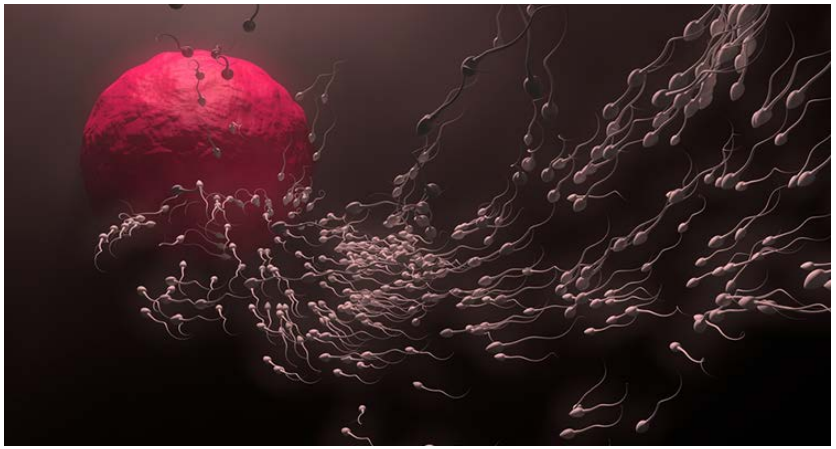
USDA United States Department of Agriculture
USDA's 94th Annual Agricultural Outlook Forum
THE ROOTS OF PROSPERITY
February 22-23, 2018 • Crystal Gateway Marriott Hotel, Arlington, Virginia

Contemporary Science Boosts Fertility in Cattle

Thomas R. (Tod) Hansen, Professor and Director
Animal Reproduction and Biotechnology Laboratory
Department of Biomedical Sciences
Colorado State University

Definition of Fertility

- **Fertility**
  - ✓The capacity to conceive or to induce conception
    - *Medical Dictionary*
  - ✓The actual production of live offspring
    - Farlex Medical Dictionary
  - ✓Fertile sperm + egg + cow = Fertile offspring



Impact of Fertility in Ruminants?

- Limits productivity, livelihood of producers and consumer cost of meat
- Over $1.06 billion annually lost to beef producers alone
- Dairy, beef, and sheep industries contribute $81 B in farm receipts with an estimated overall production value of $192 B.
- These industries support over 2.3 million jobs
- USDA-NIFA-sponsored efforts to improve fertility and manage infertility
- World population increasing at rate of 1 billion people/10 years

- **USDA NIFA W3112:** Reproductive Performance in Domestic Ruminants.
- **USDA NIFA W3171**: Germ Cell and Embryo Development and Manipulation for the Improvement of Livestock

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Got Bull?

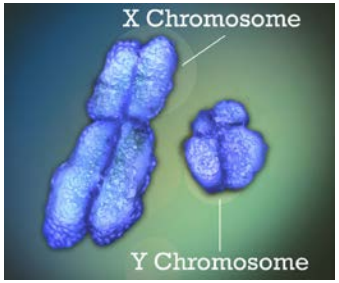
- "Buy a neighbors bull"
- Cross-breeding
- AI with superior genotype
- Sperm quality
- Genetic testing for fertility
- AI using sexed sperm

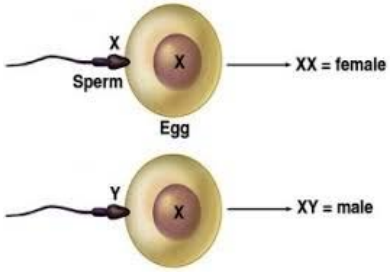
Still the most powerful tools:

✓ *Ovulation synchronization with hormones and AI with genetically superior semen*

Reproductive Priorities

- Get the cow pregnant
- Make genetic improvement
- Use technology that is convenient, effective and affordable
- Use new tested approaches
  - ✓ Test in different breeds of cattle prior to application





Sexed Semen: X vs Y

- Sexed Semen
  - 90% sort on X vs Y DNA
  - 2 million doses of bovine semen are sexed annually in USA
    - Heifer calves for expansion of herd or replacement
    - IVF to produce males for beef
  - For broader application, requires lower costs and higher fertility

Seidel, Jr. 2014, Colorado; USDA NIFA NC2117

Other Improvements in Male Fertility

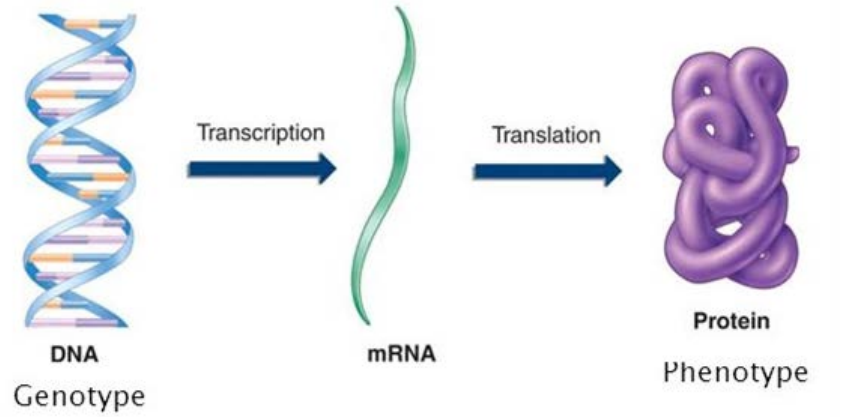
- Fertility biomarkers on sperm
- Removal of abnormal sperm
- Genetic selection for fertility
- Cryopreservation of gametes and embryos
- Identifying best sperm for IVF or ICSI

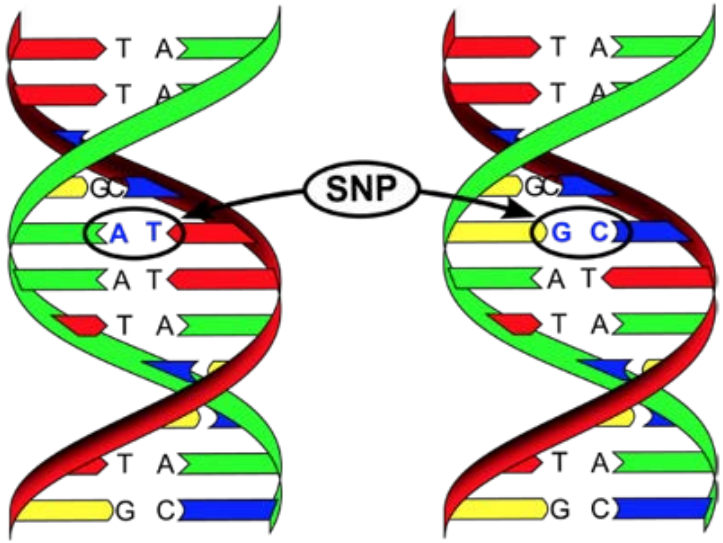
Therio.vetmed.lsu.edu

W3112: Collaborators from: Nebraska, Washington State, Montana, Missouri, Penn State, Kansas State, Wyoming and Alaska

Genetic Markers

- Genes encode mRNAs, which are translated to proteins
- New analysis of genes using single nucleotide polymorphism (SNP) can improve reliability of selection for fertility traits
  - SNP identification through mRNA and genome sequencing
  - SNP Screening: SNP Chips





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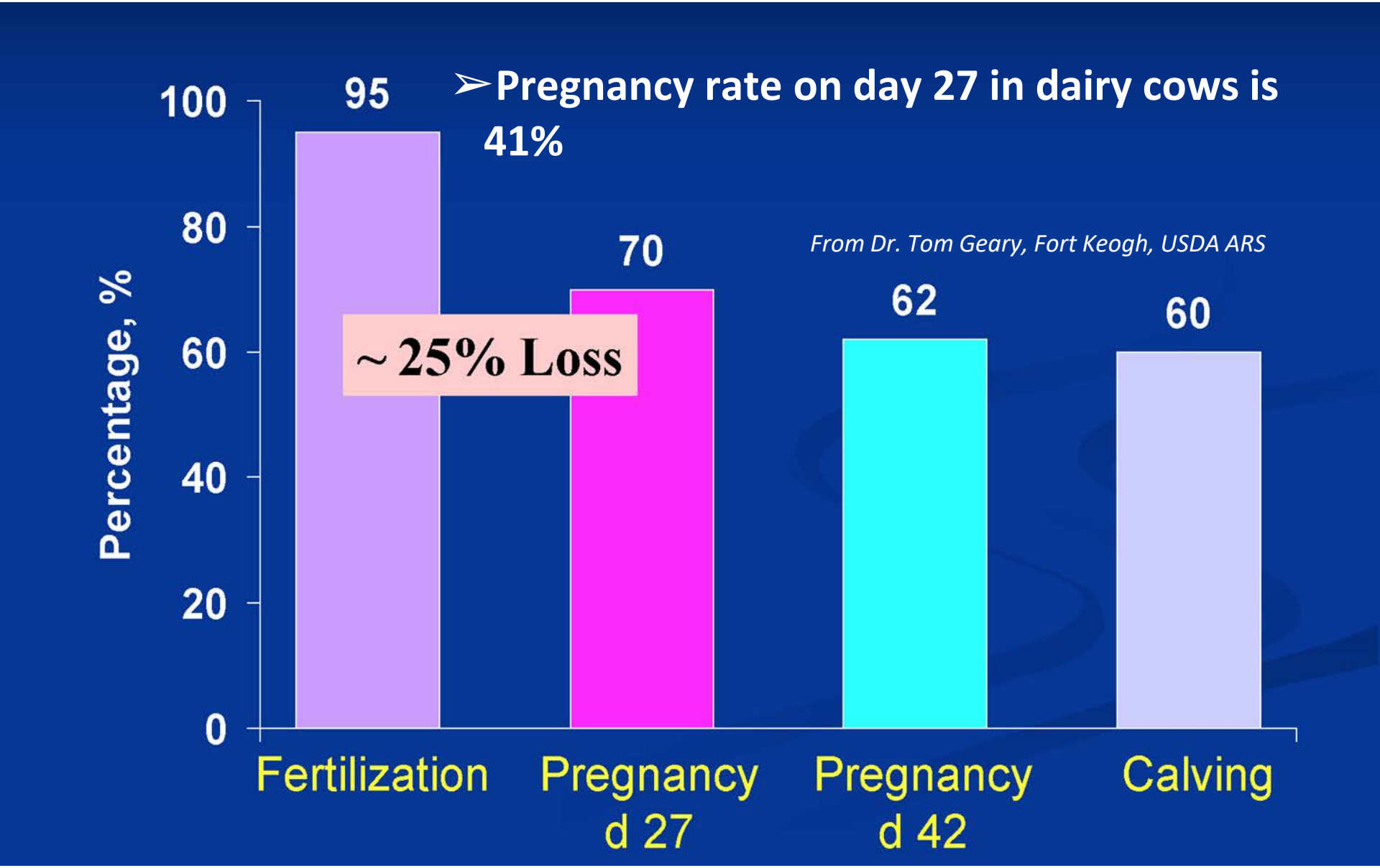
Colorado, Florida, Idaho, Missouri, Montana, Texas

Fertility of Single Service Beef Cows



Fertility in Dairy cows

- As selection towards milk production increased, fertility in dairy cattle decreased
- Less than 35% of lactating dairy cows subjected to AI carry gestation to term (*Santos JE. 2004; Florida*)
- Causes of reproductive failure
  - Dystocia and delayed resumption of ovulation after parturition
  - Impaired metabolic (energy) status
  - Impaired follicular development
  - Improper timing and amount of hormones
  - Poor uterine receptivity
  - Embryo mortality

Advances in Female Reproduction

- Ultrasound
  - ✓ Follicle development, Corpus luteum, Pregnancy, Pathologies, Sex of fetus
- Hormone diagnostic assays
  - ✓ Real-time upload to cloud/tag readers
- Synchronization of ovulation
- Detection of estrus and timed AI
- Ovarian reserve, oocyte quality and screening

From Gametes to Embryos

Superovulation to Embryo Transfer
(3-10 fold increase in egg production)

Seidel GE Jr. Science. 1981. 23;211:351-8

- ➢Superovulation
- ➢Fertilization/ in vitro fertilization
- ➢Embryo transfer
  - 1.6 M embryos world wide
  - ½ from USA
    - 2016 IETS

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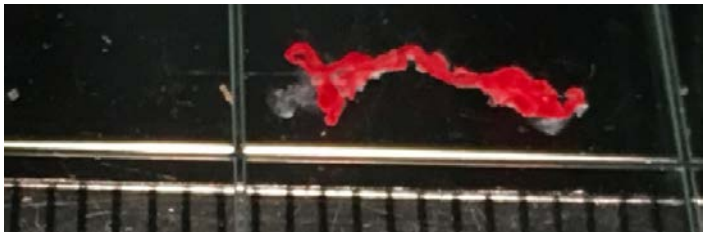
IVF slide from Dr. Jennifer

Maternal Recognition of Pregnancy and Embryo Mortality

Day 16 Embryo Mortality



Markers of EM

Discovery

Day 16 Healthy Viable Embryo

Markers of Pregnancy

IFNT, ISGs & microRNA

➢ **Embryo mortality costs USA producers $1.4 Billion Annually**

- **C. Lamb; Beef Cattle Handbook, Kansas**

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Colorado, Idaho, Pennsylvania, Missouri, Tennessee, Texas

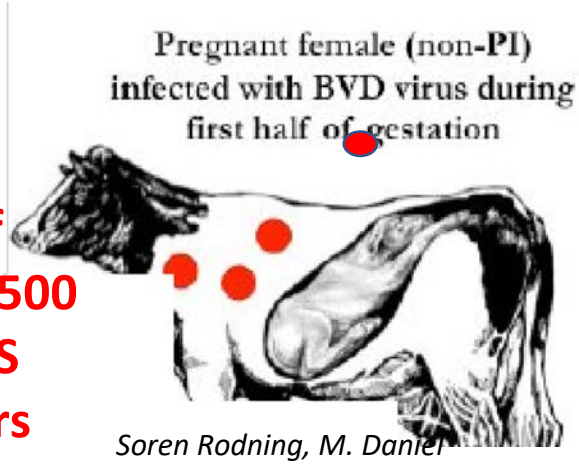
Fetal Development and Epigenetic Programming

Fetal origins of post-natal/adult disease

- Maternal Infections & pregnancy outcomes
- Heat stress
- Hypoxia
- Metabolic stress
- Nutritional stress
  - Obesity and Undernutrition
- Placental insufficiency
- Intrauterine growth restriction: IUGR

Maternal Infections & Pregnancy Outcomes

Losses because of BVDV alone are $500 M annually for US cow-calf producers



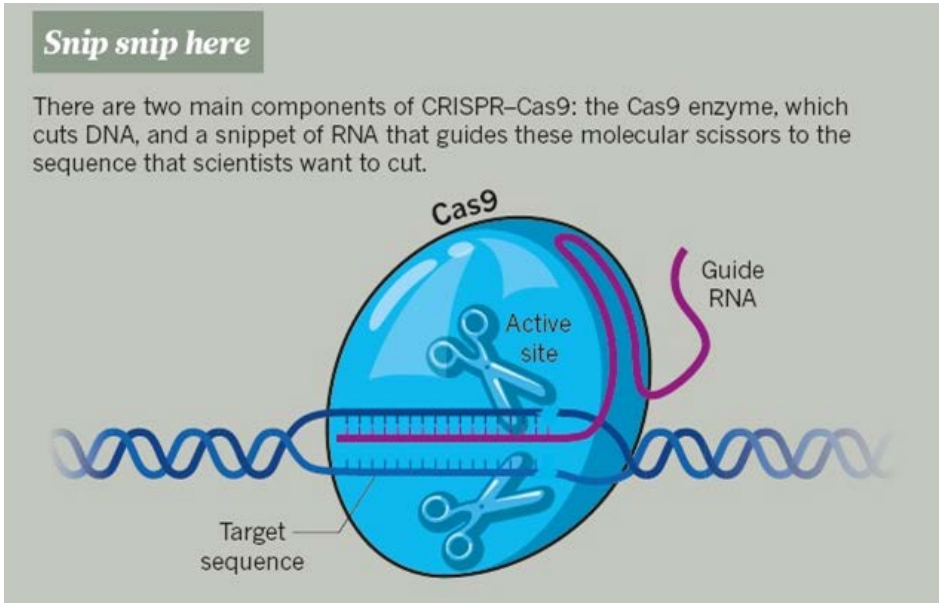
Soren Rodning, M. Daniel Givens PubID: ANR-1367

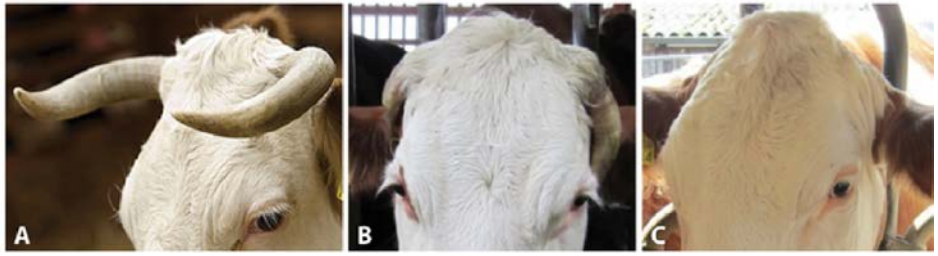
Postnatal Bovine Respiratory Disease

USDA NIFA WAAESD

AZ, CA, CO, FL, ND, NE, WY

Cloning and Gene Editing

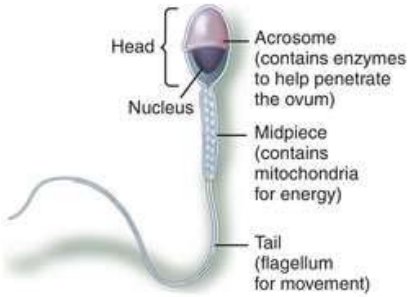




- Somatic cell cloning is inefficient (1-5%), costly and labor intensive
- Improvements using embryonic stem instead of somatic cells
- CRISPR-Cas 9
  - Cas-9 protein enzyme (scissors)
  - Guide RNA binds to Cas 9 and the specific gene target
- Gene editing
  - Insertion
  - Deletion (knocking out)
  - Replacement
  - Modification
- Insert polled gene from beef to genetically silence horned gene in dairy cows
- *"Transgene" DNA under F.D.A. Guidance for Industry187 (FDA 2009), which initiates regulatory action*

Transgenic Res (2016) 25:321–327

Contemporary Science and Fertility



Male

1. Capacitation of bovine spermatozoa in vitro
2. Improved fertility of sexed semen
3. Sperm cryopreservation/success in IVF
4. Maintenance of fertility by spermatozoa in the epididymis
5. Removing defective sperm

Female

1. Improved in vitro bovine oocyte maturation and IVF
2. ⬇ Variability and increase efficacy of bovine superovulation
3. Differentiation of ovarian primordial follicles and oocyte health
4. Diagnostics of reproductive status: P4, AMH, IFNT, miRNA
5. Optimal nutrition for pregnant and milking cow
6. Improved ovulation synchronization and AI
7. Pregnancy/placentation/fetal development/postnatal health

Improving Fertility in General

1. Genetic and production trait screening tools to select for fertility
2. Vaccines to prevent infectious disease
3. Management of large data sets: automated systems
4. Mechanisms of reprogramming: gene editing and cloning
5. Treat humanely to minimize pain with good experimental design

Contemporary Science Boosts Fertility in Cattle

➢Impact on Graduate Education

- USDA NIFA W2112 project supported research training for more than:
  - ➢ 100 undergraduate students
  - ➢ 50 MS students
  - ➢20 PhD students
- USDA NIFA NNF program recently supported six PhD students (CO)

➢ Outreach

- National and regional symposia and outreach programs

CSU/ARBL DVM/PhD students

WAAESD

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