Global Patterns of Insect Resistance to Bt Crops: The First 25 Years

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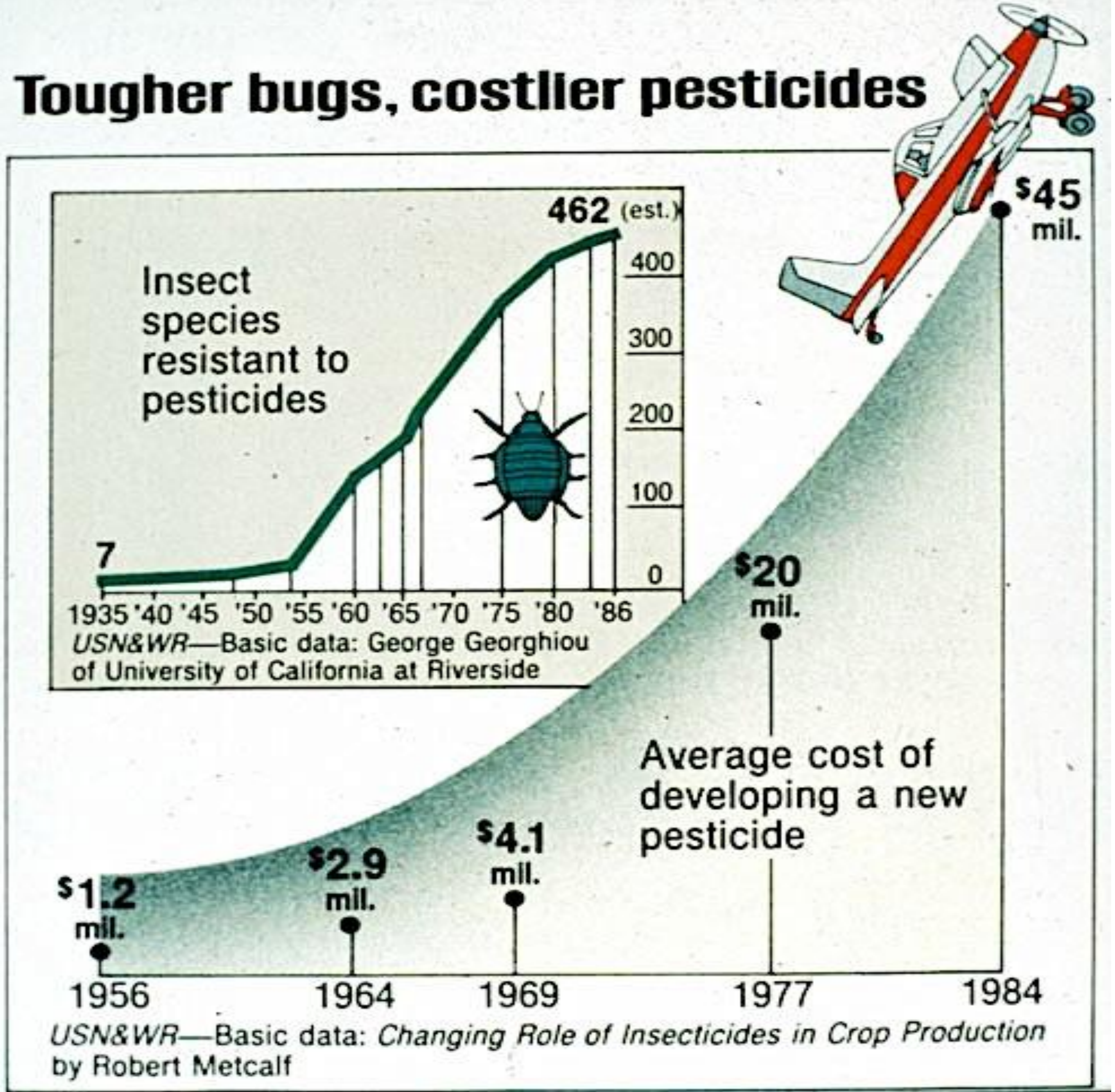
University of Arizona

ARIZONA

United States Department of Agriculture

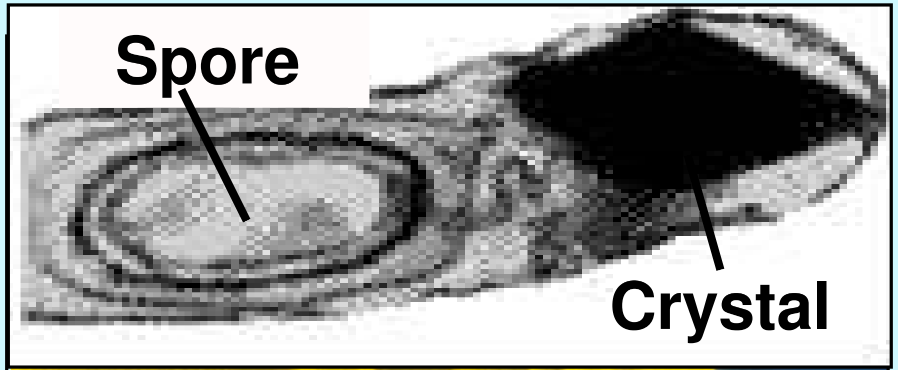
National Institute of Food and Agriculture

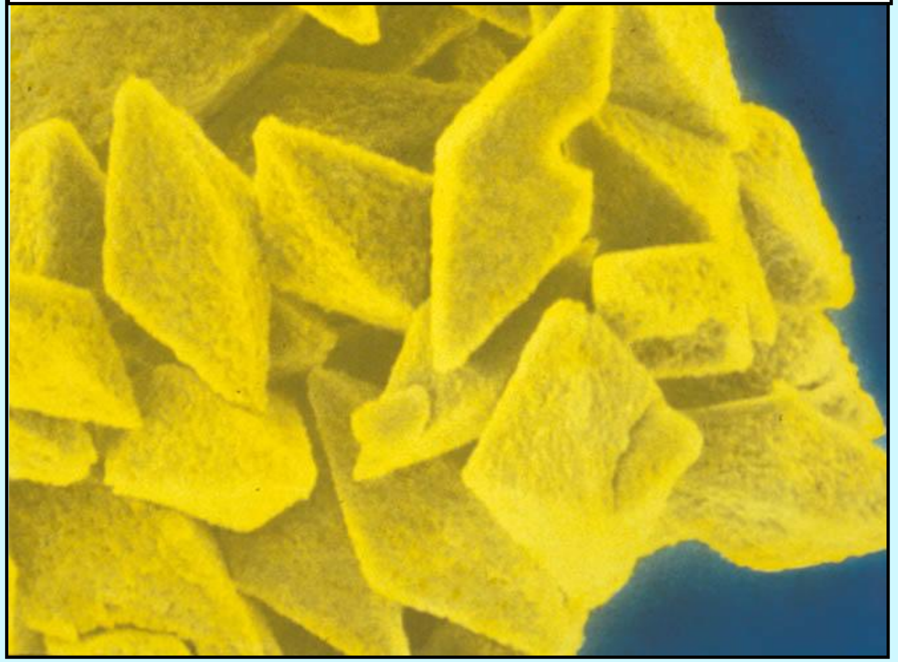
AZ Cotton Growers Association, AZ Cotton Research & Protection Council, Cotton Inc., Bayer, BASF, Corteva, Syngenta, USDA-APHIS


Tougher bugs, costlier pesticides
Insect species resistant to pesticides
7
462 (est.)
400
300
200
100
0
1935 '40 '45 '50 '55 '60 '65 '70 '75 '80 '86
USN&WR—Basic data: George Georghiou of University of California at Riverside
Average cost of developing a new pesticide
$1.2 mil.
$2.9 mil.
$4.1 mil.
$20 mil.
$45 mil.
1956
1964
1969
1977
1984
USN&WR—Basic data: Changing Role of Insecticides in Crop Production by Robert Metcalf

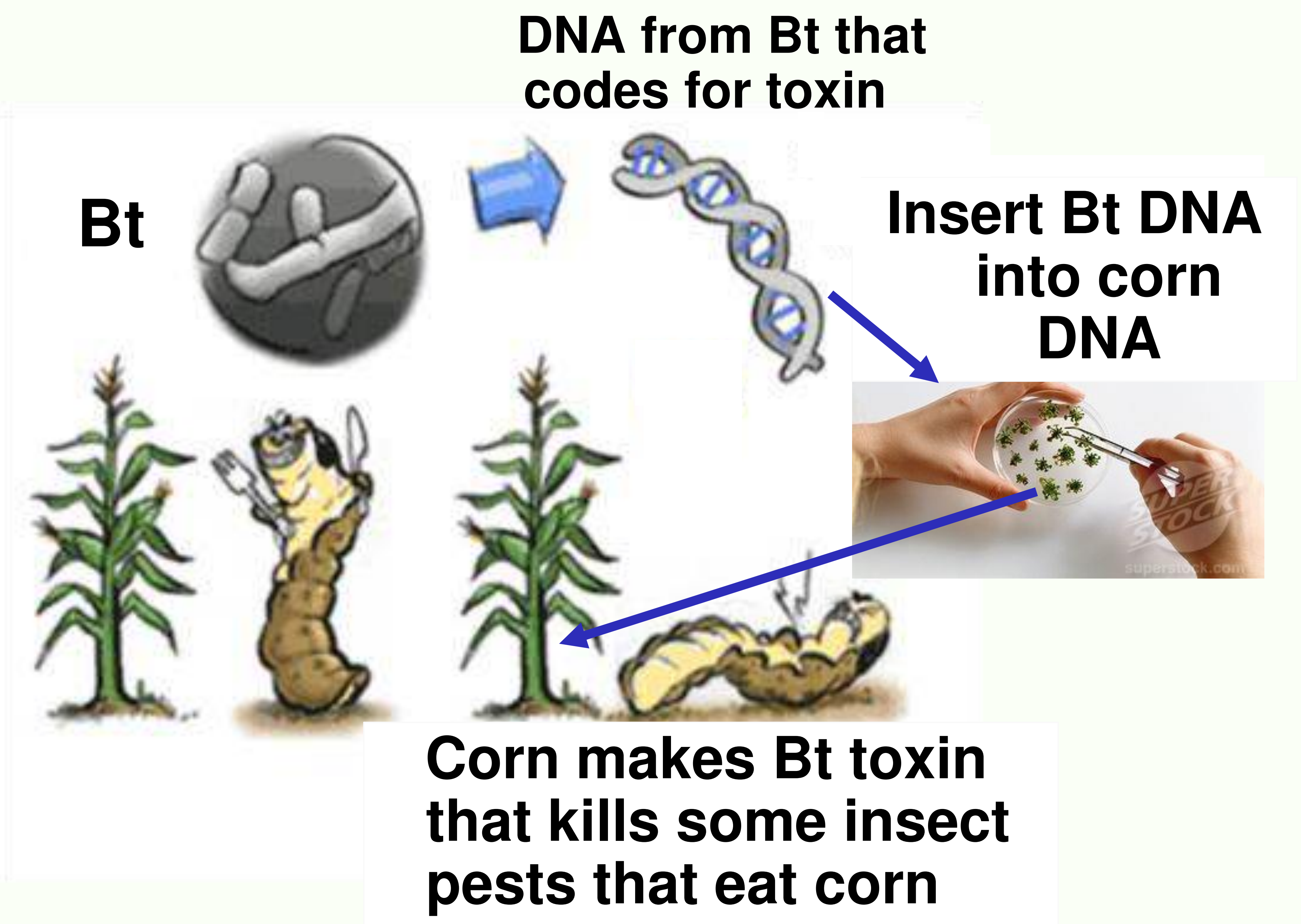
Bacillus thuringiensis

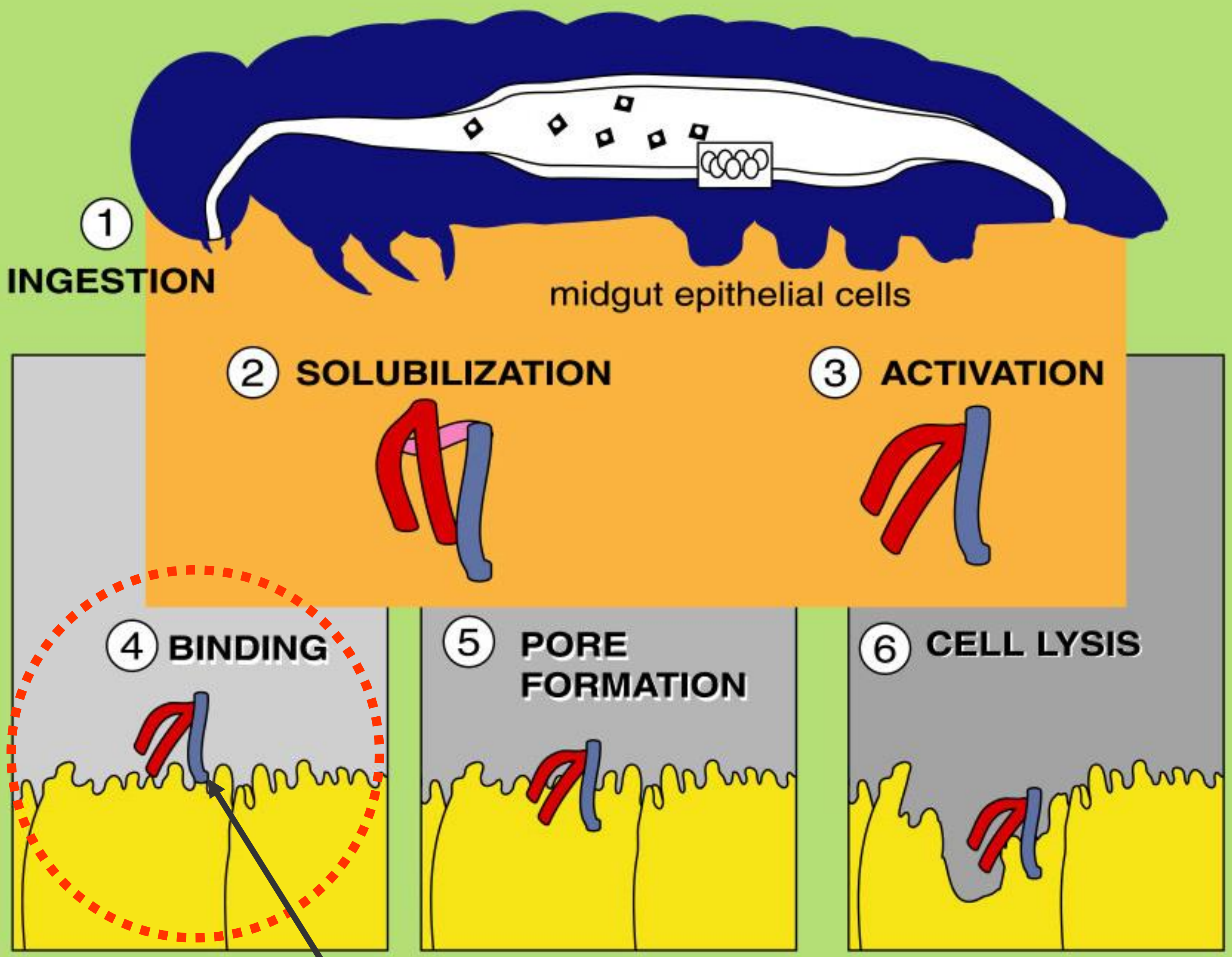
- Natural, widespread bacterial pathogen of some insects
- Bt proteins used in sprays for >80 years to control disease vectors, forest & crop pests
- Bt proteins not harmful to most non-target organisms including natural enemies & people
- Genes encoding Bt proteins engineered into crops





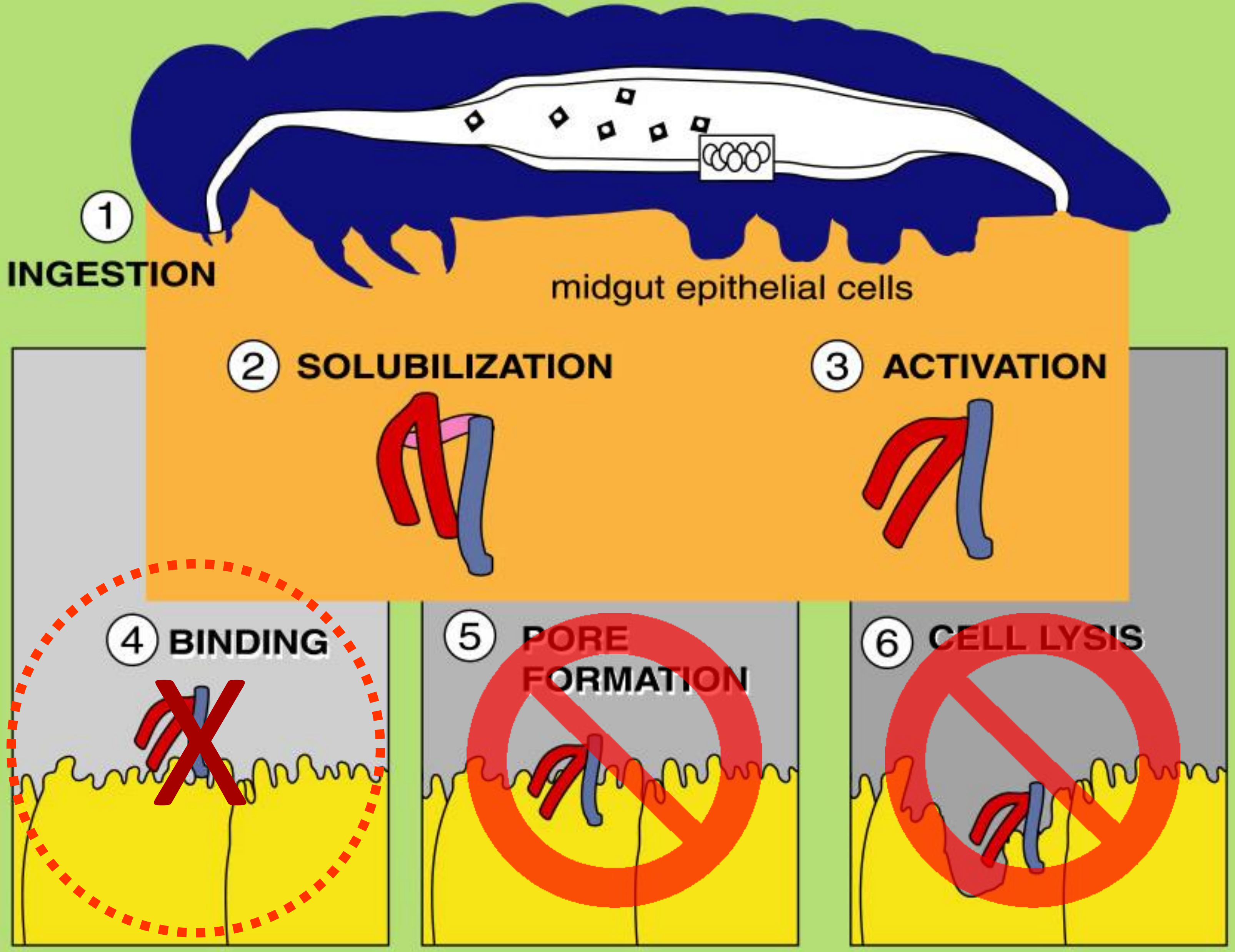
Bt crystalline (Cry) proteins


DNA from Bt that codes for toxin
Bt
Insert Bt DNA into corn DNA
Corn makes Bt toxin that kills some insect pests that eat corn



Toxins bind specifically to midgut target sites (e.g., cadherin & ABC proteins)

Artist: V. D'Amico



Artist: V. D'Amico

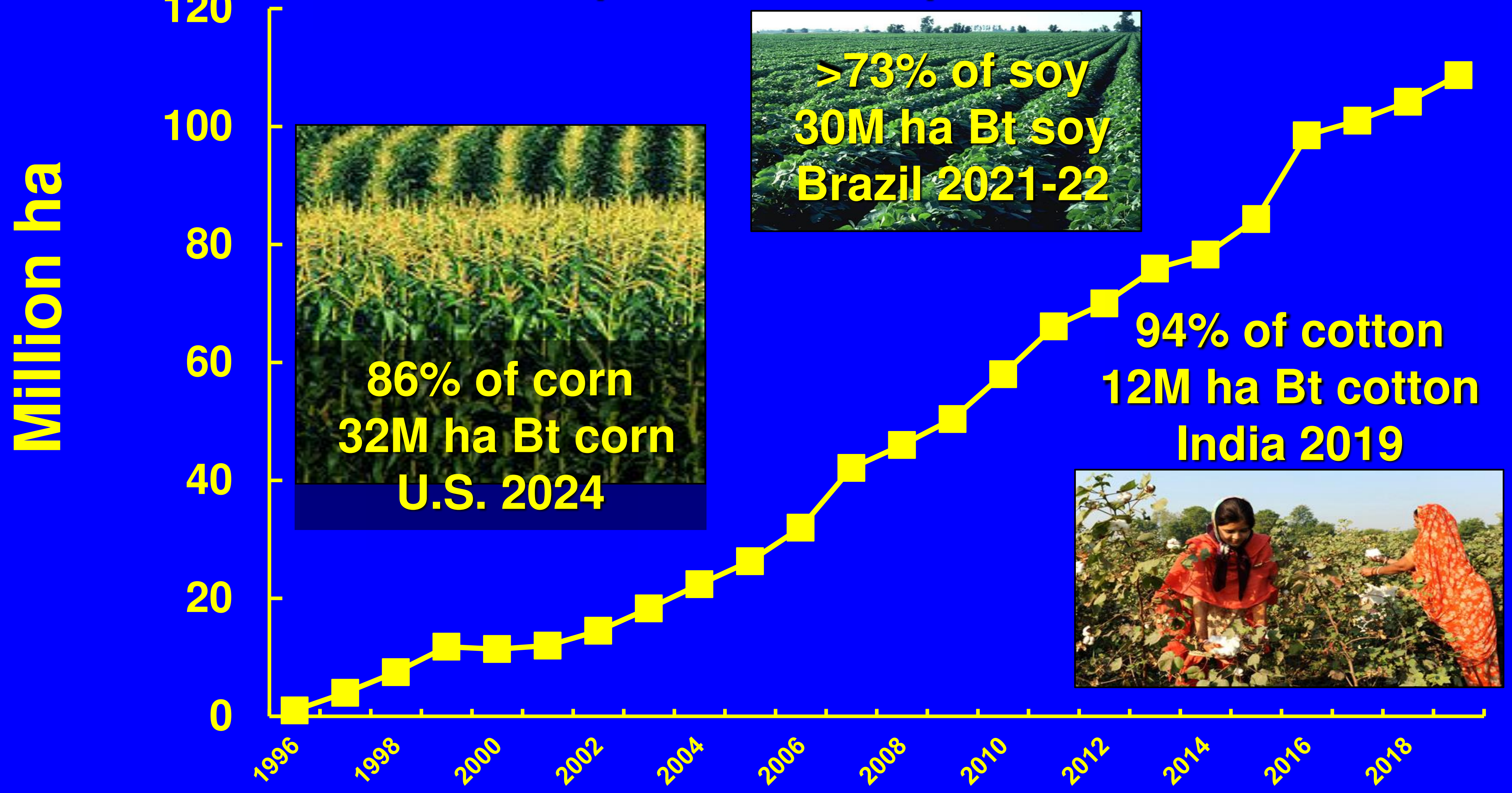
Disruption of toxin binding causes resistance

Benefits of Bt crops!

- Effective against target insect pests!
- Kill boring pests!
- Little or no toxicity to most other species!
- Reduce insecticide use!
- Economic, environmental & health benefits!

European corn borer!
Ostrinia nubilalis!

Global Adoption of Bt Crops: 27 Countries in 2019



ISAAA Brief 55 (2019), Goday et al. (2022), USDA ERS (2024)

Experts' prediction from modeling: Pest resistance to Bt crops in as few as 3 years!

- Roush. Pesticide Science (1997) 51: 328!
- Gould et al. PNAS (1997) 94: 3519!

Can we apply evolutionary principles and knowledge about resistance to make Bt crops more sustainable?

Conclusions

- Resistance management matters.
- Refuges of non-Bt host plants can delay evolution of resistance to Bt crops (even if the high-dose standard is not met).
- Combining Bt crops with other control tactics can be highly effective.

Field-Evolved Resistance to Bt Crops!
Categories!

Significant, genetically based decrease in susceptibility

"Practical resistance" !

- **> 50% of individuals resistant !**
- **reduced efficacy reported!**

"Early warning"!

!

No significant decrease in susceptibility

!

Susceptible

Tabashnik et al. JEE (2014), Tabashnik & Carrière Nature Biotechnology (2017) !

Field-Evolved Resistance to Bt Crops

Case = Response of one pest species to one Bt protein in one country

Example: Practical resistance of *Helicoverpa zea* to Cry1Ac in the US

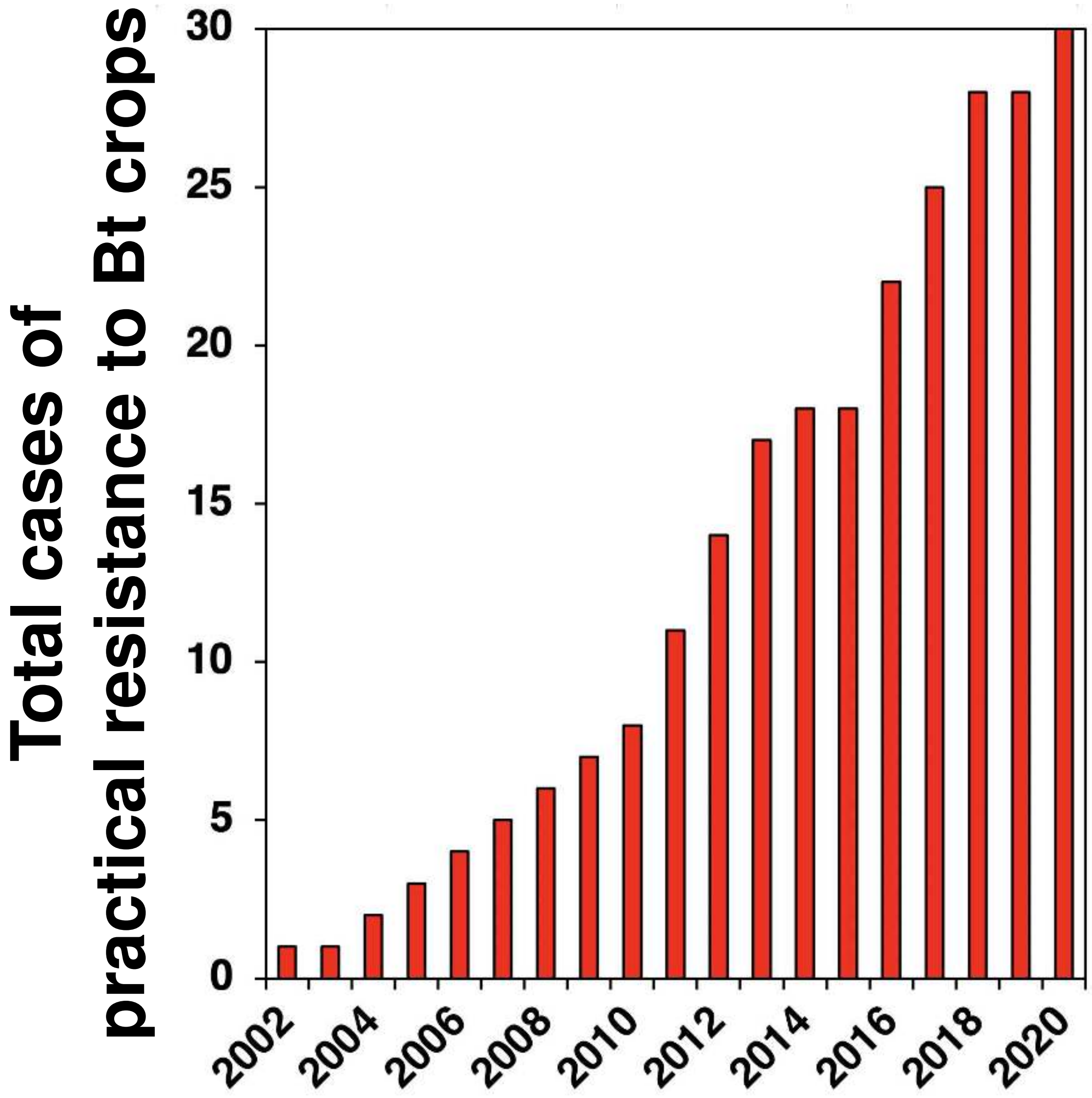
80 cases: 73 cases Tabashnik et al. 2023 JEE, 7 more as of 20 August 2024

Photos by Alex Yelich, University of Arizona

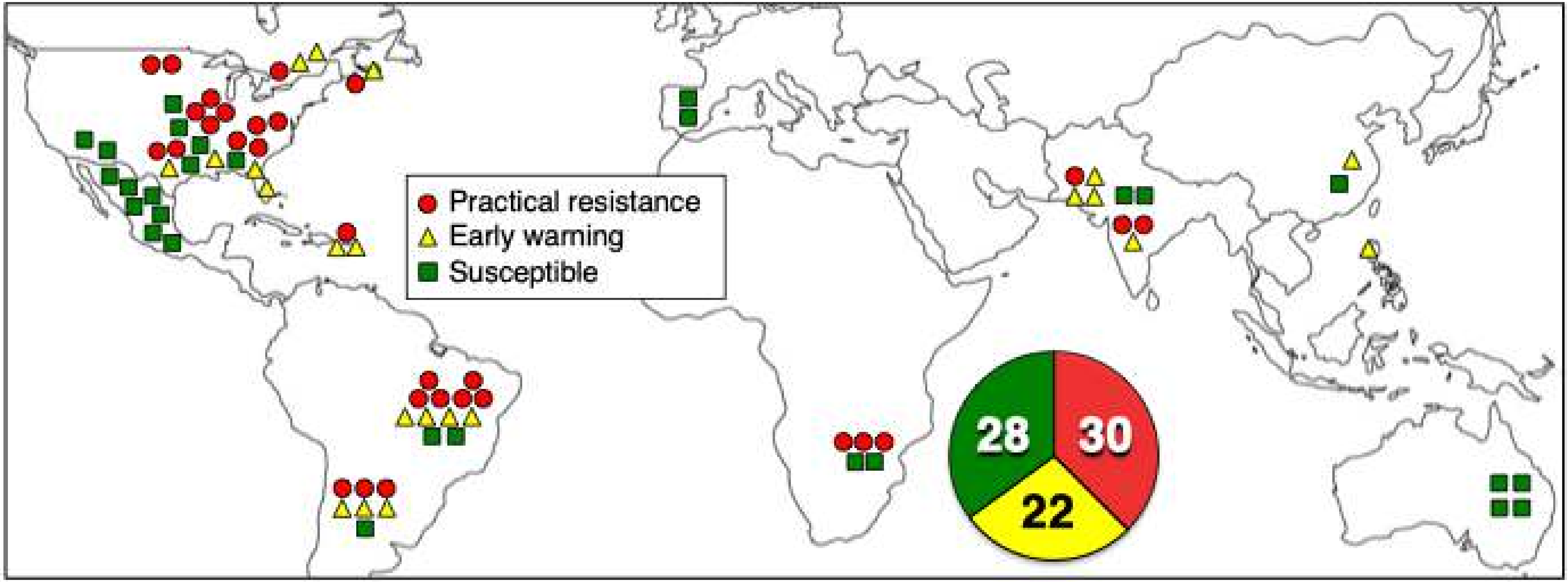
Field-Evolved Practical Resistance to Bt Crops

2022: 30 cases
11 pests:
9 moths, 2 beetles
9 Cry toxins
7 countries

Tabashnik et al. 2023 JEE
Updated 20 August 2024



Global status of field-evolved resistance to Bt crops



Tabashnik et al. 2023 JEE, Updated 20 August 2024

Refuge Strategy
Plants: 1 Bt toxin
Insect resistance: 1 gene, 2 alleles (r & s)

ss = susceptible homozygotes

rs = heterozygotes

rr = resistant homozygotes

"High-Dose"/Refuge Strategy: Ideal Conditions

Resistance is recessive

- r alleles rare
- only extremely rare rr survive on Bt crop
- rr mate with ss to produce rs
- rs killed by Bt

Taylor & Georghiou JEE 1979, Tabashnik & Croft Environ Ent 1982
Gould Annu Rev Ent 1998

Predictions Confirmed by Field Outcomes

Resistance evolves slower with:

1) recessive inheritance of resistance to Bt crops
2) abundant refuges of non-Bt host plants

Tabashnik et al. 2013 Nature Biotechnology
Tabashnik & Carrière 2017 Nature Biotechnology
Tabashnik & Carrière 2019 JEE
Huang 2021 GM Crops & Food

Pink Bollworm

Pectinophora gossypiella

Resistance Risk in AZ: High

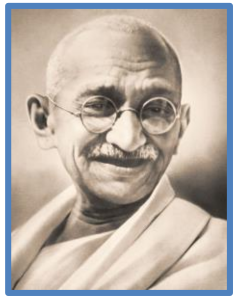
- Lab-selected resistance
- Feeds mainly on cotton
- >50% Bt cotton in Arizona since 1997
- 5 generations per year

Invasive, major pest of cotton worldwide

Henneberry & Naranjo IPM Rev 1998

CABI Invasive Species Compendium 2016

Pink Bollworm (*Pectinophora gossypiella*) an Invasive Pest: Resistance to Bt Cotton in the World's Top 3 Cotton-Producing Countries



India Refuges of non-Bt cotton were scarce, resistant to Cry1Ac + Cry2Ab in <10 years

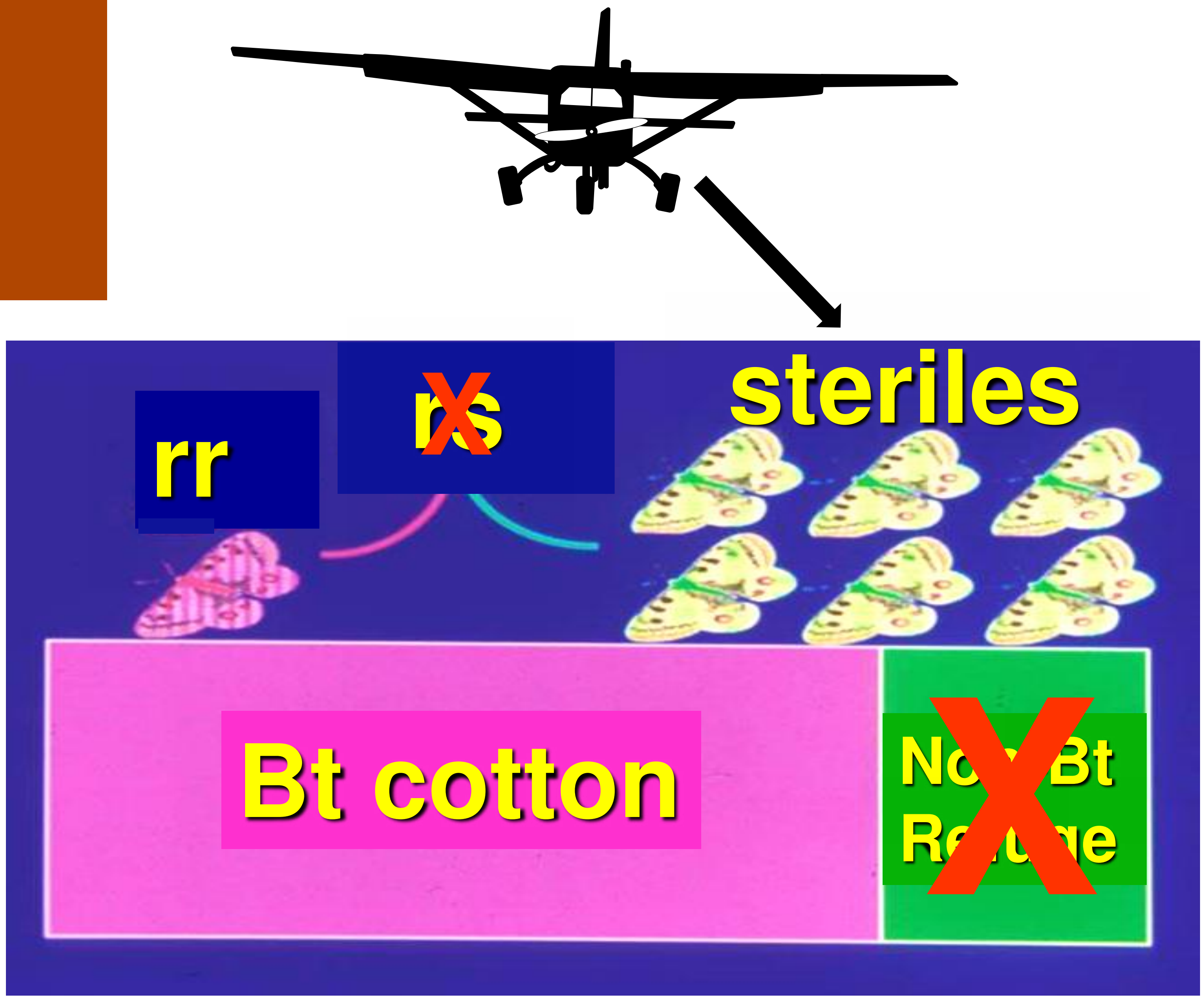
China Resistance to Cry1Ac rose initially when refuges were scarce, then fell when refuge abundance increased

USA No resistance >28 years: refuges for first 10 years, then eradication with Bt cotton + sterile moth releases

Dhurua & Gujar PMS 2011, Naik et al. PMS 2018, Wan et al. PNAS 2017, Tabashnik & Carrière JEE 2019, Tabashnik et al. PNAS 2021

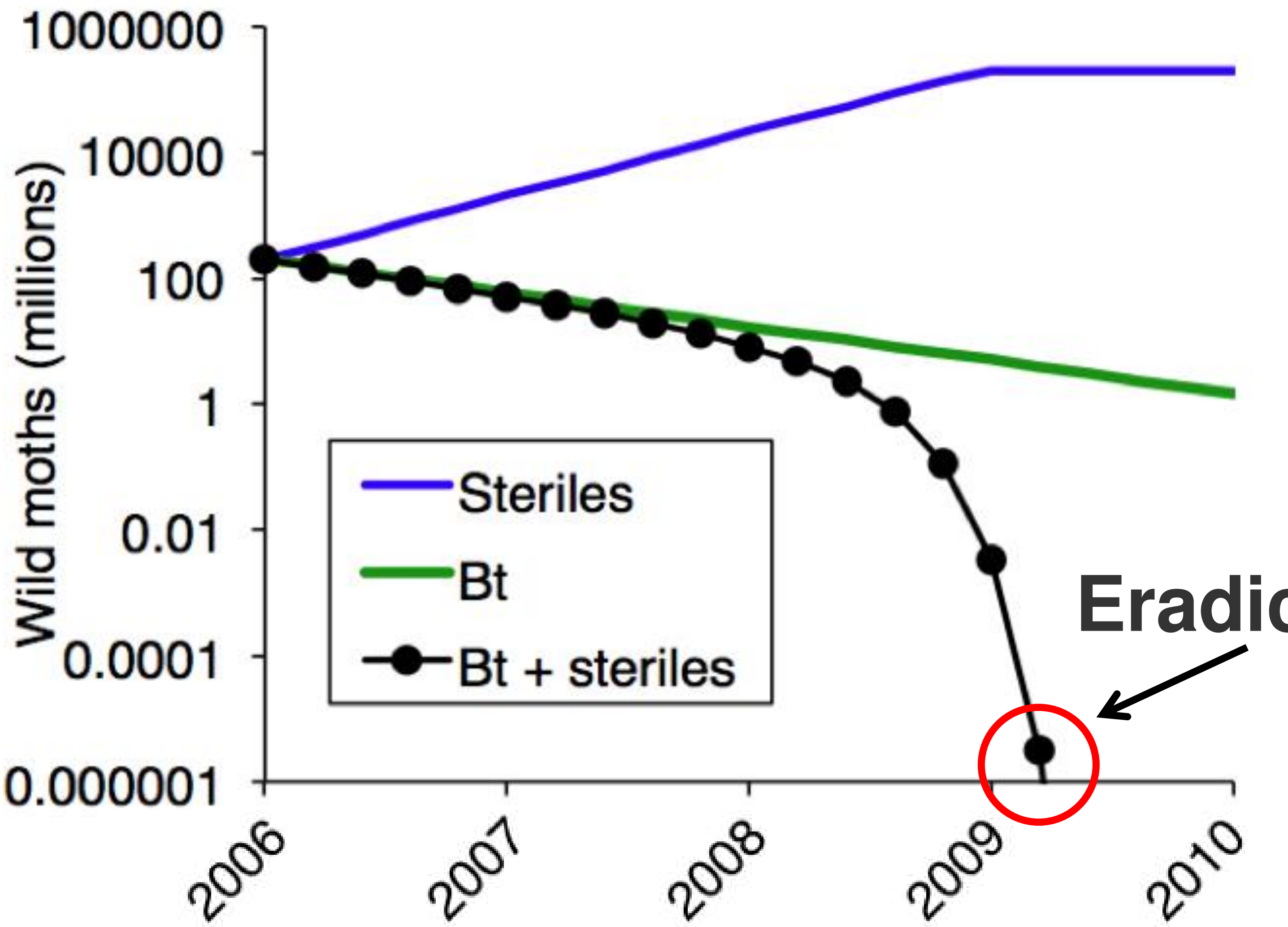
Sterile Insect Technique + Bt Cotton

- r alleles rare
- rr mate with steriles
- No fertile progeny

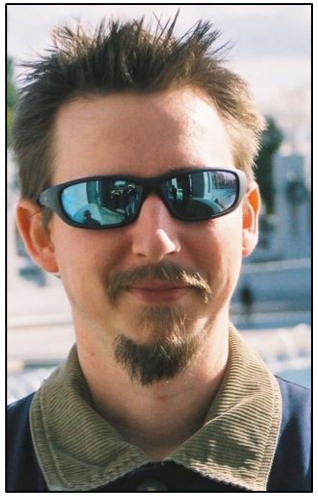


Tabashnik et al. 2010 Nature Biotechnology, 2021 PNAS

Simulations: Bt cotton + steriles synergistically suppress PBW



Eradication



Mark Sisterson

Refuge (observed):
7% non-Bt cotton, 93% Bt cotton

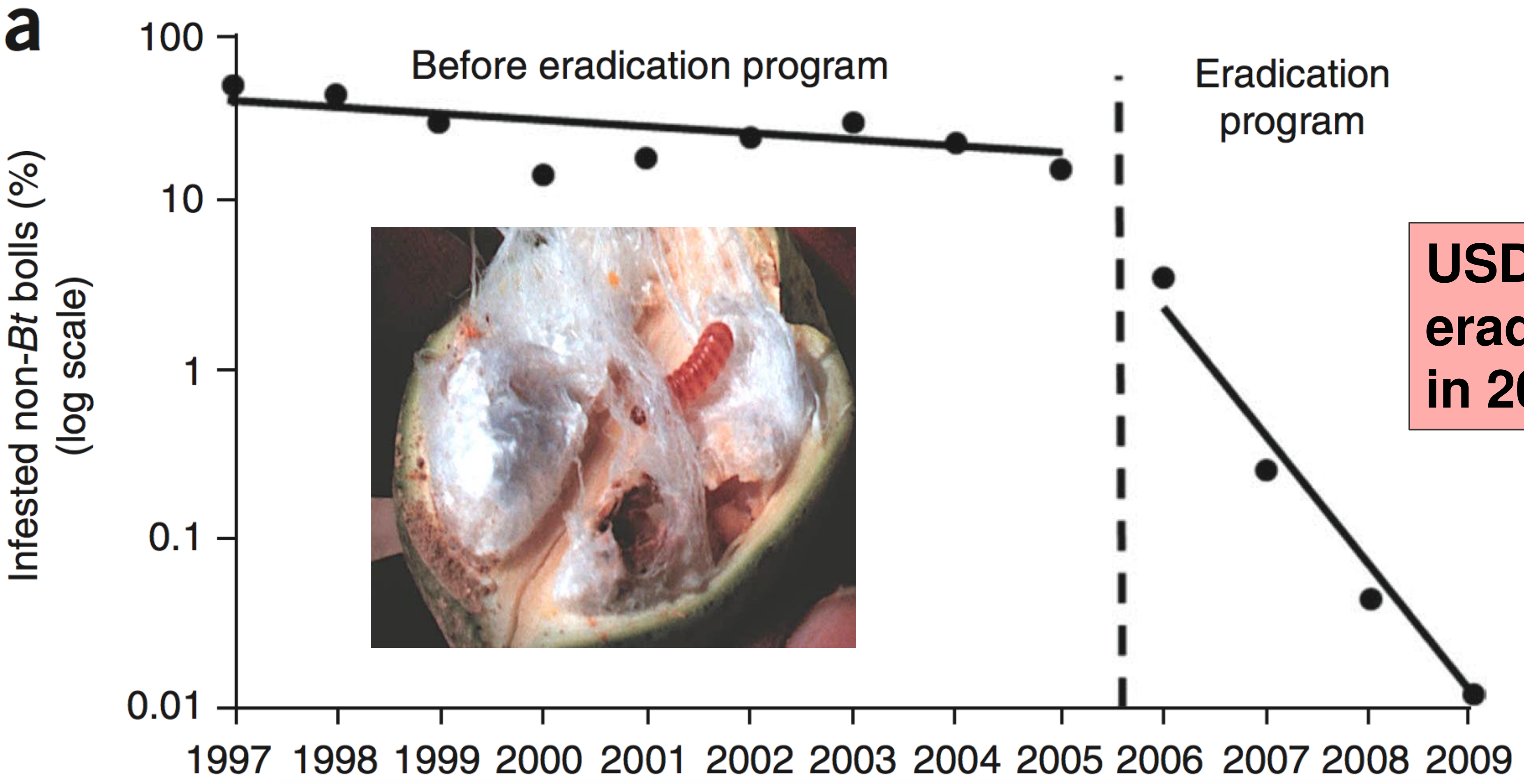
Tabashnik et al. 2021 PNAS

PBW Sterile Moth Releases in AZ

2-3 releases per week per field
April – October
11.4 billion moths: 2006 to 2014

Bt cotton: 400 moths/ha/week
Non-Bt cotton: 4,000 moths/ha/week

Pink Bollworm Larvae in Non-Bt Cotton Bolls



USDA declared eradication in 2018

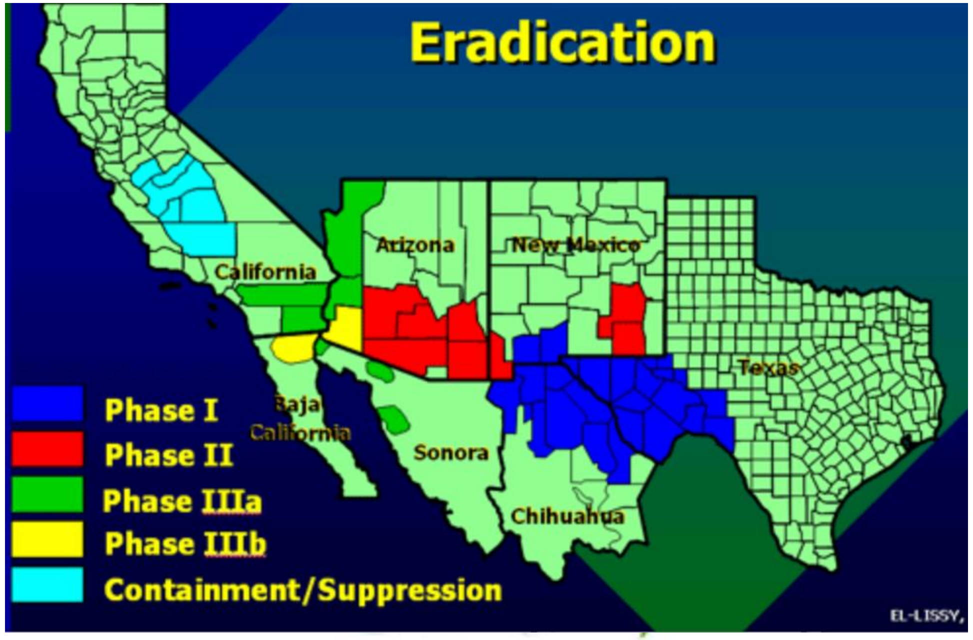
2010 to 2018: No larvae in 86,413 bolls

Tabashnik et al. Nature Biotechnology (2010) & PNAS (2021)

Benefits of eradicating pink bollworm from the US

- Insecticide use in cotton reduced by 82%
- 11 million kg of insecticides avoided
- Farmers saved $192M from 2014-2019

Tabashnik et al. 2021 PNAS



Pyramid Strategy:
2 or More Toxins that Kill the Same Pest
Ideal Conditions

- No cross-resistance between toxins
- Each toxin kills nearly all susceptibles
- Resistance is rare & recessive
- No overlap with single-toxin plants
- Refuges are sufficiently abundant

Roush (1998) Phil Trans Royal Society
Carrière et al. (2015) Nature Biotech & (2016) Trends in Biotech

Bt cotton: Cry1Ac, Cry1Ac + Cry2Ab (Bollgard II)
Cry1Ac: not high dose vs. *Helicoverpa* species

Australia: *H. armigera* & *H. punctigera*

1996-2003 Cry1Ac: 70% refuge

Susceptible to both toxins: 2004

2004-2015 Cry1Ac + Cry2Ab

No overlap

Still susceptible to both toxins

Downes et al. GM Crops & Food 2012,
Downes Monitoring Report 2015-16

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Downes Monitoring Report 2015-16

USA: *H. zea*

1996-2010 Cry1Ac: min 4% refuge

Resistant to Cry1Ac: 2002

2003-now Cry1Ac + Cry2Ab

Overlap: 8 years (2003-2010)

Resistant to Cry1Ac & Cry2Ab

Ali et al. JEE 2006, Ali & Luttrell JEE 2007 and others

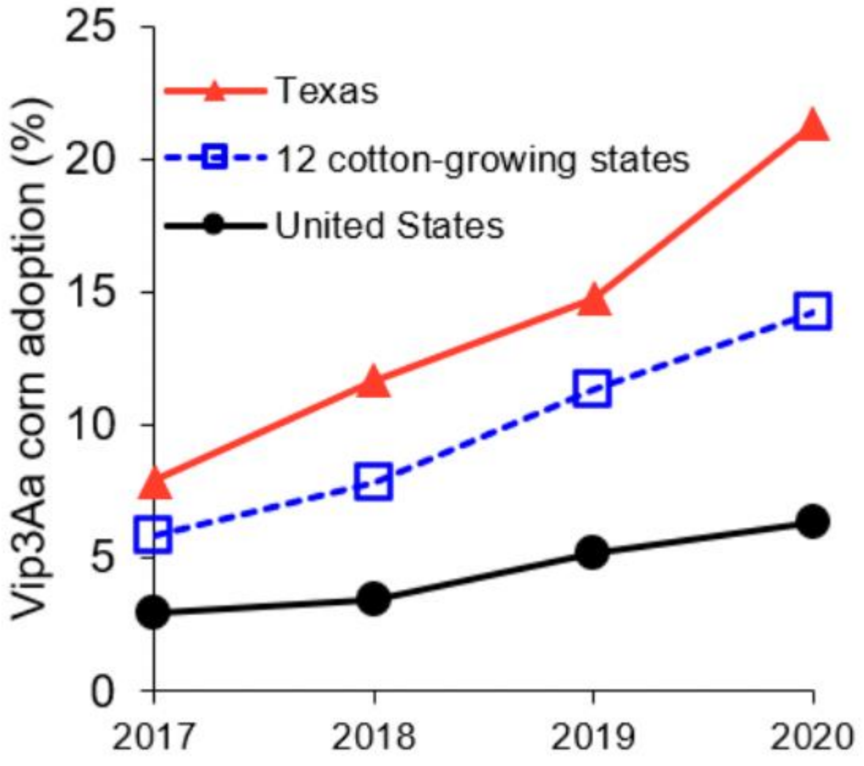
Bt cotton with 3 toxins
Cry1Ac + Cry2Ab + Vip3Aa (Bollgard 3)
Cry1Ac + Cry1F + Vip3Aa (Widestrike 3)

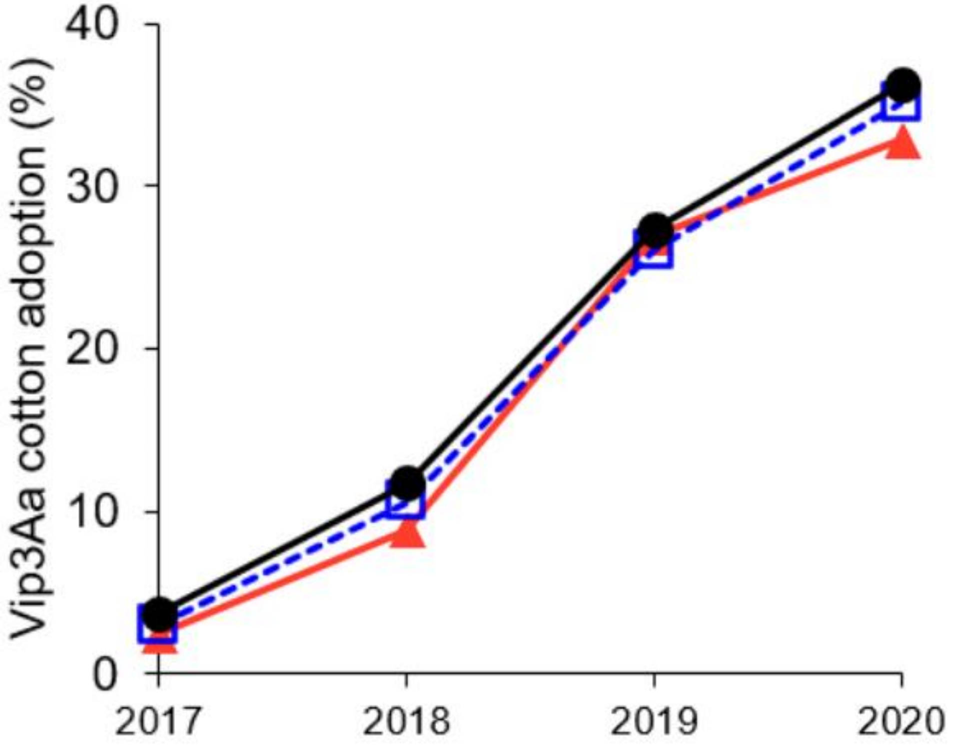
Australia: *H. armigera* & *H. punctigera*
Susceptible to Cry1Ac & Cry2Ab
2016: Switch to Bollgard 3 (92%)
3-toxin pyramid
Susceptible to all 3 toxins

USA: *H. zea*
Resistant to Cry1Ac & Cry2Ab
Cry1F not effective
2016: cotton ca. 1% Widestrike 3
1-toxin product vs. many populations

Tabashnik & Carrière Nature Biotechnology (2017)

Early Warning of Resistance to Vip3Aa in *Helicoverpa zea* (corn earworm & cotton bollworm)





Yang et al. Toxins (2021)

The battle continues…