

35th Remington Winter Course
in Infectious Diseases

**Exanthemas in Adults and
Children**

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FINANCIAL DISCLOSURE:

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*In the past 12 months, I have **not** had a significant financial interest or other relationship with the manufacturer(s) of the product(s) or provider(s) of the service(s) that will be discussed in this presentation.*

Objectives

- To review the six “classic” toxic erythemas
- To discuss causes of toxic erythemas
- To summarize clinical manifestations, diagnosis and prevention of these exanthems

Toxic Erythemas: Six Diseases of Childhood

Category	Disease	Year described
First	Rubeola (measles)	1627
Second	Streptococcal scarlet fever	1627
Third	Rubella (German measles)	1881
Fourth	Staphylococcal scarlet fever “Dukes disease”*	1900
Fifth	Erythema infectiosum	1905
Sixth	Roseola (exanthem subitum)	1910

* Mild form of SSSS characterized by generalized scarlatiniform eruption with exfoliation

Rubeola (measles; first disease)

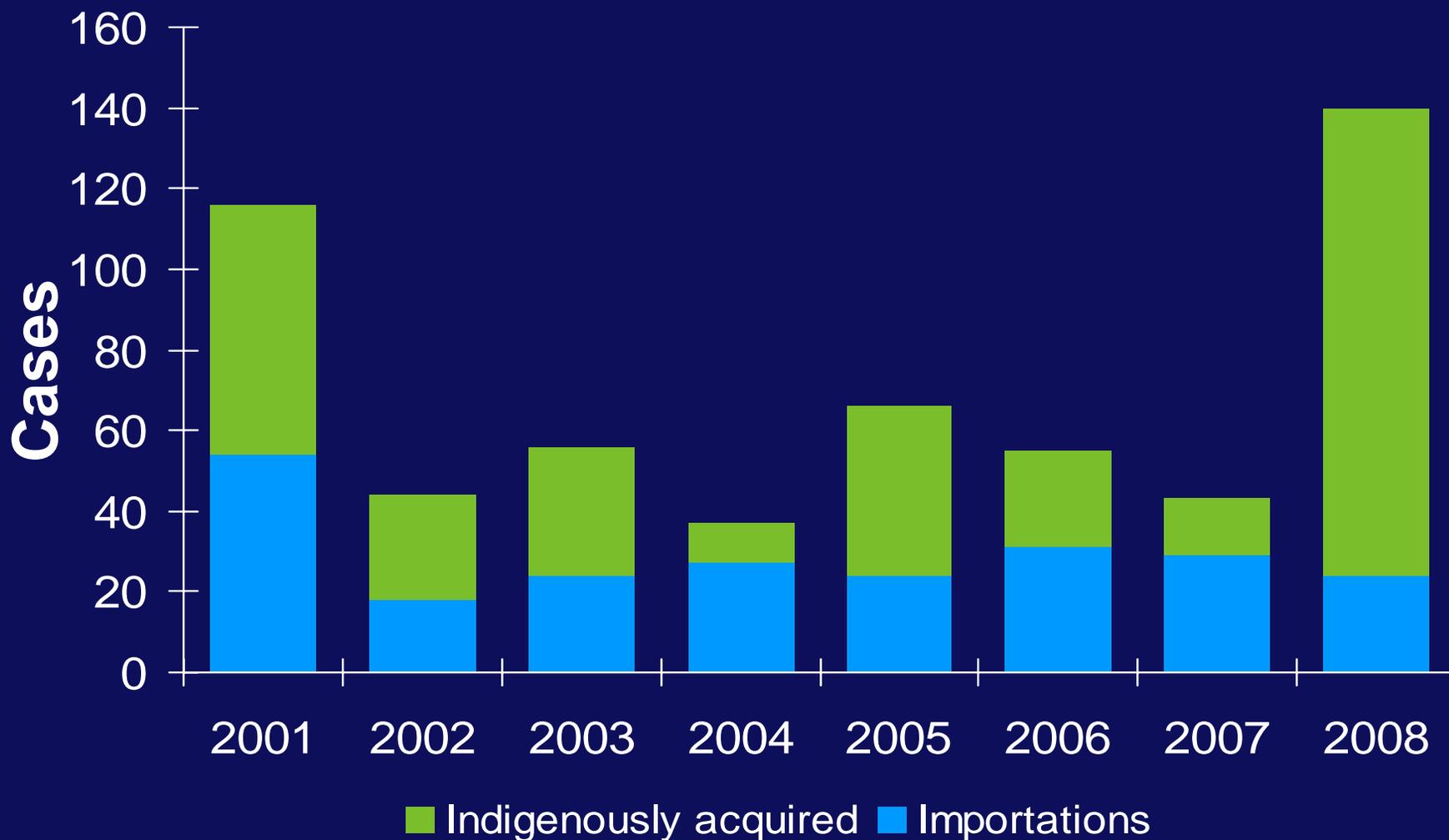
- **Cause** RNA virus
- **Clinical** Fever, cough, coryza, conjunctivitis, maculopapular rash, Koplik spots
- **Diagnosis** Serology, isolation of measles virus and genotyping of isolates (CDC)
- **Treatment** Supportive, vitamin A

Measles Burden

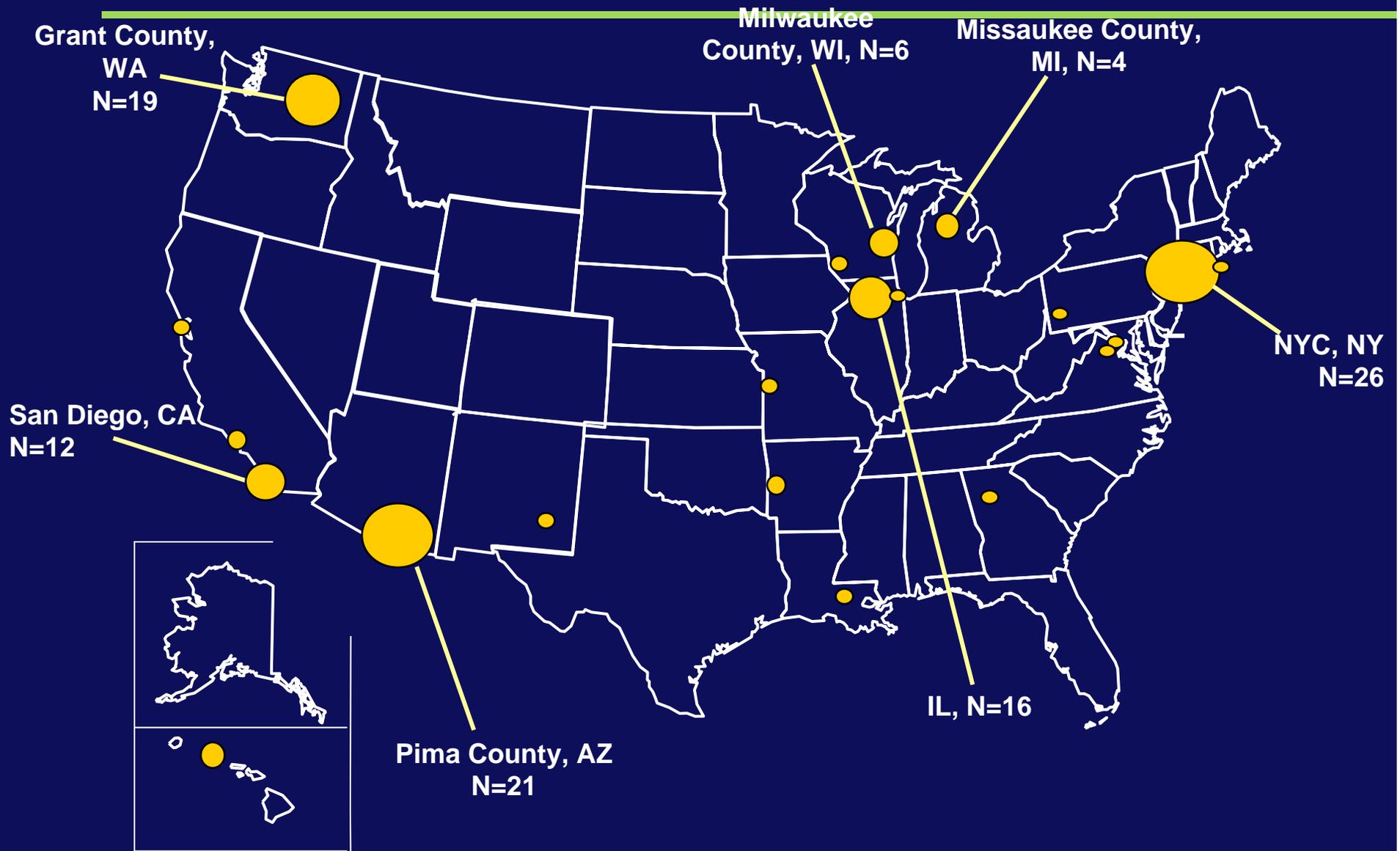
- Pre-vaccine era:
 - 3-4 million cases annually
 - 1 in 20 developed pneumonia
 - 1 in 2000 developed encephalitis
 - 1000 developed chronic disability from measles encephalitis
 - 48,000 hospitalized
 - 1 in 3000 died
 - 1 in 1 million developed SSPE



Reported Measles Cases U.S., 2001- 2008



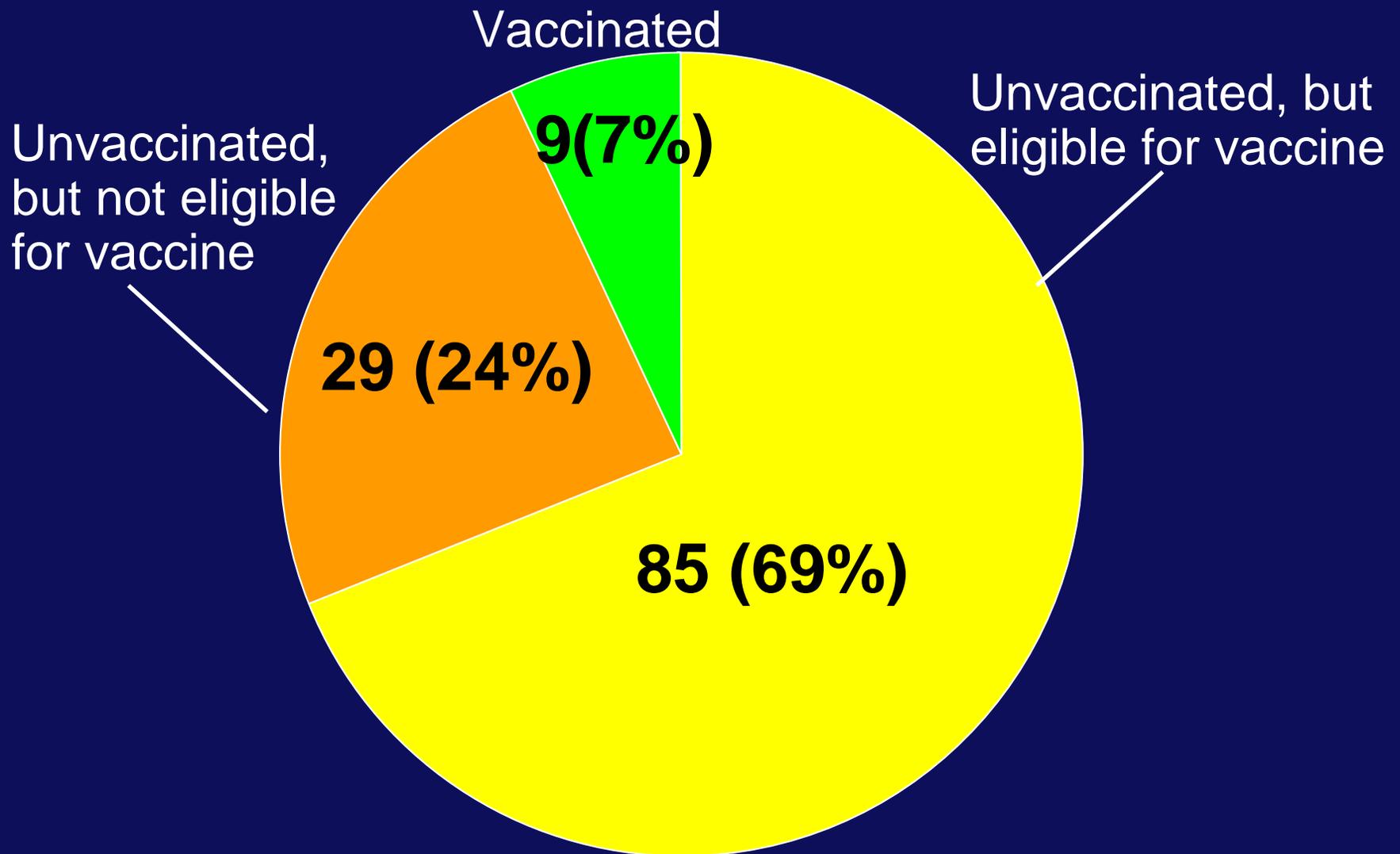
Measles Cases Reported to CDC/NCIRD January 1 - June 20, 2008 (N= 123)



Importations

- 106 (86%) cases were import-associated
- 10 source countries for the 17 imported cases
- 116 (94%) U.S. residents
- 17 U.S. states involved
- The viruses isolated had a variety of genotypes (i.e. D4, D5, H1)

Proportion of Case-Patients by Vaccination Status, N= 123



Summary of Measles Outbreak

- Import-associated cases are stable in U.S.
- Most cases are occurring in unvaccinated U.S. residents
- Primary reason for lack of vaccination is personal belief exemptions
- Until better global control is achieved, cases will continue to be imported into the U.S. and outbreaks will persist as long as there are communities of unvaccinated people

Streptococcal Scarlet Fever (second disease)

- Cause *S. pyogenes* which produces pyrogenic exotoxin (A,B,C)
- Clinical Diffuse erythematous eruption (head, neck, extremities sparing palms and soles) usually with pharyngitis
- Diagnosis Culture
- Treatment Antimicrobial agent



Mechanisms of Streptococcal Infections

Direct infection of skin

Cellulitis/impetigo

Immunologically mediated

Erythema marginatum
Subcutaneous nodules

Toxin mediated
(pyrogenic exotoxin)

Scarlet fever

(production of super
antigens)

Toxic shock syndrome

Invasive

Bacteremia
Necrotizing soft tissue

Rubella (third disease)

- Cause Positive stranded RNA virus
- Clinical Subclinical and clinical disease
 Congenital rubella syndrome
- Diagnosis Serology
- Treatment Supportive
- Prevention Immunization





Achievements in Public Health: Elimination of Rubella and Congenital Rubella Syndrome --- United States, 1969-2004

On March 21, this notice was posted as an MMWR Early Release on the MMWR website (<http://www.cdc.gov/mmwr>).

In October 2004, CDC convened an independent panel* of internationally recognized authorities on public health, infectious disease, and immunization to assess progress toward elimination of rubella and congenital rubella syndrome (CRS) in the United States, a national health objective for 2010 (1). Since rubella vaccine licensure in 1969, substantial declines in rubella and CRS have occurred, and the absence of endemic transmission in the United States is supported by recent data: 1) fewer than 25 reported rubella cases each year since 2001 (Figure), 2) at least 95% vaccination coverage among school-aged children, 3) estimated 91% population immunity, 4) adequate surveillance to detect rubella outbreaks, and 5) a pattern of virus genotypes consistent with virus originating in other parts of the world. Given the available data, panel members concluded unanimously that rubella is no longer endemic in the United States. This report summarizes the history and accomplishments of the rubella vaccination program in the United States and the Western Hemisphere and the challenges posed by rubella for the future.

Clinical Manifestations of Human Parvovirus B19 Infection (fifth disease)

Conditions

Erythema infectiosum
(fifth disease)

Polyarthropathy syndrome

Chronic anemia/pure red
cell aplasia

Hydrops fetalis/congenital
anemia

Persistent anemia

Papular-purpuric glove
and sock syndrome
(PPGSS)

Usual Hosts

Immunocompetent children

Immunocompetent adults
(more common in women)

Immunocompromised hosts

Fetus (first 20 weeks of
pregnancy)

Immunocompromised people

Rare



Exanthem Subitum (Roseola; sixth disease)

- Cause Human herpes virus 6
- Clinical Rash, high fever without rash, seizures, encephalitis; fever followed by rash
- Diagnosis Seroconversion; isolation HHV-6 (research laboratories)
- Treatment supportive



Erythema by Cause

Erythema

Erythema infectiosum
(fifth disease)

Erythema marginatum

Erythema migrans

Erythema multiforme

Erythema nodosum

Cause

Parvovirus B-19

Rheumatic fever

Lyme disease

Herpes simplex plus
others

Many infectious and
noninfectious

Other Toxic Erythemas

- Drug associated eruptions
 - Stevens-Johnson syndrome
 - Toxic epidermal necrolysis (TEN), Lyell's syndrome
- Staphylococcal scalded skin syndrome
- Toxic shock syndrome
- Kawasaki syndrome
- Diseases associated with animal contact or vectors

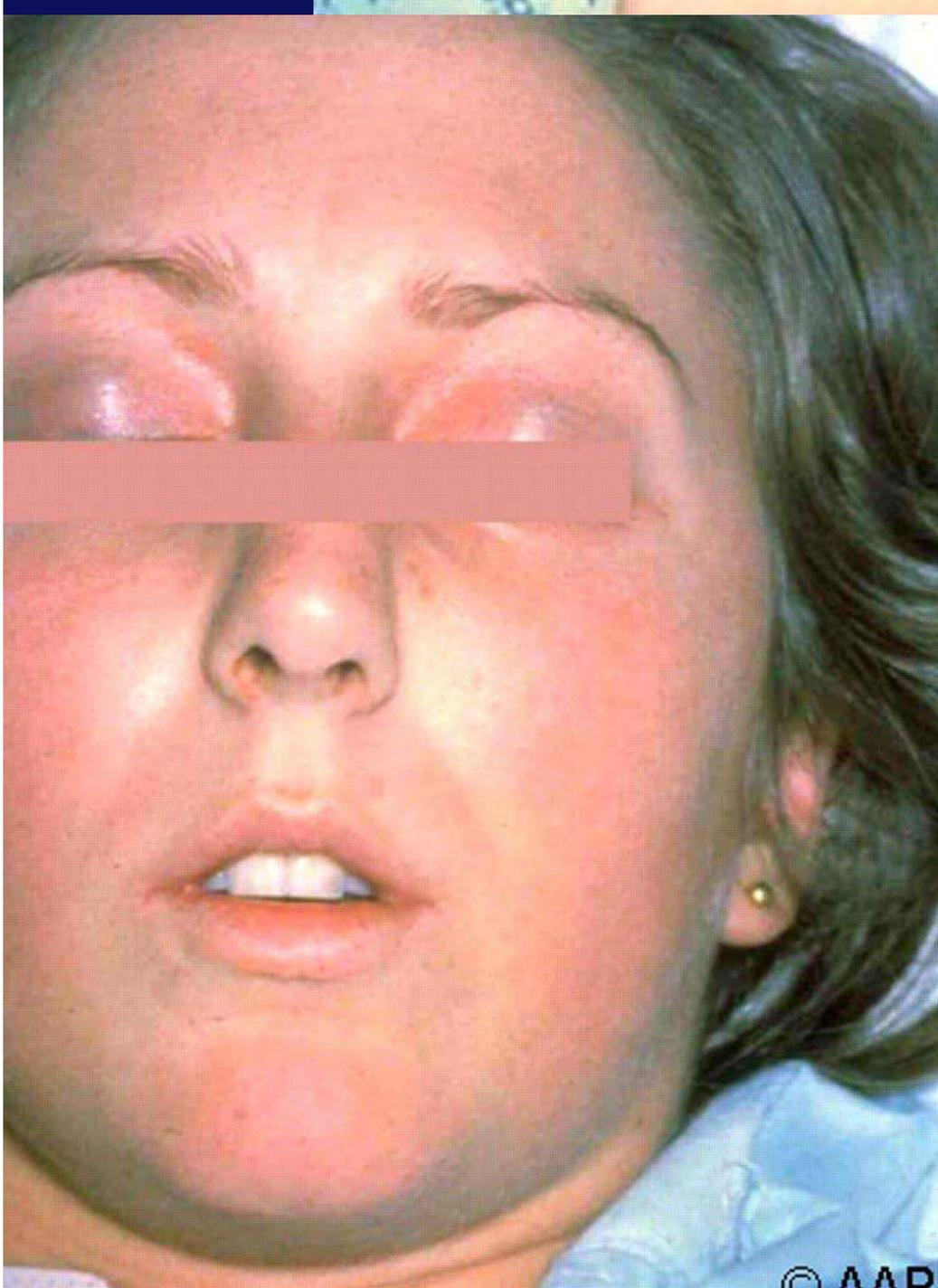
Staphylococcal Scalded Skin Syndrome (SSSS, Ritter's Disease)

- **Cause** Epidermolysin or exfoliatin toxins; 5% of *S. aureus* produce exfoliatin toxin
- **Clinical** Blistering, tender skin disorder varying from localized blisters to generalized exfoliation usually occurs in neonates or young children; normal mucous membranes and conjunctivae
- **Diagnosis** Nikolsky sign; skin biopsy for cleavage plane
- **Treatment** Antistaphylococcal antibiotic

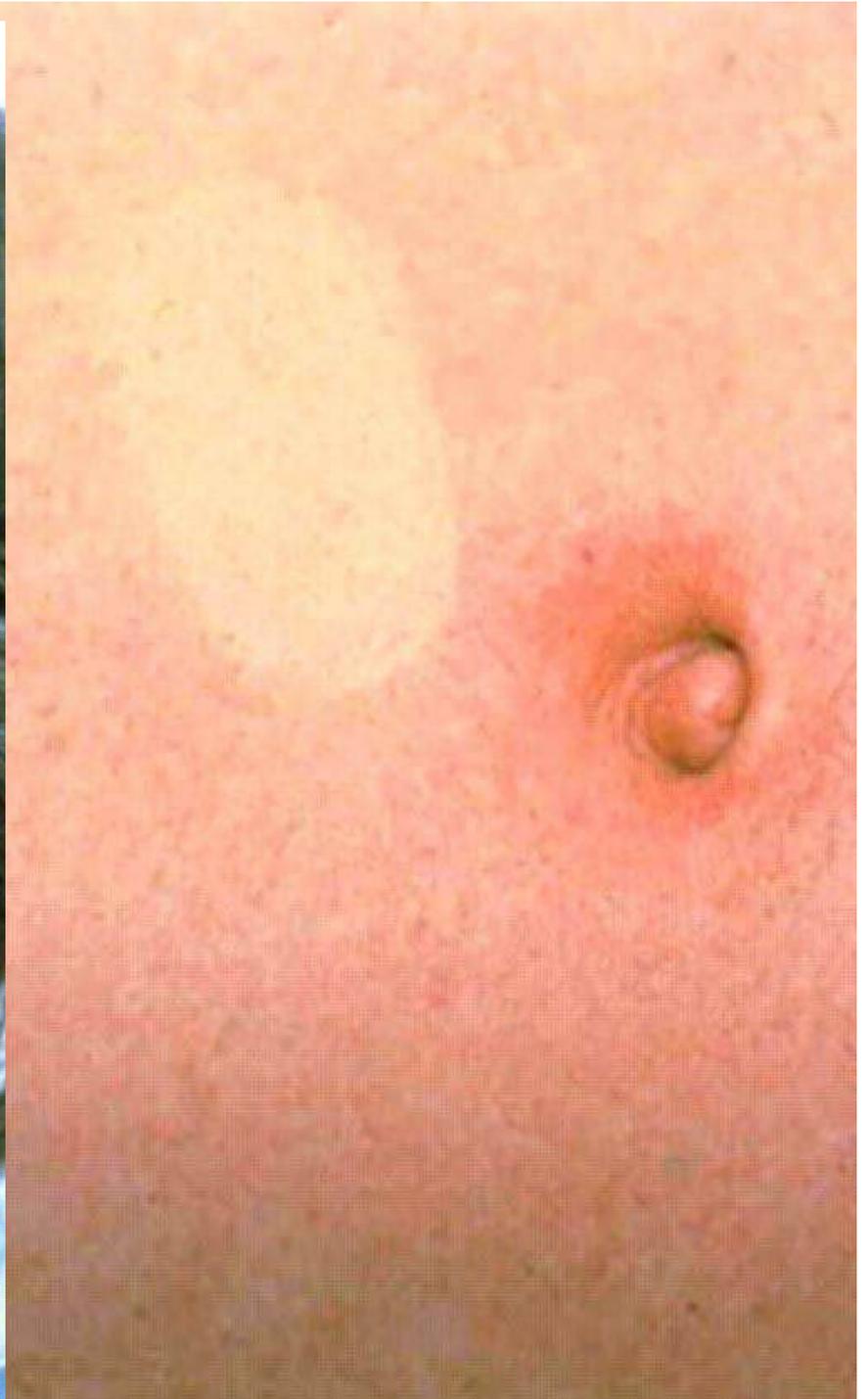


Toxic Shock Syndrome (TSS) due to *S. aureus*

- **Cause** TSS toxin 1 acts as a super antigen that stimulates T cells
- **Skin** Acute febrile illness with generalized, tender erythroderma on hands, feet (with edema) and trunk; desquamates 7-10 days (hands and feet)
- **Mucous membranes** Hyperemia of oral and vaginal mucosa
- **Conjunctivae** Markedly injected
- **Treatment** Fluid management, antistaphylococcal antibiotic, manage organ failure, 10% mortality



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Special Category of Macular Papular Rash

- Erythema multiforme
- Stephens Johnson –TEN complex (includes mucocutaneous intolerance reactions; several subgroups)
- Self-limited, acute intolerance reactions characterized by
 1. target lesions (stable circular erythemas or urticarial plaques with areas of blistering and necrosis)
 2. histologically satellite-cell necrosis of epidermis

Stevens Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis

- 1866 erythema multiforme described as a relatively mild self-limited skin diseases that tends to recur
- Two related mucocutaneous disorders with high rates of morbidity and mortality
 - 1922 Stevens-Johnson syndrome described
 - 1956 Lyell introduced the term toxic epidermal necrolysis

Erythema Multiforme

Cause *H. simplex*, *M. pneumoniae*, drugs

Clinical Acute, self limiting exanthem, usually mild and relapsing; round to oval macules and papules on trunk and extremities; target lesions; mild oral (mouth) mucosal involvement

Diagnosis Absent Nikolsky sign
HSV, other viral causes,
drug history, biopsy

Treatment Supportive, acyclovir for recurrent herpes



Stephens Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)

Cause	Adults: drugs Children: infection (often <i>Mycoplasma pneumoniae</i>)
Clinical	Severe, episodic, acute mucocutaneous reactions. Two syndromes are closely related; differ in extent of amount of body surface area involved (<30% SJS, >30% TEN)
Diagnosis	Skin biopsy with immunofluorescence
Treatment	Discontinue offending drug; aggressive burn unit intervention; mortality SJS (1-5%), TEN (30-40%)

Stevens Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)

	<u>SJS</u>	<u>TEN</u>
Mucosal lesions	Erosions at ≥ 2 sites	Erosions at ≥ 2 sites
Typical skin lesions	Small blisters on purpuric macules or atypical targets	Individual lesions like SJS
	Less areas of confluence	Confluent erythema
	Detachment of $\leq 10\%$ of body surface area	Nikolsky's sign Large sheets of necrotic epidermis Total detachment of $\geq 30\%$ of body surface area

Stevens Johnson Syndrome and Toxic Epidermal Necrolysis

	<u>SJS</u>	<u>TEN</u>
Signs and symptoms	10-30% have fever, lesions of respiratory and g.i. tracts	All have fever, all have acute skin failure, leukopenia, lesions of respiratory and g.i. tracts
Drug induced	50%	> 80%
Fatal	< 5%	30%

Diffuse Erythemas That Desquamate or Peel

Condition

Cause

Toxic shock syndrome (TSS)

S. aureus, GAS

Staphylococcal scaled skin
syndrome (SSSS)

S. aureus

Toxic epidermal necrolysis (TEN)

Many

Stephens Johnson syndrome

Many

Kawasaki (mucocutaneous lymph
node syndrome)

Unknown

Epidermolysis bullosa

Genetic

Skin Conditions with Nikolsky Sign

- Bullous impetigo
(local disease)
- Staphylococcal Scalded Skin Syndrome
- Stevens Johnson Syndrome
- Toxic Epidermal Necrolysis
- Pemphigus vulgaris
(drug induced)
- Epidermolysis bullosa