Immunising older cohorts
Pros and cons

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Vaccines depend for their impact at the population level by reducing transmission and true herd immunity

Transmission has to be blocked
without transmission disease disappears irrespective of whether those vulnerable to infection have serum antibody or not

This why catch up programmes are so important

Immunising older women is a catch up programme

As an example

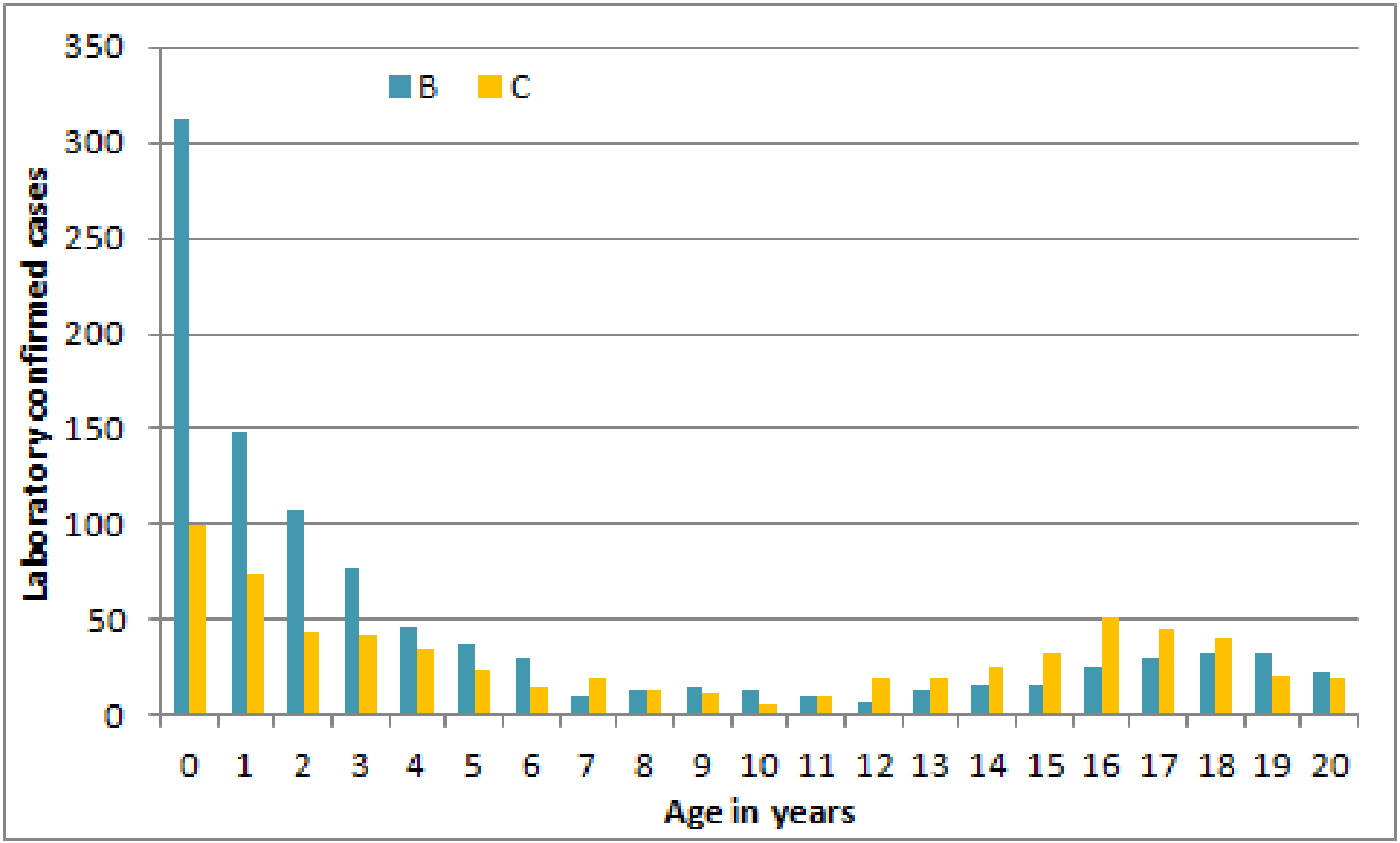
Meningococcal vaccines

Immunising infants

The UK story

Slides courtesy Adam Finn@adamhfinn
University of Bristol UK

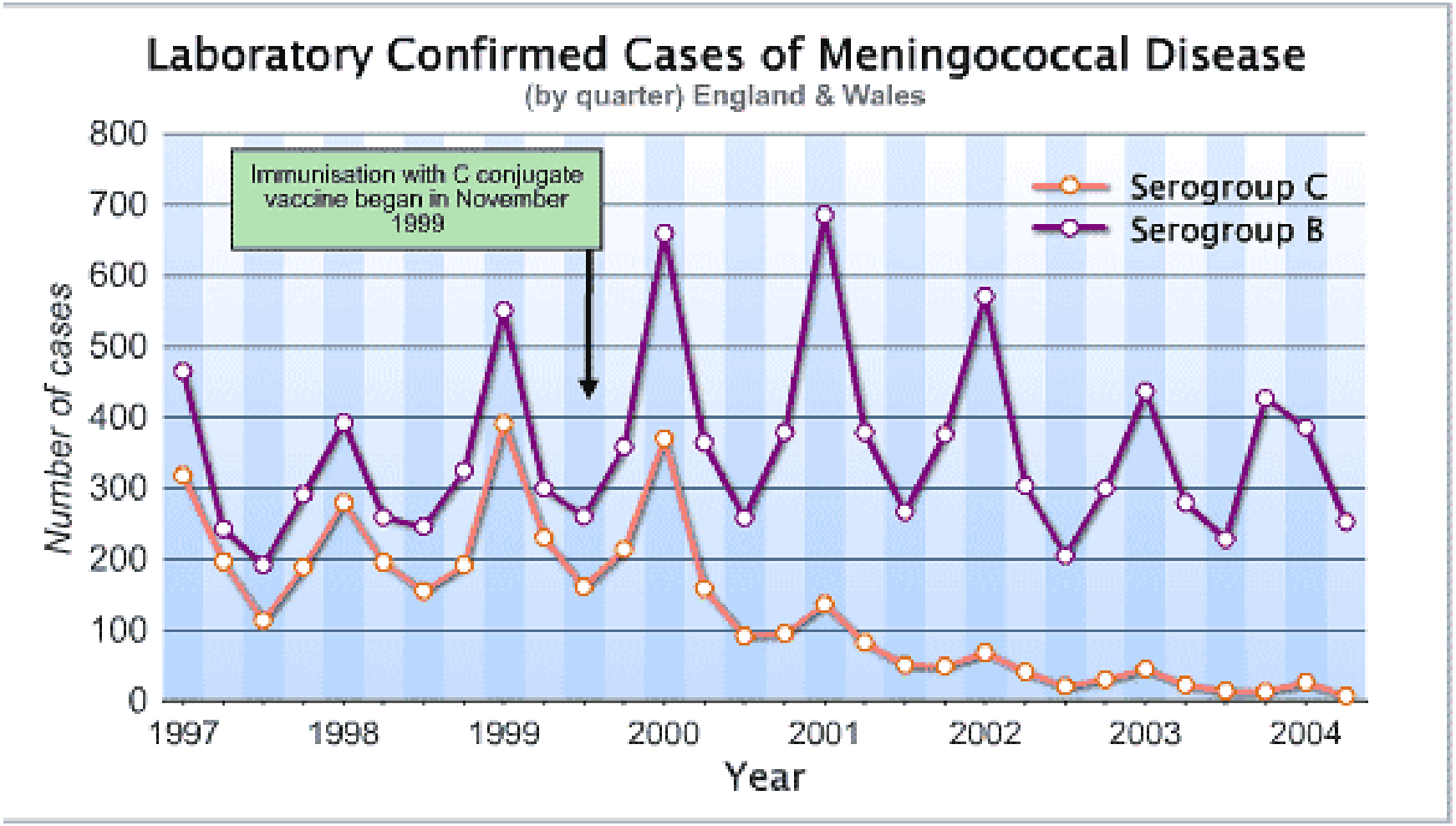
Age – UK 1998/9


B
C
Laboratory confirmed cases
350
300
250
200
150
100
50
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Age in years

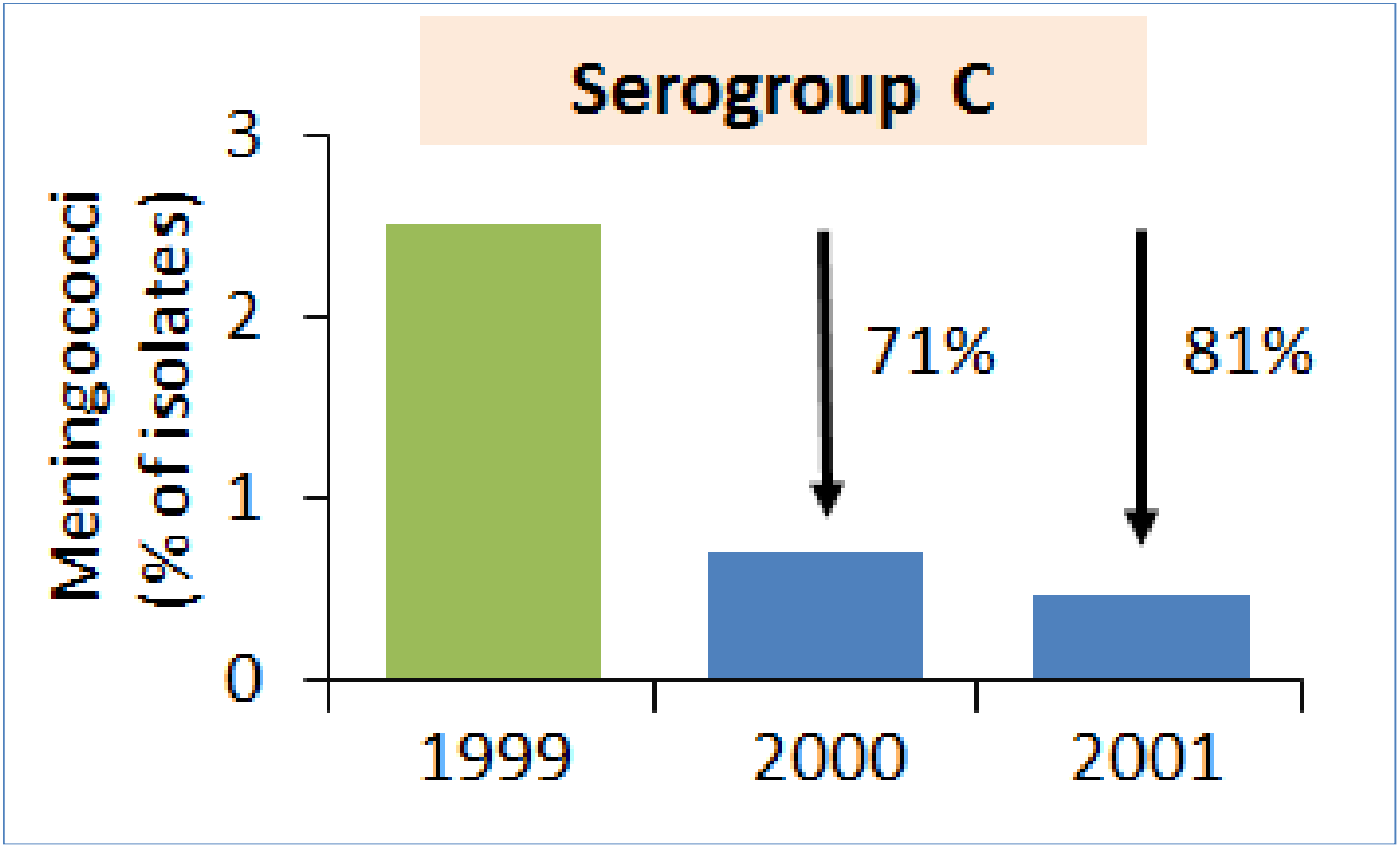
One off "catch up"programme 2000

- One dose MenC conjugate
- All children up to the age of 20y
- (Eventually extended to 23y)

MenC disease carried on disappearing but not by inducing long lasting antibody in vulnerable recipients



UK Students - carriage



Maiden MC, et al. ***J Infect Dis. 2008;197:737-743***

The catch up programme worked by blocking transmission

immunising teenagers protected younger children

teenagers are the group with highest rates of carriage

young children have the highest rates of disease

Transmission was blocked

Take home message

- Think fundamentally
- blocking transmission is the name of the game

Immunising older women

Pros

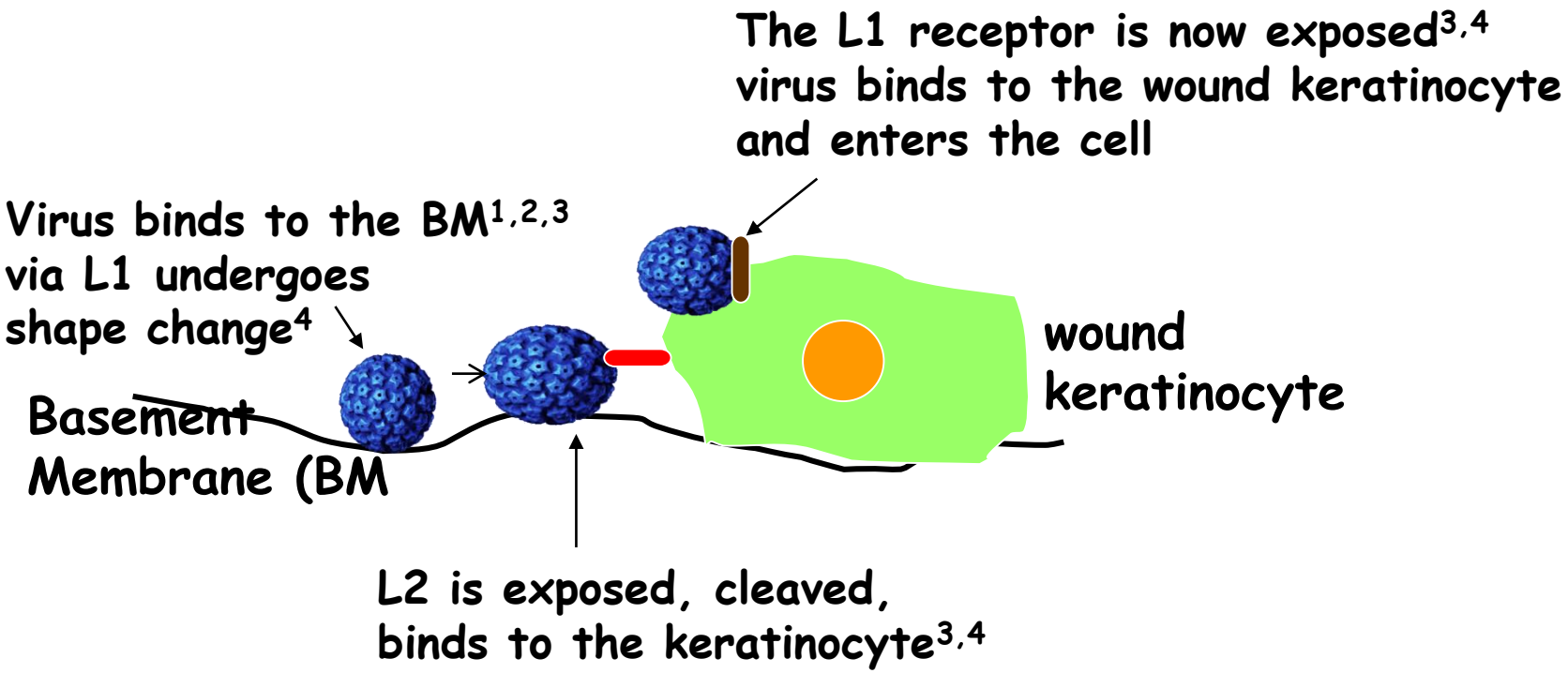
- Transmission of vaccine types blocked rapidly
- Rapid impact on disease in older cohorts – herd protection

Cons

- Cost – current models predict even 1 dose vaccination not cost effective in >26 year olds
- What about those already infected and shedding virus will serum antibody block transmission? Possibly

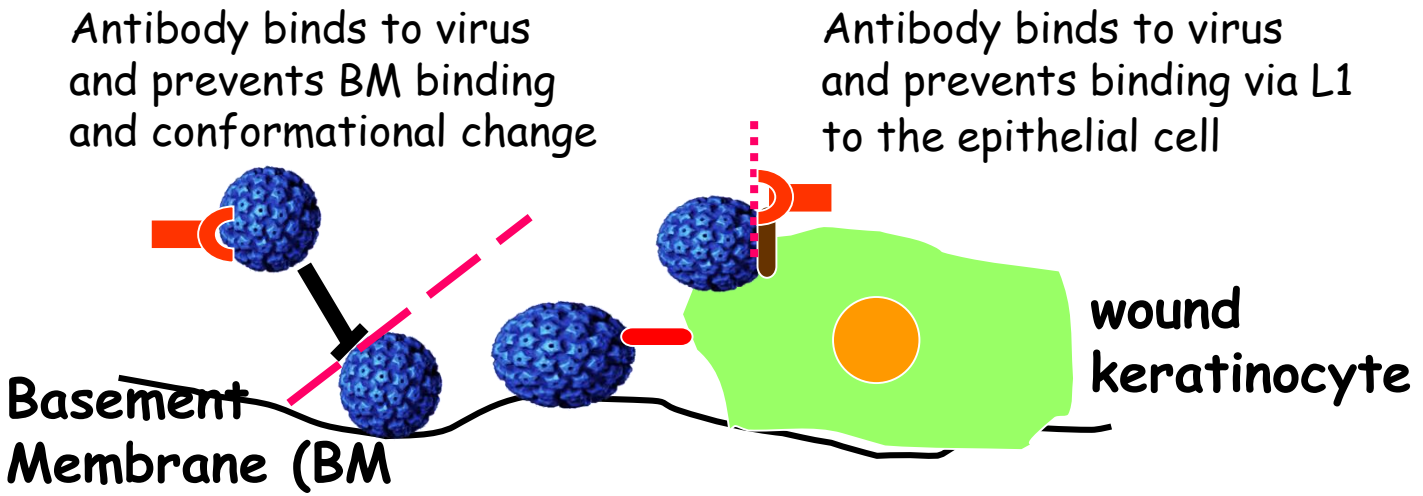
How does serum neutralising antibody against HPV L1 prevent virus entry?

Proposed mode of HPV entry



[1]Roberts etal Nature Med 2007 13 857. [2]Day etal J Virol 2008 82 4638
[3]Day etal J Virol 2007 81 8784 [4]Day et al 2010 Cell Host Microbe

Neutralisation after HPV 16L1 VLP immunisation



HPV 16 L1 antibodies that prevent conformational change neutralise at very low concentrations (10^{-12}M)
Passive immunisation shows very low levels of antibody prevent virus entry

Very low levels of antibody are needed to prevent HPV infection

Antibody to L1 can prevent HPV infection by

Blocking binding to the basement membrane

Blocking binding to the epithelial cell receptor

Both types of antibody are generated after vaccination with HPV VLPs

Passive immunisation experiments show that very low levels of these antibodies are sufficient to prevent HPV entry into cervical epithelial cells

Day et al 2010 Cell Host Microbe 16;8(3):260-70.

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- *What about those already infected and shedding virus will serum antibody block transmission? Possibly*

If virus is shed as free particles into the vaginal lumen in a productive infection then antibody in the cervico/vaginal mucus and fluids should coat the particle and prevent autoinoculation and/or infection of the sexual partner

Transmission would be blocked

If cell associated virus is shed this mechanism would not operate