Are the Major Impediments Now to Resistance Management for Crops In the Social Sciences and Governance?

Rick Roush

Overview

Mechanisms, genetics & management theory adequately understood by about 1990-95, yet successes in delaying resistance in the field are few

Problem is implementation

Most or all successes have included some gov’t intervention; a proposal discussed intensely in 1984

History of Debate on Gov't Role

Dover and Croft, 1984: US EPA should do more to regulate resistance management because resistance typically leads to more environmentally risky pesticide use (more applications, toxic compounds)

US National Academy of Science, Wash DC, Nov 1984, esp. Miranowski & Carlson; generally rejected intervention

Miranowski & Carlson (NAS pub 1986)

Conditions Favoring R Management by a Single Technology Company

Highly profitable technology with no potential or actual close substitutes

Monitoring of resistance (and RM practices) not costly

Monopoly permits the company to market the compound to manage resistance

Pest mobility is such that voluntary management by growers is uneconomic

A Tale of Two Monsanto Technologies

Conditions Favoring R Management by a Single Technology Company

Bt Crops:

Resistance problems modest after 16 years, with some actual or potential competitors along the way

Round-up Ready Crops:

Monopoly on the crops, not the herbicide

Now >14 weeds; profit losses of about $99M

A Tale of Two Monsanto Technologies

In this most dramatic example, with "Conditions (Nominally) Favoring Resistance Management by a Single Technology Company",

Why has Resistance Management been relatively more successful for Bt Crops than for Round-up Ready Crops?

Insecticide resistance management:

Choices from a short menu (Roush 1989)

- High vs low doses depended migration, refuges & persistence
- Rotations/Mixtures/Mosaics
- Non-chemical controls and avoidance of use

High dose

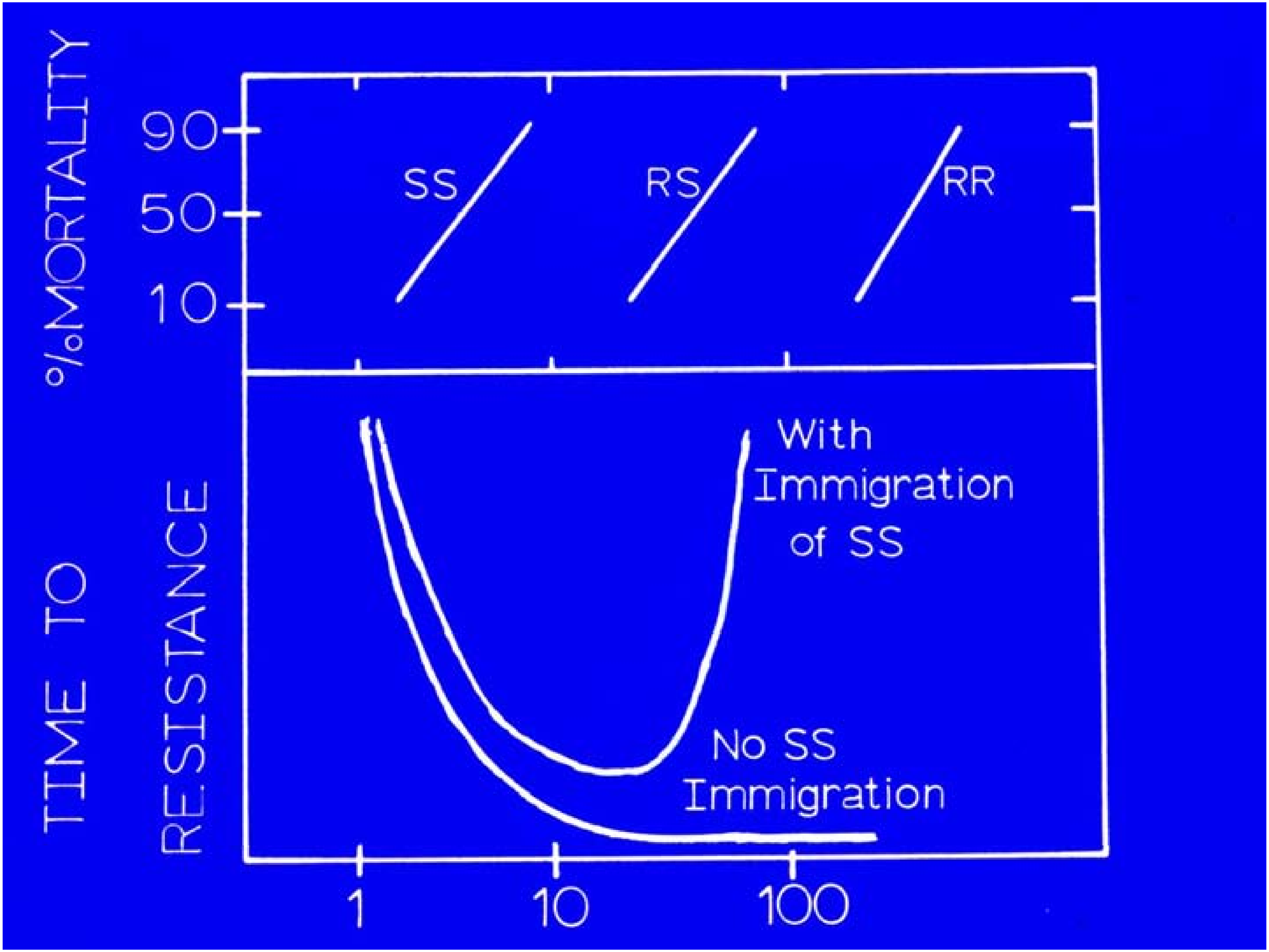
Kill RS, the most common carriers of resistance, ie., where p=frequency of R (10^{-4}) :

RR	RS	SS
p^2	$2pq$	q^2
10^{-8}	$2X10^{-4}$	about 1

High Dose Strategy Depended on:

- Low initial R frequency (<10^{-3})
- Mortality of RS > 95%, even across different life stages exposed and in the face of residue decay
- **Effective Refuges**, not deterred by insecticide residues ("seed bank" for weeds are refuges)

(essentially worked out by Tabashnik and Croft 1982, Environmental Entomology)


%MORTALITY
90
50
10
SS
RS
RR
TIME TO RESISTANCE
With Immigration of SS
No SS Immigration
1
10
100

1980s Pyrethroid Resistance Mgt in Australian Cotton: Seasonal "Windows"

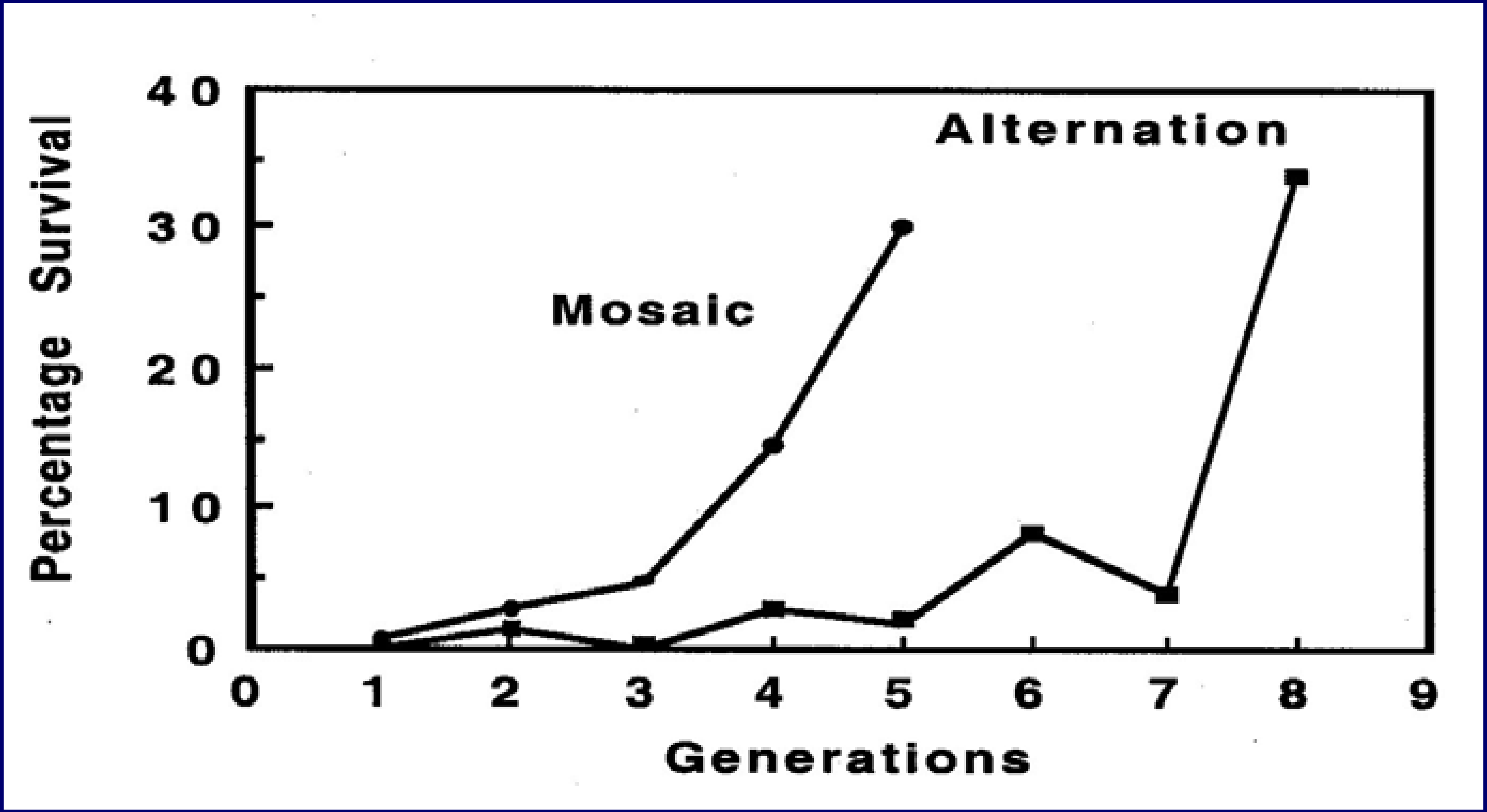
I. Endosulfan (GABA)

II. Pyrethroids (Na channel)

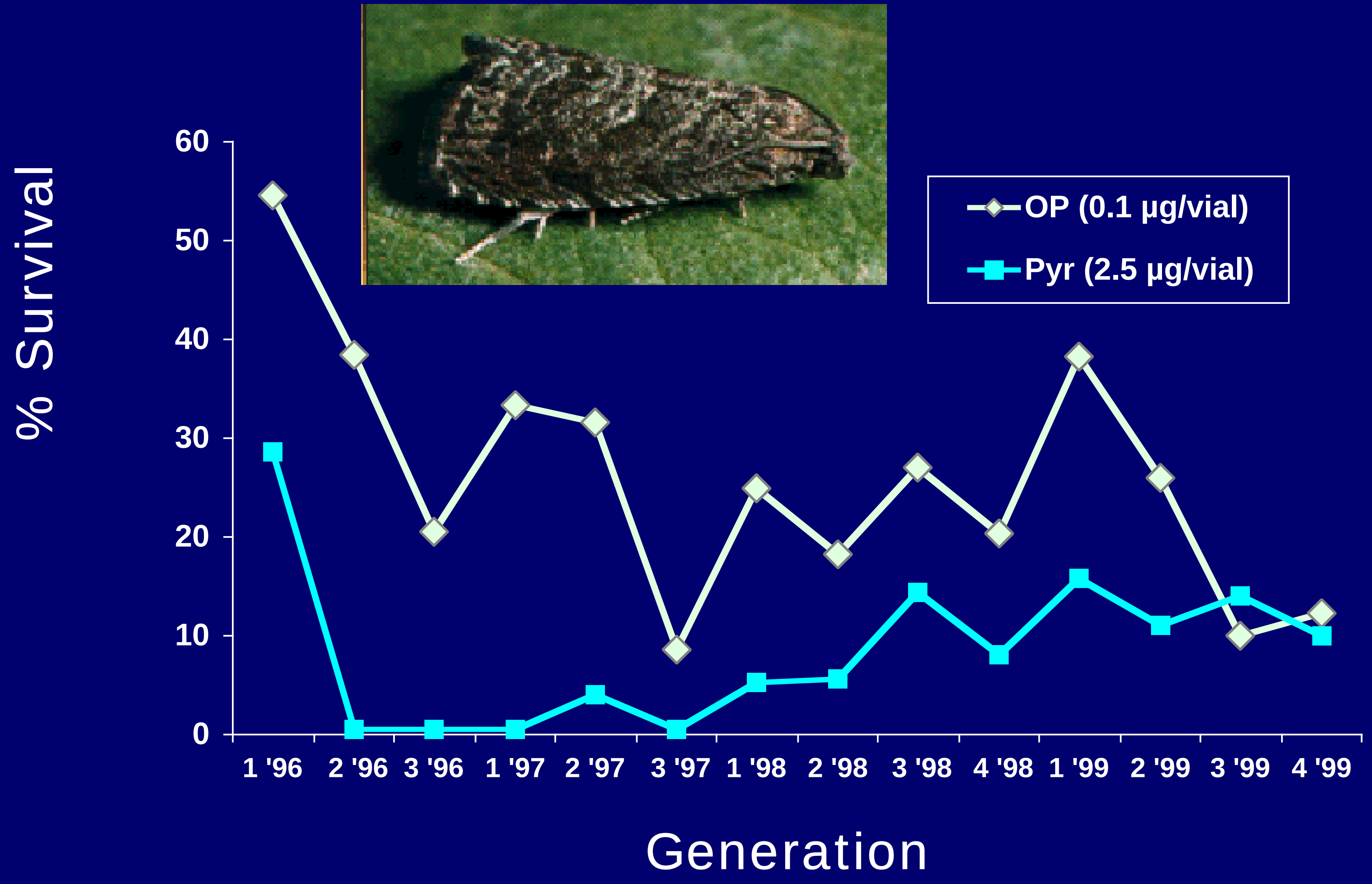
III. Organophosphates & carbamates (AChE)

(Rotation "soft" regulated by inclusion of time intervals on pesticide label)

Avoid mosaics, the least efficient way of using both insecticides



Effect of Rotation of Insecticides on the Evolution of resistance in Oriental Fruit Moth in Ontario, Canada (D. Pree)



What's needed in Mixtures to Delay R?

- Low initial R frequency (< 0.1%)
- No cross-resistance between compounds; guessed at by target
- Resistance to at least one of the toxins needs to be somewhat recessive (Mani in Genetics 1985)
- Redundant killing of SS & Refuges

More precise statement of the underlying theory:

- Mixtures work by "Redundant Killing" of SS

(Comins 1986, Gould 1986)

- Same for GM pyramids for Bt (1994-1998)

Need not just equal decay rates;

Mixtures not promising because of

- loss of redundant killing from

incomplete coverage or

-kill of different age classes,

& residue decay

AND

twice as much pesticides!

To Make Robust Mixtures:

Consider frequencies of genotypes

p^2 x p^2	$S^A S^A S^B S^B$	about 100%
$2pqXp^2$	$R^A S^A S^B S^B$	2 x 10^{-4}
p^2x2pq	$S^A S^A R^B S^B$	2 X 10^{-4}
$4p^2q^2$	$R^A S^A R^B S^B$	4 x 10^{-8}

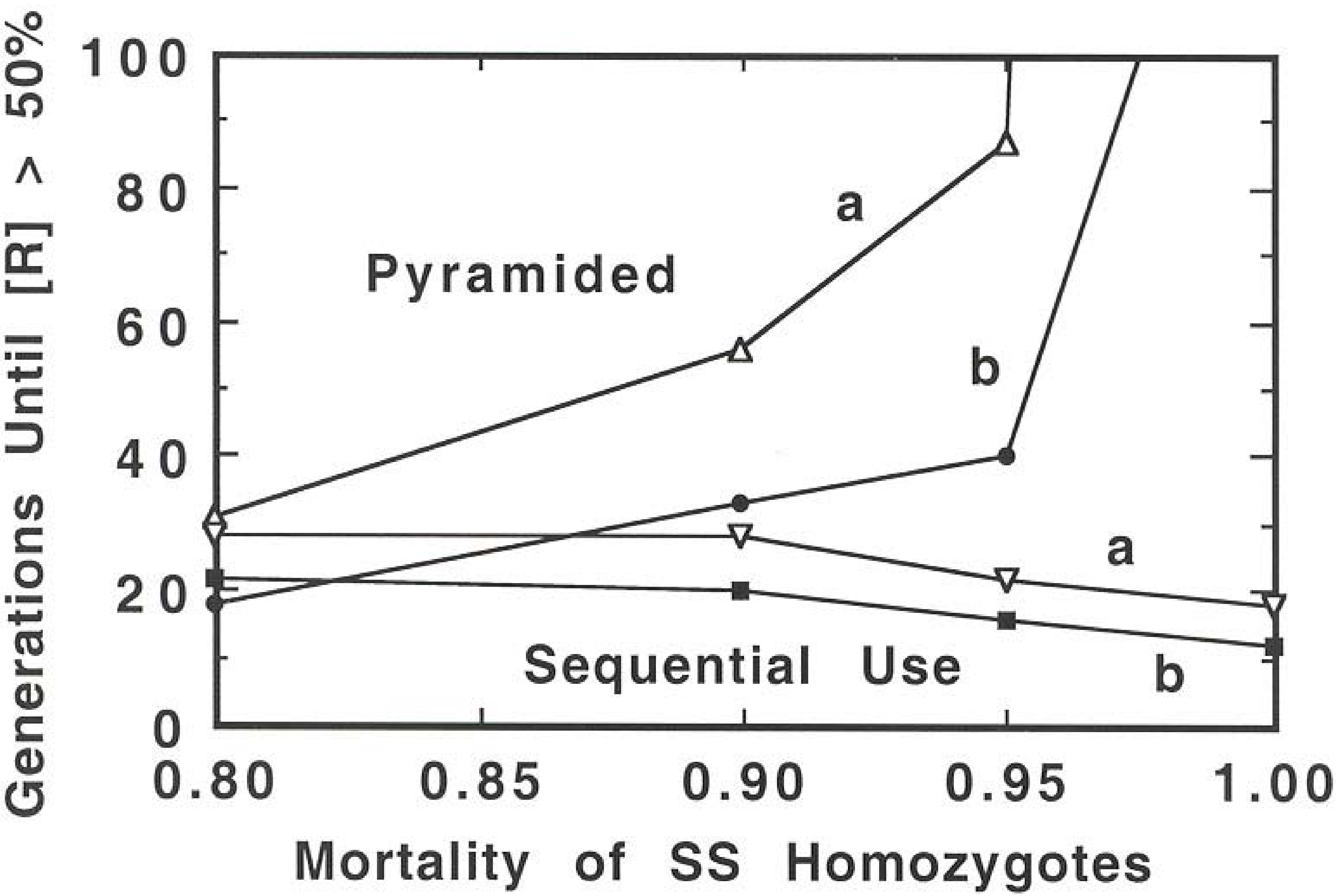
Doubly resistant individuals <u>are</u> very rare, but it's survival of the RSSS and SSRS individuals that cause resistance!

Mixtures (& Pyramids)

$2pqXp^2$	$R^AS^AS^BS^B$	2×10^{-4}
p^2x2pq	$S^AS^AR^BS^B$	$2 X 10^{-4}$

The key is redundant killing: mortality of these SS-bearing genotypes must be more than 95%

E.g., if residues decay to the point where only 80% of SS genotypes are killed, no real benefit to mixing (or pyramids!).



Generations Until [R] > 50%
100
80
60
40
20
0
Pyramided
a
b
a
Sequential Use
b
0.80
0.85
0.90
0.95
1.00
Mortality of SS Homozygotes

Single and Double Gene Bt Plants

Zhao et al. 2003 Nature Biotech

Transgenic Herbicide Crops

- Introduced in 1997, little widespread adoption of resistance management tactics as Entomology would know them
- No government regulation

Transgenic Herbicide Crop RM

- In Australia, resistance to glyphosate from from 1996 (Powles and Preston)
- 1998, Best Practice Guidelines: “Don’t include same herbicide resistance in two GM crops within same rotation”
- Clean equipment between fields to avoid spreading weed seeds
- No relationship between RR canola and resistance to glyphosate over 5 years


UC Statewide IPM Project
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Glyphosate resistance risk factors (Preston)

Intensive use of glyphosate (15-20 years), especially if 3-4 times per year (orchards)

No other herbicides used

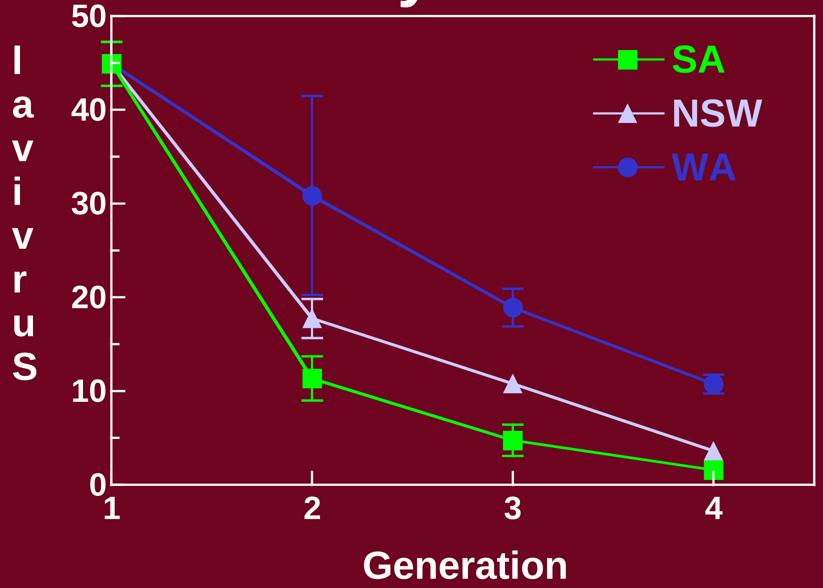
Little or no tillage (small seed bank more important than weed kill?)

Glyphosate resistance genetics in Oz ryegrass

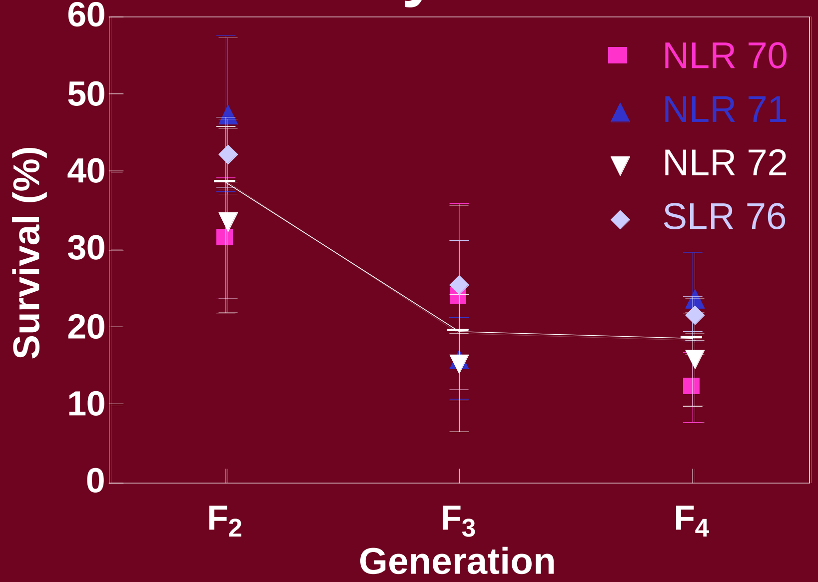
- Most of resistance due to one gene
- Resistance low (3-7 fold)
- Why so slow to evolve compared to other herbicides?

Fitness Penalty for Glyphosate Resistance (Preston)

1 population, 3 sites, 3 years



4 populations, 1 site, 2 years



Glyphosate resistance management

Fitness costs (about 50% decline per generation)

Not a great fitness advantage (only 3-7 fold R)

Rotate herbicides! (>1 yr in 3?)

Avoid treating large weeds

Transgenic Herbicide Crop RM

Tactic proposed by not adopted in USA:

Not introduce Round-up Ready corn at all to reduce glyphosate use in crop rotations, thereby enforce pesticide rotations

- There were alternative herbicides

- RR corn eventually much less rapidly adopted than RR soy or cotton, suggesting less value

Insect Resistance Management for Genetic Engineered Crops: Patterns of Success

Conservative List of Problematic Cases

Armyworm *(Spodoptera frugiperda)* to Cry1F in Bt corn in Puerto Rico

Maize stem borer (*Busseola fusca) to* Cry1Ab in Bt corn in South Africa

Pink bollworm (*Pectinophora gossypiella)* to Cry1Ab cotton in India (controversial)

Bt corn in the beetle Western corn rootworm, *Diabrotica virgifera,* in USA

Also increased R frequency in *Helicoverpa*

Why Has Transgenic Bt R Mgt Been Successful?

"Field outcomes support theoretical predictions that factors delaying resistance include recessive inheritance of resistance, low initial frequency of resistance alleles, abundant refuges of non-Bt host plants and two-toxin Bt crops deployed separately from one-toxin Bt crops" (Tabashnik et al. 2013, Nature Biotech 31: 510)

Field Control Failures Due to Failure to Plan or Implement?

Spodoptera frugiperda to Cry1F in Bt corn in Puerto Rico: few structured refuges, poor efficacy

Busseola fusca to Cry1Ab in Bt corn in South Africa; few structured refuges

Pink bollworm, *Pectinophora gossypiella,* in India: refuges?

Bt maize for *Diabrotica*: low efficacy, refuges difficult

Helicoverpa: low efficacy and small refuges

Successes in Planned Resistance Management for Bt Crops

Bt corn in mainland USA: relatively large mandated refuges and high expression relative to pest sensitivity

Pink bollworm, *Pectinophora gossypiella,* in Arizona cotton: same

Tobacco budworm, *Heliothis virescens* on cotton in the USA: same

Helicoverpa spp in USA and Australia; not well controlled by Cry 1A toxin, but large refuges and pyramided two Bt genes

A Tale of Two Monsanto Technologies: Heroines and Heroes?

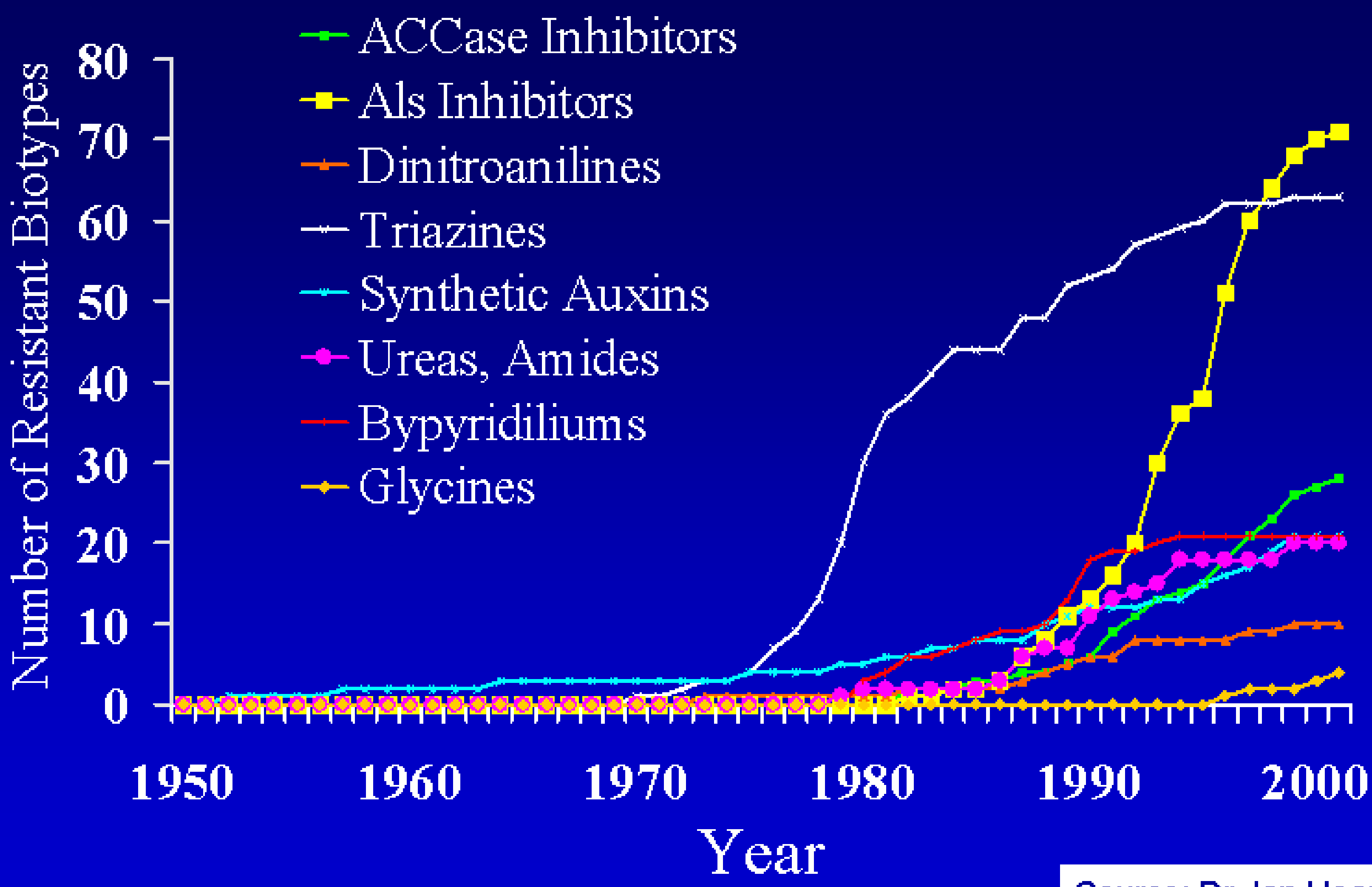
For Bt crops within Monsanto,

Pam Marrone, Steve Sims and Terry Stone selected for Bt resistant *Heliothis virescens*, the tobacco (cotton) budworm

For Round-up Ready Crops, a strong view within Monsanto that resistance to glyphosate was (nearly) impossible?

Slow in field, was hard to do even by GM!

Herbicide Resistant Weeds



Source: Dr. Ian Heap
www.weedscience.com

Why Were Refuges and Two-toxin Bt Crops Mandated in US and Australia?

US EPA lobbied to protect Bt which was seen as a public good

(Why not glyphosate?)

In Australia, cotton growers were very concerned due to history of R to insecticides, & encouraged government to adopt public sector recommendations

Summary

Government intervention usually needed to preserve refuges & drive adoption of pyramided varieties, was part of successful insecticide strategies, but not part of Round-up Ready crops

Revisit “soft” gov’t intervention with 30 years of hindsight?