caused Dreadful illness
- Severe sores of the genitals
- Abscesses on the face and body
- Foul smell
- Necrotizing tissue of unknown cause

Treatments

Mercury used for four centuries (1500-1800's)

Side effects:

Ulcers

Loss of teeth

Neuro muscular damage

Death

One may say at the time...

“A night in the arms of Venus leads to a lifetime on Mercury.”

Treatments continued...

In 1908, Paul Ehrlich tried to find the 'Silver Bullet' (also known as the magic bullet), a perfect drug to cure a disease with no danger of side effects.

He found: Salvarsan....and known today as **'Arsenic'**



Rats loved it!

And cured them of syphilis!!

The Cure....

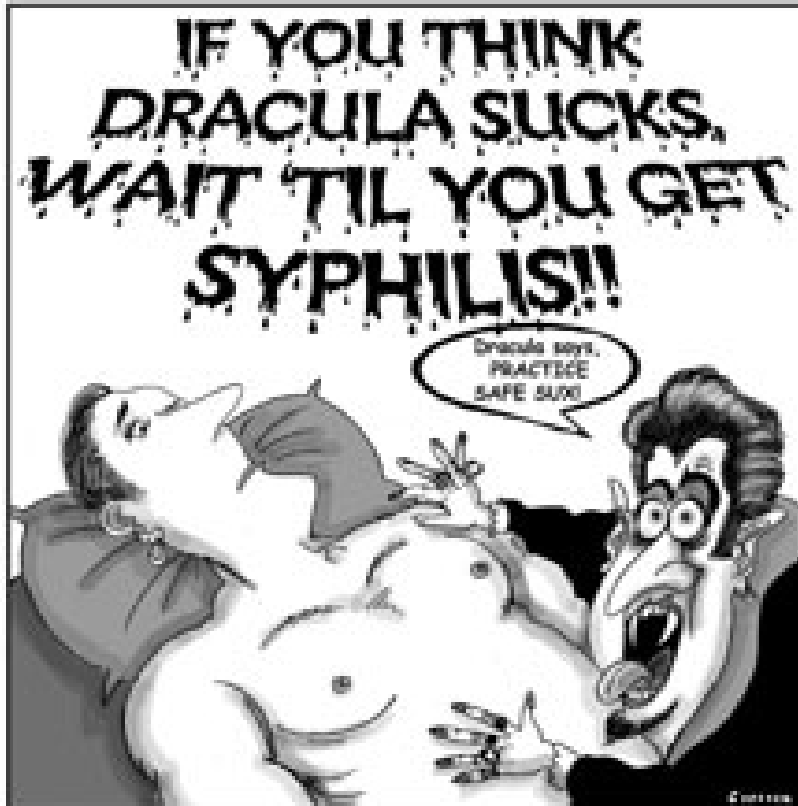
Alexander Fleming:

- Discovered the Mold *Penicillium* in 1929, and published a paper.
-Little interest in the medical community!!

Howard Florey and Ernst Chain:

- Picked up Flemings work & mass-produced drug
- Used for Syphilis in 1943

Press & News Media try to use their influence on curbing the spread of Syphilis



Unethical Trials

Tuskegee Study:

- US Study conducted in Alabama started in 1932, when 399 African-American men were given Syphilis and not-treated **...even when treatment was available in 1947**
- **Did not end until Press found about in 1972!!**

Unethical Trials

Guatemala: 1946 - 1948 study

- Inoculated prison inmates, insane asylum patients, and soldiers using infected prostitutes
- Also used direct inoculation
- Included Children
- 1300 people infected
- Results NEVER published

Unethical trials paved the way for the standardization for today's research trials!!

Diagnosis of Syphilis

Most persons present without symptoms or signs

Syphilis is usually diagnosed with serologic tests

2 types of tests

1. Non-treponemal tests
2. Treponemal test

T. pallidum has never been successfully cultured

Blood Tests for Syphilis

Non-treponemal test:

- Rapid plasma reagin (RPR) is an antibody like substance present in syphilis infected individuals and occasionally in persons with other acute or chronic conditions.
- Simple test: Carbon-particle cardiolipin antigen can bind with reagin
- False positives with HIV, HSV, malaria, IV drug use, SLE, RA, pregnancy, leprosy, etc

Blood Tests for Syphilis continued...

Treponemal tests: -Detects specific ABS to T.Pallidum

- Chemiluminescence ImmunoAssays (CIA)
- Enzyme ImmunoAssay (EIA)
- Enzyme-Linked ImmunoSorbent Assay (ELISA)
- Treponema pallidum particle agglutination assay (TPPA)
- Microbeadimmunoassays (MBIA)
- Fluorescent treponemal antibody absorbed (FTA-ABS)
- Microhemagglutination assay MHA-TP

- **Antibody (IgG) stays positive for life!**

2 Syphilis Algorithms

Traditional

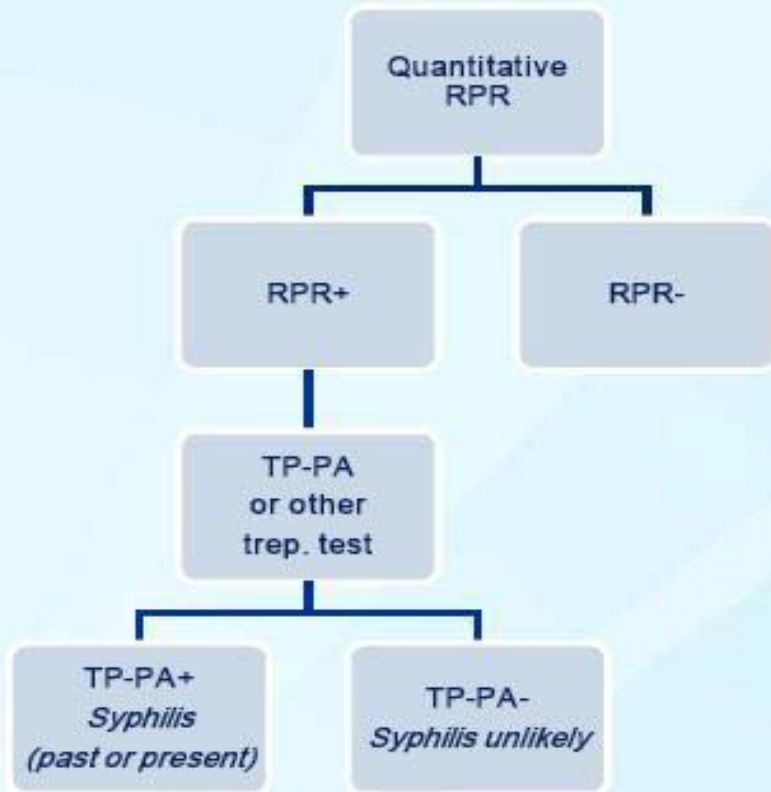
- Screen with non-treponemal test
- Confirm with treponemal test
- Detects active infection
- Can miss early, latent or treated infection

Reverse

- Begin with EIA/CIA
- Confirm with RPR
- Good for high throughput screening
- Cost effective when done in bulk
- Catch early & latent infection
- Can't differentiate treated from untreated

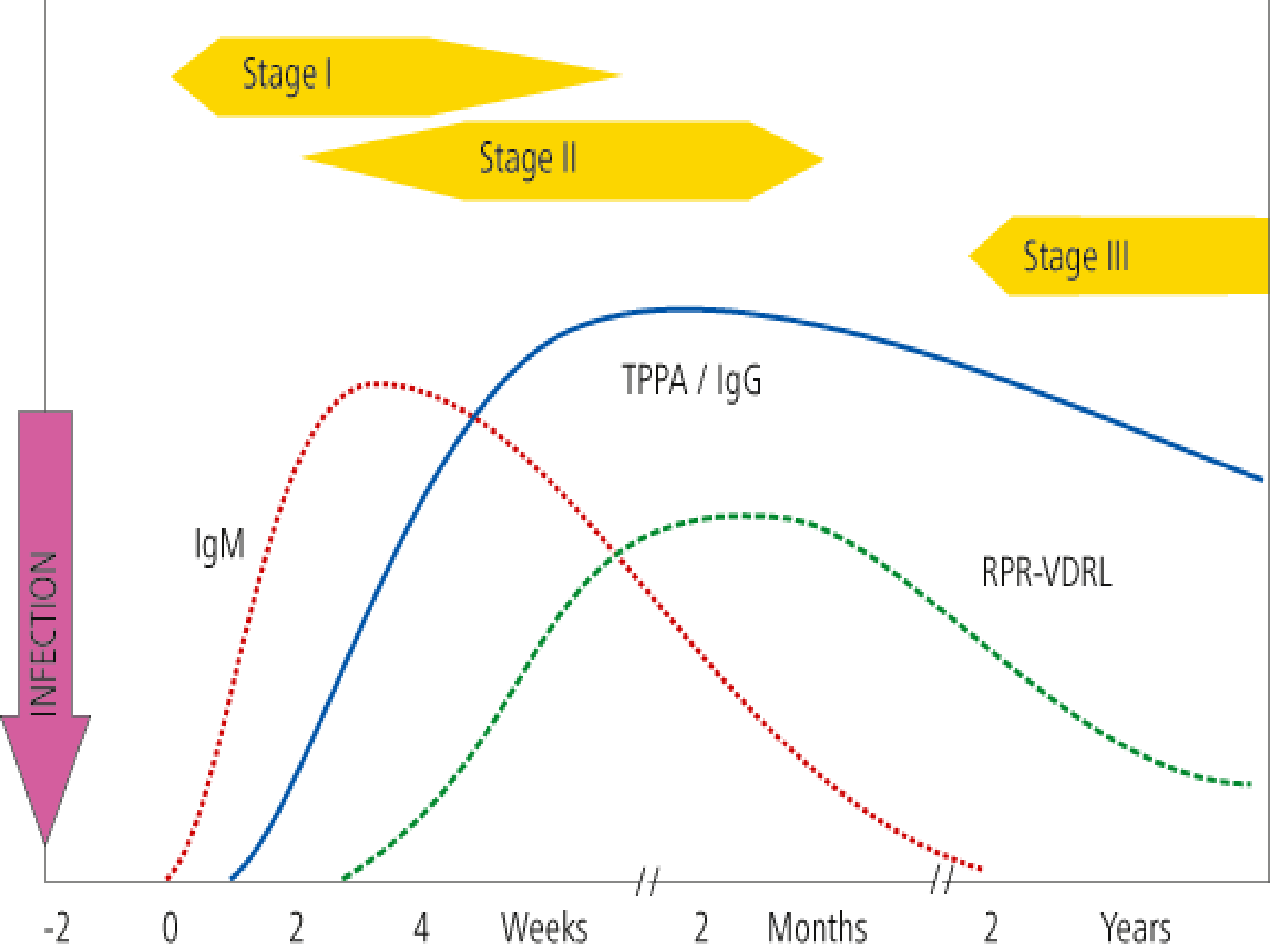
Syphilis serologic screening algorithms

Traditional



Reverse sequence





Which is best?

Up to 2010, the US Center for Disease Control (CDC) recommended the traditional algorithm....

Now (2014), a little less clear.

Traditional algorithm

- + Only detects active infection
- + Easy to follow
- High rate of biologic false Pos
- Can miss early primary, treated, and latent infection

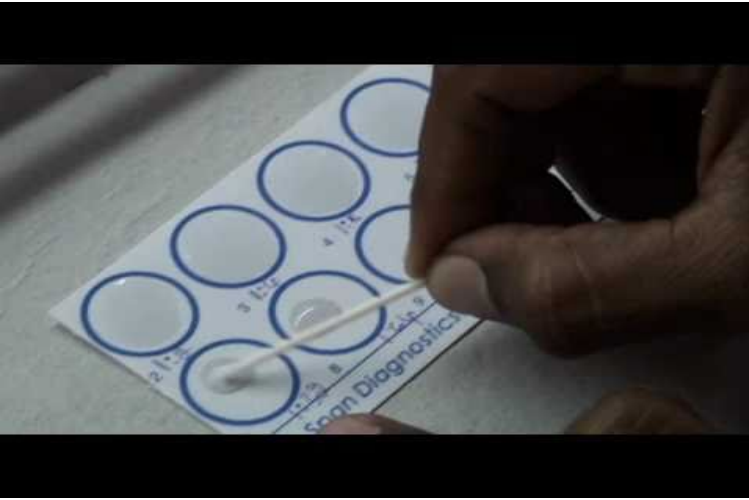
Reverse algorithm

- + Detects early primary infection & latent Infection
- + Fast screen results
- + No false negatives at screening due to prozone
- More complicated algorithm
(2 antibody tests will be required)
- Varies by risk of population



Many medical institutions in the US have switched over to the reverse algorithm, and suspect all will be changing in short time.

Why switch to CIA or EIA screening method?



or



What do you think?

Possible outcomes for Reverse Algorithm

<u>Syphilis IgG</u>	<u>RPR</u>	<u>TPPA</u>	<u>Interpretation & treatment</u>
Negative	(Not performed)	(Not performed)	Syphilis infection unlikely
Positive	Positive	(Not performed)	Syphilis – recent infection likely Evaluate clinically, determine if treated for syphilis in the past, assess risk of infection, and administer therapy according to CDC’s STD Treatment Guidelines if not previously treated
Positive	Negative	Positive	Syphilis – past or present infection Evaluate clinically, determine if treated for syphilis in the past, assess risk of infection, and administer therapy according to CDC’s STD Treatment Guidelines if not previously treated
Positive	Negative	Negative	Infection unlikely – false positive syphilis If at risk for syphilis, repeat RPR in several weeks

Syphilis has affected our world in many ways:

- ❖ Practice of medicine
- ❖ Art, literature
- ❖ Drug development
- ❖ Ethical research on human subjects
- ❖ Laboratory medicine and how we view it

And also affected (& infected) these famous people...

Adolf Hitler

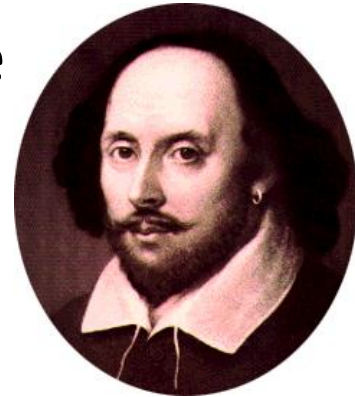
➤ 1908 - Contracted syphilis from a Jewish prostitute



Pope Alexander VI



Shakespeare



Ivan the Terrible



Henry VIII

Benito Mussolini



Al Capone



Questions?

