Occupational and Environmental Concerns of Veterinary Pharmaceuticals, Biologicals and Antibiotics

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Topics De Jour

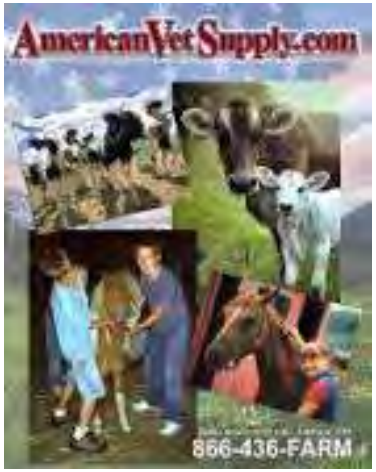
- **Pharmaceuticals used in livestock production & Human Health Risks**
- **Where do they get it?**
- **Regulations of use**
- **How are people exposed**
- **Immunization products**
- **Antibiotics**
- **Hormones**
- **Needle sticks**
- **<u>Prevention</u>**

So what is used in Animals & why (emotional vs. factual perspective)

Product	Why Used
Biologicals	Increase immunity to infections (all animals)
Antibiotics	• Treatment of infections • Growth promotion • Prevention • Antibiotic Resistance
Hormones:	• Treatment – obstetrics, catabolic state • Estrous synchronization • Growth promotion • Enhanced Milk Production

Where do producers get Vet Drugs?

- Most over the counter from local farm store (except DVM Rx)
- Farm service and supply companies
- Veterinary Clinics
- Online
- Mail order



Veterinary and Poultry SUPPLY, INC.

Regulation and Control of Drugs Used in Animals

- **USDA and FDA**
  - Regulate for safety and effectiveness
  - USDA – Animal Vaccines
  - FDA – Animal and Human Drugs.
- **Vet Rx drugs** require a veterinarian to properly diagnose, treat, and administer the drug according to labeled directions
- **FDA Veterinary Feed Directive –** (2017- Vet oversite to reduce low level antibiotics for growth)
- **Veterinarians can use drugs** approved for humans in pets, **non-**food animals

Prevention of Animal Drugs in the Food Chain (Producer, Regs, Vets)

- **On the farm**
  - **Producer**
  - **Veterinarian**
  - **USDA**
- **At the processing/slaughter plant**
  - **Sampled for bacteria, hormone & antibiotic residues before a food item**
    - **Veterinarian inspection**
    - **USDA: Meat**
    - **FDA: Milk, Eggs**
- **At the Store**
  - **USDA - randomly sampled**
  - **Local Health Departments**

How are Producers Exposed?

- Needle sticks
- Direct contact
- Inhalation
- Prevention for allergic workers
  - PPE
  - Respirator
  - safety glasses
  - nitrile gloves

Self Injection Injuries

- > 80 % of farmers self report self injecting[1,2] in previous year
- Current techniques need to change
- Particularly if using injected vaccines with **oil based adjuvant**

References

1. Sustainable Farm Families program participants
2. RIST Sheep Health courses participants

Stuck by One of These Needles?

- Multiple use needles common in cattle and swine = **Hazard**
- Trauma (large bore, barbed needle)
- Contaminated (feces & skin surface organisms)
- Toxic/infectious material in syringe
- Highly concentrated products for large animals

Human Hazards from Animal Biologics (Immunization Products)

- Biologics (e.g., vaccines) used to prevent infections
- Hazards from:
  - **1. Inflammation**
    - **Oil adjuvants**
  - **2. Infection from the product**

What biologic injections may cause harm to humans?

- Live products infections:
  - RB51 – Cattle Brucellosis
  - Erysipelas – Swine
  - Contagious Ecthyma – Sheep
- Killed products =Inflammation
  - E Coli
  - Johne's disease – Cattle, Sheep
    - (disease like Crohn's in humans)
  - Circo virus – Swine

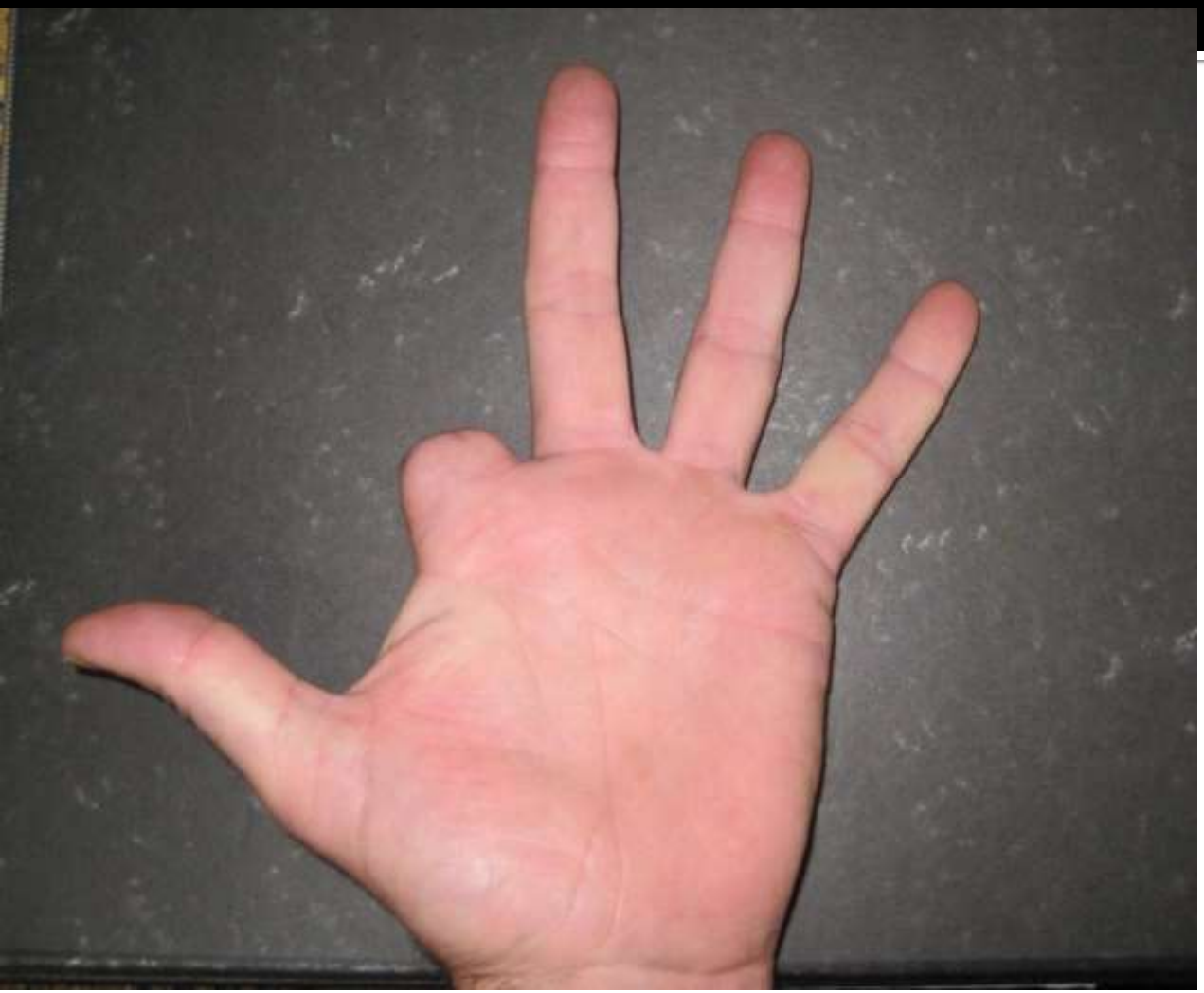
Accidental Inoculation with Gudaire vaccine in sheep

4 operations over 5 months after self injection of Gudair vaccine

5 months after self injected Gudair Vaccine

Oct

Accidental Vaccination with Gudair vaccine



- **Oil adjuvant is Mobile & inflammatory in tissue**
- **4th operation to amputate finger saved the hand**

Hazards of Antibiotic Use

Use of antibiotics in Agriculture

- **In Animals**
  - **Treatment** –
    - Specific antibiotic
    - Specific condition
    - Specific dose
    - Specific length of time
  - **Prevention** – used @ treatment levels in an outbreak
  - **Growth** Promotion
- **Orchards**

Streptomycin use in apple orchards did not increase abundance of mobile resistance genes
Duffy et a;.*FEMS Microbiology Letters*, Volume 350, Issue 2, January 2014, Pages 180–189

- **Ethanol plants**
  - Paulus 2013, J Amim.Sci 91(5) pp2395-404.

Antibiotics as feed/water additives

- Sub-therapeutic levels
  - Faster growth with less feed (1% – 4% gain)
- Treatment levels
  - For sick animal
  - Prevent herd outbreak
- Risks – Resistant infections in animals, producers, public

Tilmicosin (Micotil)

Possible Acute hazard !

- **34-year-old farmer administered Micotil® to cows for respiratory infection.**
- **Put syringe in his pocket**
- **Cow kicked him driving 2 cc into his inner thigh.**
- **In 15 minutes feeling ill.**
- **Taken to his local hospital.**
- **Died 2 hours later of cardiac failure**

Tilmicosin (Micotil®)

- A macrolide antibiotic
- Used in ruminants (cattle and sheep) for respiratory infections
  - One IM dose = 5 – 7 days effective blood level
  - 81,000 beef feeding operations in U.S.
  - 65,000 dairy farms

- Cardio-toxic to Humans, primates, horses, pigs
  - Calcium channel blocker
- Sx:
  - Pain at injection site
  - Chest pain
  - Ventricular arrhythmia (Super calcium channel blocker)
  - Hypotension
  - Heart failure – death

Tilmicosin (Micotil®) poisoning cases

- 2,392 cases world-wide from 1992-2000
- 2,200 reports U.S. (2017)
  - Mostly spray to the eyes, nose, mouth, skin (strong irritant)
- 25 deaths (16 possible suicides??)
- Systemic Sx with 0.5 ml
- 700 – 1400 mg fatal to humans (2 – 4 cc)

- Rx only from DVM

(https://www.avma.org/News/JAVMANews/Pages/171115j.aspx)

Tilmicosin (Micotil®) – Treatment

- **Slow the absorption (ice packs, tourniquet)**
- **Dog studies**
  - **IV Calcium**
  - **Dobutamine (Beta agonist, increases cardiac contractility)**
- **Get to the ER**
- **Cardiac monitoring**
- **Avoid**
  - **Epinephrine**
  - **Beta blocker/sympatholytic (e.g., propranolol)**
- (*Clin Toxicol [Phila]*. 2016;54[8]:812.)

Tilmicosin (Micotil®) – Prevention

- **Responsible people:**
  - Veterinarians, Health Care Providers, Farmers, Employers, Workers, drug companies
- **Substitute to safer antibiotic**
  - Enrofolxacin (Bytril) Class fluroquinalone
  - Tulathromycin (Draxxin) Class Macrolid
  - Florfenicol (Nuflor) Class Chloramphenicol
- Proper restraint of animals
- **Education: includes emergency procedures**
  - get signature of understanding from veterinarian
  - Proper storage
  - Proper sharps disposal
  - One dose per syringe fill
  - Keep needle cover on until use
  - Do not carry loaded syringe in pocket, mouth

1. Chronic Health Risks of Antibiotics

Antibiotic resistance

1. **General**
   - **Animals rapidly develop resistant gut flora**
   - **Build-up of resistant organisms in the environment**
     - ⇧ **Shedding**
     - ⇧ **Mutation/ transduction/conjugation**

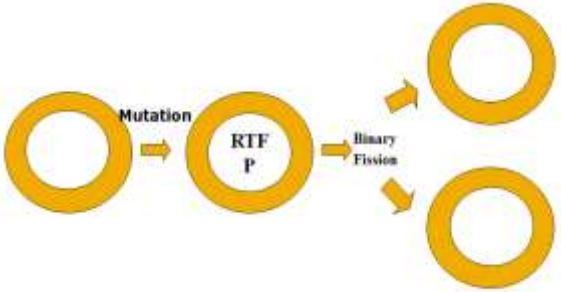
http://www.bsas.org.uk/about_the_bsas/issue_papers/antibiotic_use_in_farmed_livestock/

2. Chronic Health Risks of Antibiotics

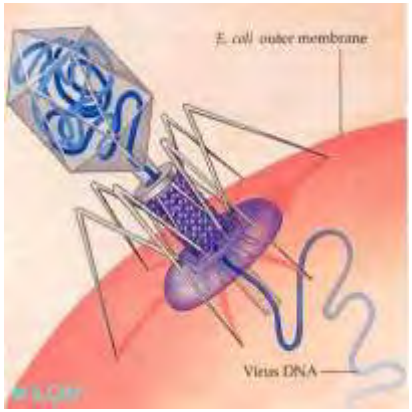
2. **Occupational contact - animals/feed/environment**
   - **Farmers rapidly take on resistant patterns of animals**
3. **General public (low risk)**
   - **Food chain**
   - **Water contamination**
4. **Health effects?**
   - **Enhanced growth of existing resistant pathogens**
   - **Methicillin Resistant S. aureus ? (MRSA)**

How Bacteria Gain Antiboiotic Resistance

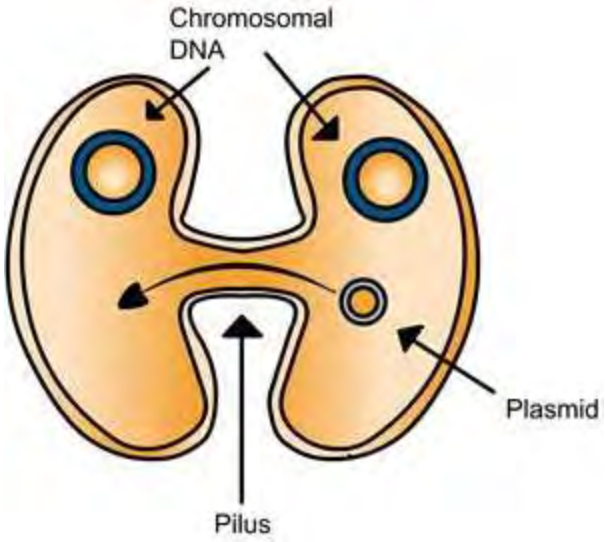
1.CHANCE MUTATION & BINARY FISSION



3. Bacterial phage



2. CONJUGATION



Methicillin Resistant Staph aureus (MRSA)

- Is this the "smoking gun" for overuse of antibiotics?
- Pigs, Cattle, Poultry, Pets
- Swine strains also resistant to tetracyclines

Environmental Risks:

- Found in lagoons, drainage ditches, drainage wells, test wells, and field tiles:
- Antibiotics, resistant bacteria, pharmaceuticals, and trace minerals (Cu, Se) from animal feeds
- In general – Antibiotics in agriculture – uncertain in degree of antibiotic resistance in publics health. But less general use the better.

Hormones Used in Livestock

Treatment

1. Oxytocin (may cause abortion in women)
    1. Dystocia
    2. Milk let down
2. Prostaglandins (may cause abortion in women)
    1. Not cycling , pyometra, Retained placenta
    2. Synchronization
3. Anabolic Steroid (Trenbelone) (misused in body builders) Increased appetite, manage stress in cattle

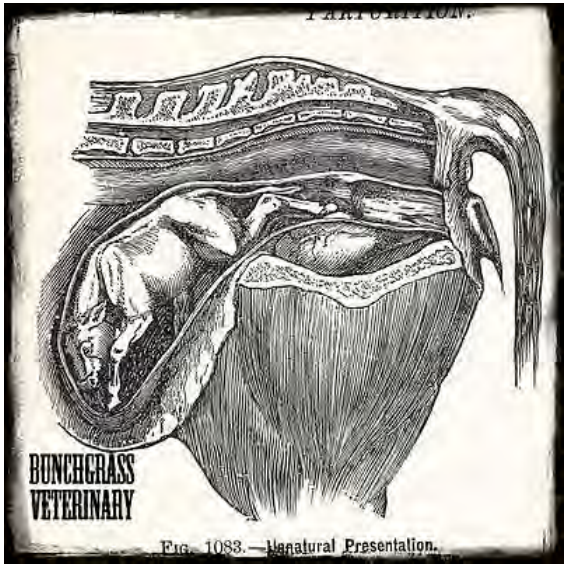
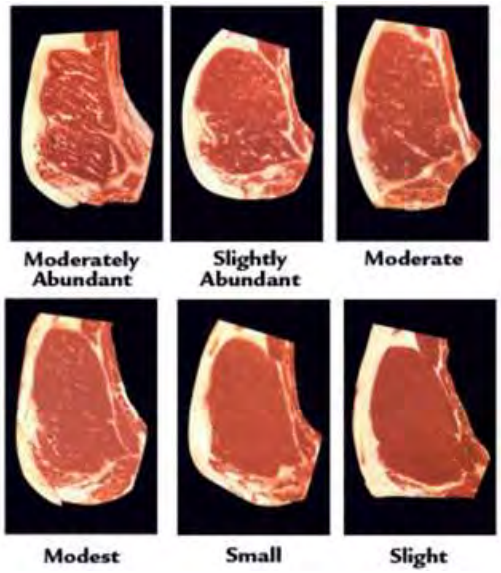


Fig. 1083.—Unnatural Presentation.

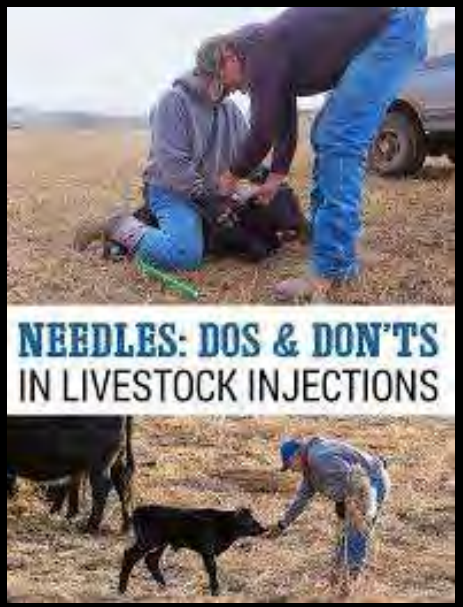
Hormones Used for Production



Increased Growth/ on less feed

- **Estrogens** (growth promotion in steers & meat quality)
  - DES banned for pregnant women.
- **Progesterone & testosterone** (used to increase performance in Heifers, or synchronized)
- **Bovine Growth Hormone** – Dairy Cows increased milk production
- **Ractopamine** (Beta Adrenergic agonist (adrenalin-like) swine and Cattle

Prevention of of Needle Sticks



Donham, K, Rendell, D. Health Risks to Veterinarians and Associated Personnel: Handling Pharmaceuticals and Biolgoicals. The American Assoc. Bovine Practitioners Proceedings, 42:14-17, 2009.

1. Restraint and Animal Handling facilities
2. Often a two person job
3. Safety and Humane considerations

Not This

Temple Grandin

This

Better this

Needle Sticks: Consequences and Prevention

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Proper equipment, Technique, and good cattle dogs = increased safety

Prevention - Needle-Free Injection

Needle-Free Injection System Available

David Cook of Felton International demonstrated the new Pulse® needle-free, cattle-injection system.
Photo courtesy of Felton International

Prevention of Accidental Needle Sticks – General

- (See Micotil prevention above)
- Veterinarians
  - Consider substitution of safer drugs
  - Proper restraint
  - Educate clients to whom you dispense
- Employers
  - Proper storage
  - Proper training (includes emergency procedures)
  - Proper sharps disposal
- Workers
  - Proper animal restraint
  - One dose per syringe fill
  - Keep needle cover on until use
  - Do not carry loaded syringe in pocket, mouth

Safe and effective sheep and cattle injection training program

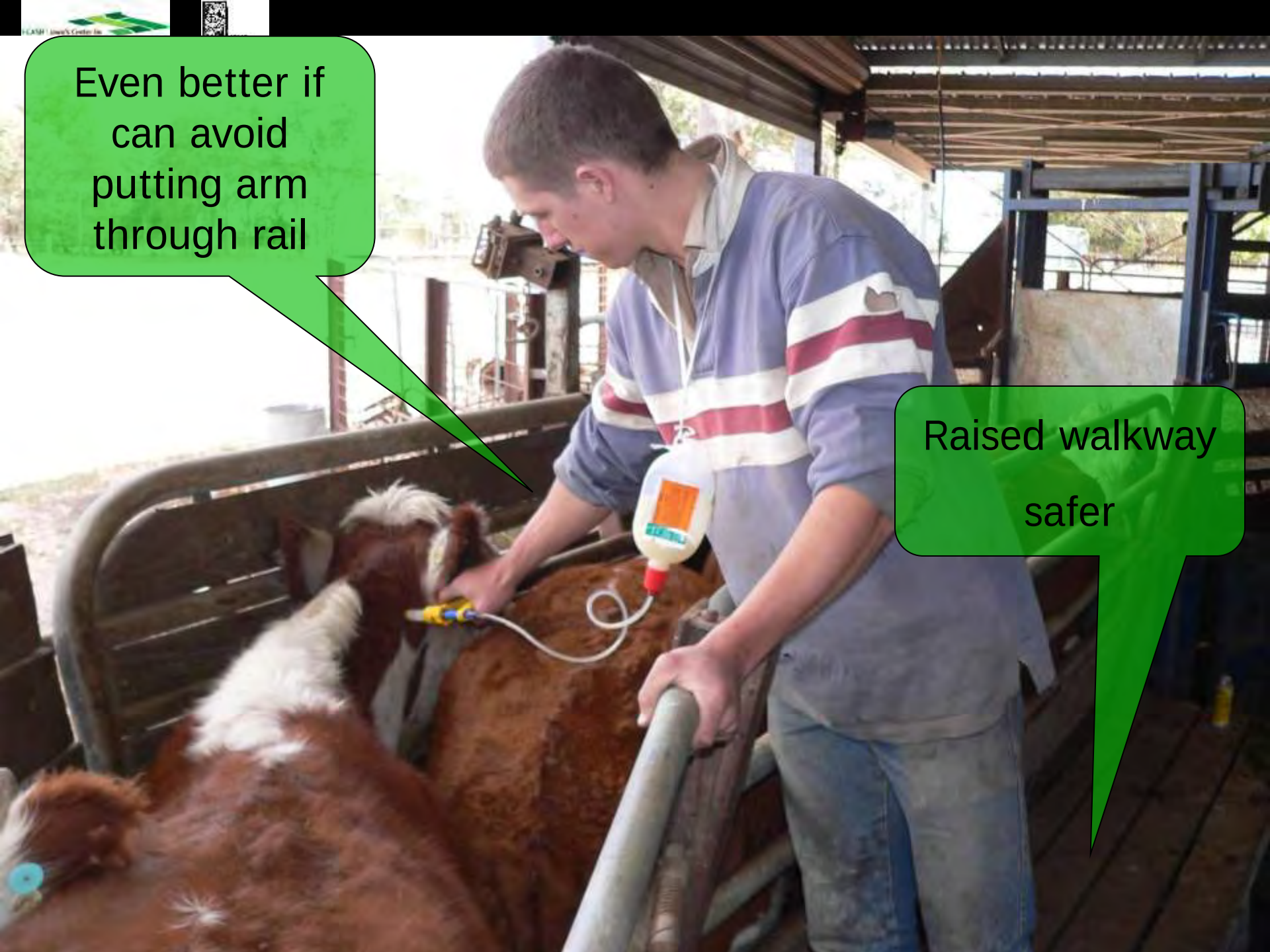
David Rendell DVM and Associates
Veterinary consultants and practice
"Livestock Logic", Hamilton, Victoria, Australia
http://www.livestocklogic.com.au/david-rendell/

- 6mm *(¼ Inch)* 18g needle
  - lambs
  - most vaccines

Longer needles increase risk of injury

Conventional 12mm (1/2”) needle

- mature woolly animals
- intramuscular injections


Even better if can avoid putting arm through rail
Raised walkway safer

Key Points - 1

- Most animal products available OTC
- FDA and USDA regulate animal products for animal safety and effectiveness, and food safety
- Needle sticks are a major risk
  - Acute toxicity (Tilmicosin)
  - Inflammation from oil-based adjuvants
  - Trauma
  - Environmental infections
  - Infection with live vaccines

Key Points - 2

- Hormones and antibiotics used for growth promotion. (antibiotics may be part of antibiotic resistance in humans)
- Prevention
  - Substitute for hazardous products
  - Good animal handling facilities
  - Safe Injection training of workers
  - Sharps management
  - Needless injection

Thanks for your attention
Lets keep these folks alive and well.

Questions? Email to Kelley-donham@uiowa.edu