MAMMARY GROWTH AND DEVELOPMENT

From Fetus to Lactation:

Fetal growth, estrus, and pregnancy

Mammogenesis

- Development of the mammary gland
- Begins early **fetus** and proceeds beyond initiation of lactation:
    1. Prenatal (fetus)
    2. Prepubertal
    3. Postpubertal
    4. Pregnancy
    5. Early lactation
    6. *Involution*

Fetal Mammary Development

- Only basic structures develop
- Development occurs at first half of pregnancy
- Very little further development before birth

Fetal Mammary Development

- Anlage: 1st group of cells to develop into a given organ (i.e. the primordium)
- Mammary tissue develops from the ectoderm in fetus
- Mesoderm is source of cellular development of blood and lymph vessels, connective tissue, fat pad, and smooth muscle

Embryonic

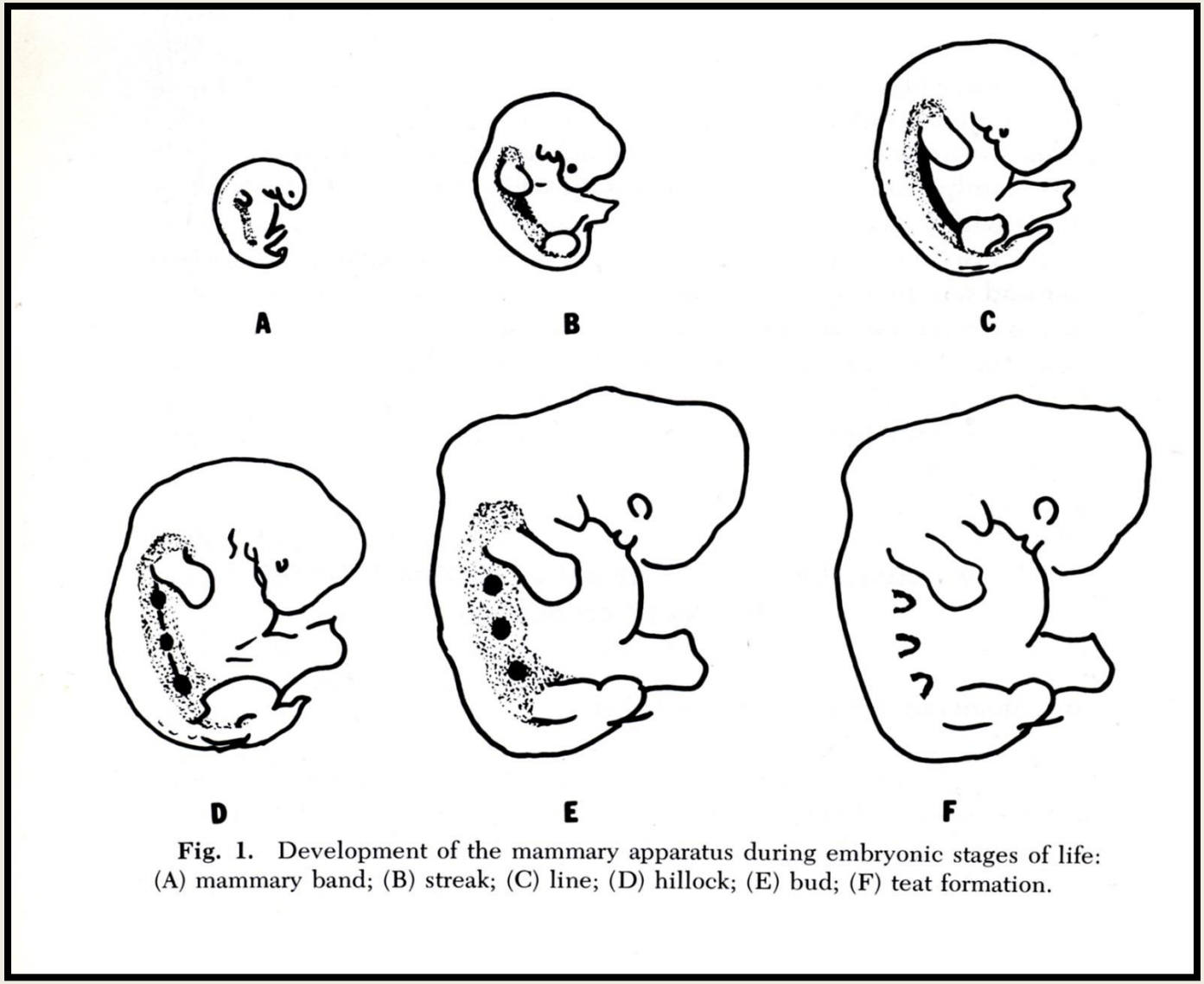


Fig. 1. Development of the mammary apparatus during embryonic stages of life: (A) mammary band; (B) streak; (C) line; (D) hillock; (E) bud; (F) teat formation.

Fetal Mammary Development

- Thickening of ectoderm on both sides of midline
- Mammary line develops by 30 days (in utero)
- Mammary buds form along mammary line (correspond to number of glands in adult)
- Mammary buds 'sink' into mesenchyme
- Teat meatus, teat and gland cisterns, and duct system form in primary sprout stage
- Primary sprout canalizes and becomes secondary sprouts, which include major ducts

Embryonic stages

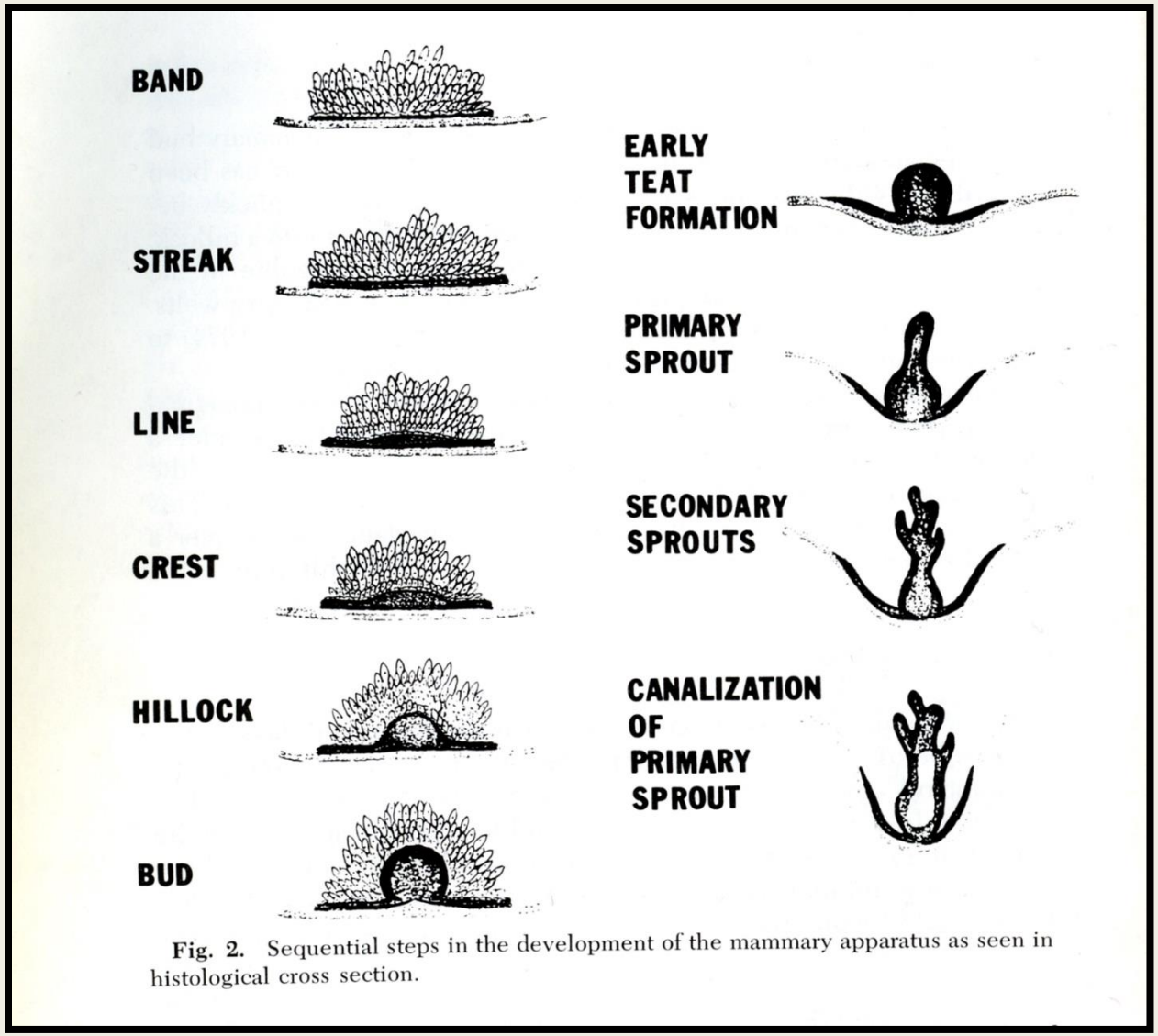


Fig. 2. Sequential steps in the development of the mammary apparatus as seen in histological cross section.

Fetal Development Summary

Developmental Stage	Role
Band, streak, line, crest, hillock	Transitional states; increased thickening
Bud	Localization of epithelium
Epidermal cone	Becomes streak canal
Primary sprout	Distal – teat sinus Proximal – gland sinus
Secondary sprout	Ductal system
Mesenchyme	Fibrous tissue, fat pad, connective tissue, blood and lymph vessels, smooth muscle

Teat Formation

- When primary sprout starts proliferating, outward and lateral pressure causes teat formation
- Epithelial ingrowth
  - Animals that crawl on ground and burrow (rat, mouse, hamster)
  - Reduce teat injury
- Proliferation
  - Most eutherian mammals
  - Horse, cow, sheep, humans, etc.
- Eversion
  - Metatherian (marsupials)
  - Resembles inverted finger of rubber glove
  - Inpocket within pouch with tiny nipple at base
  - Pocket disappears as lactation begins and teat extends

Teat Formation

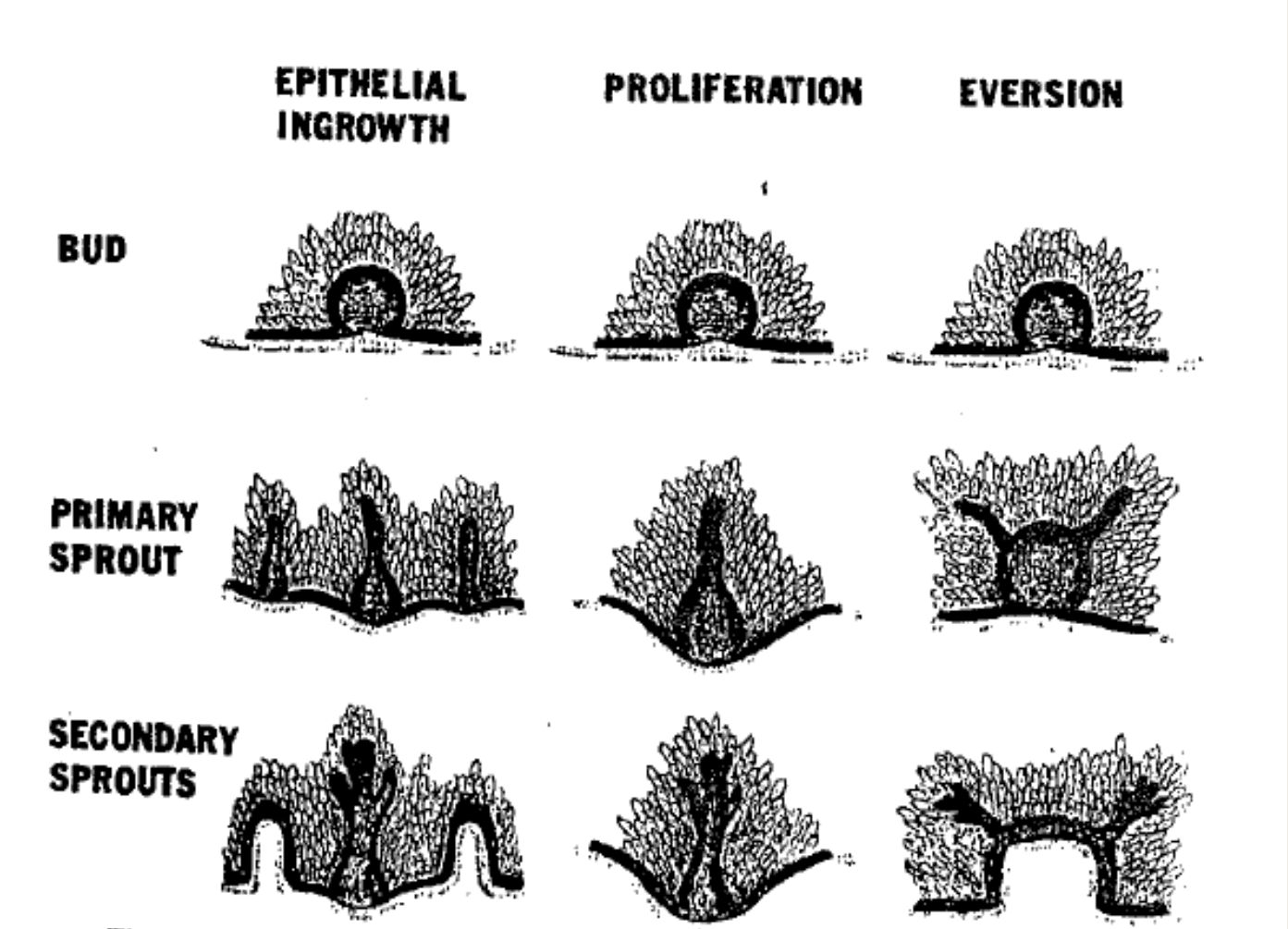


Fig. 3. Stages in development of three distinct types of teats in metatherian and eutherian mammals.

TABLE I

EMBRYONIC AND FETAL DEVELOPMENT OF MAMMARY GLANDS

Stage of mammary apparatus development	Cattle[a] Age of embryo or fetus (days)	Cattle[a] C.R. length of embryo or fetus (mm)
Mammary band	32	14
Mammary line	35	17
Mammary crest	37	19
Mammary hillock	40	21
Mammary bud	43	25
Teat formation	65	80
Primary sprout	80	120
Secondary sprout	90	160
Canalization of sprout	100	190
Gland cistern	110	230
Teat cistern	130	300
Gestation length	280	—

TABLE I *(Continued)*

Stage of mammary apparatus development	Rat[d] Age of embryo or fetus (days)	Rat[d] C.R. length of embryo or fetus (mm)
Mammary band	11	6–10
Mammary line	11–13	6–14
Mammary crest	12–14	12–17
Mammary hillock	13–15	17–18
Mammary bud	14–15	18–19
Teat formation	15–18	19–30
Primary sprout	14–18	18–32
Secondary sprout	19	40
Canalization of sprout	15–16	19–23
Gland cistern	—	—
Teat cistern	—	—
Gestation length	22	

Fetal Mammary Development

- 33 day-old cow embryo
- Embryo just formed mammary band

Fetal Mammary Development

- Castrating male fetus will result in mammary development
- Injecting a 14 day pregnant rat with testosterone will prevent mammary formation in fetuses
- No teat development in male fetuses of horse, mouse, rat, beaver. Why?

Mammary Gland at Birth

- Teats well developed
- Secondary sprouts canalized
  - Solid cell core at the end (will continue to grow and branch)
- Sprout growth limited to area around gland cistern
- Non-secretary tissue well formed
  - Connective tissue, blood vessels, lymph vessels
- Male gland similar, but not fully developed
- Secretory and glandular parts are not developed yet

Birth to Puberty

- Udder increases in both weight and capacity
  - Increase in connective tissue and fat deposition
- Fat pad deposition
  - Front and rear quarters approach each other
- Ducts continue to grow and shape into what will become a mature udder

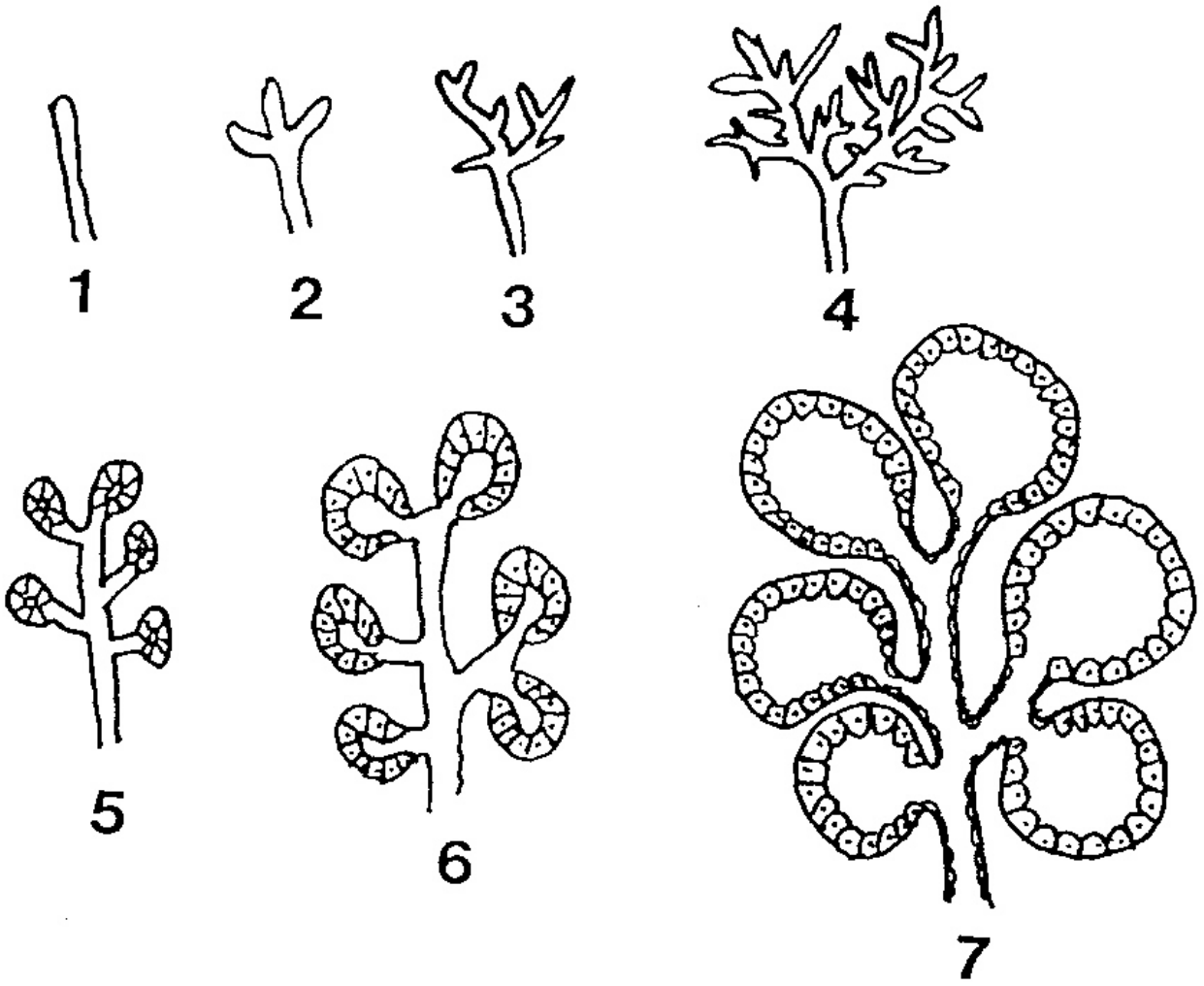
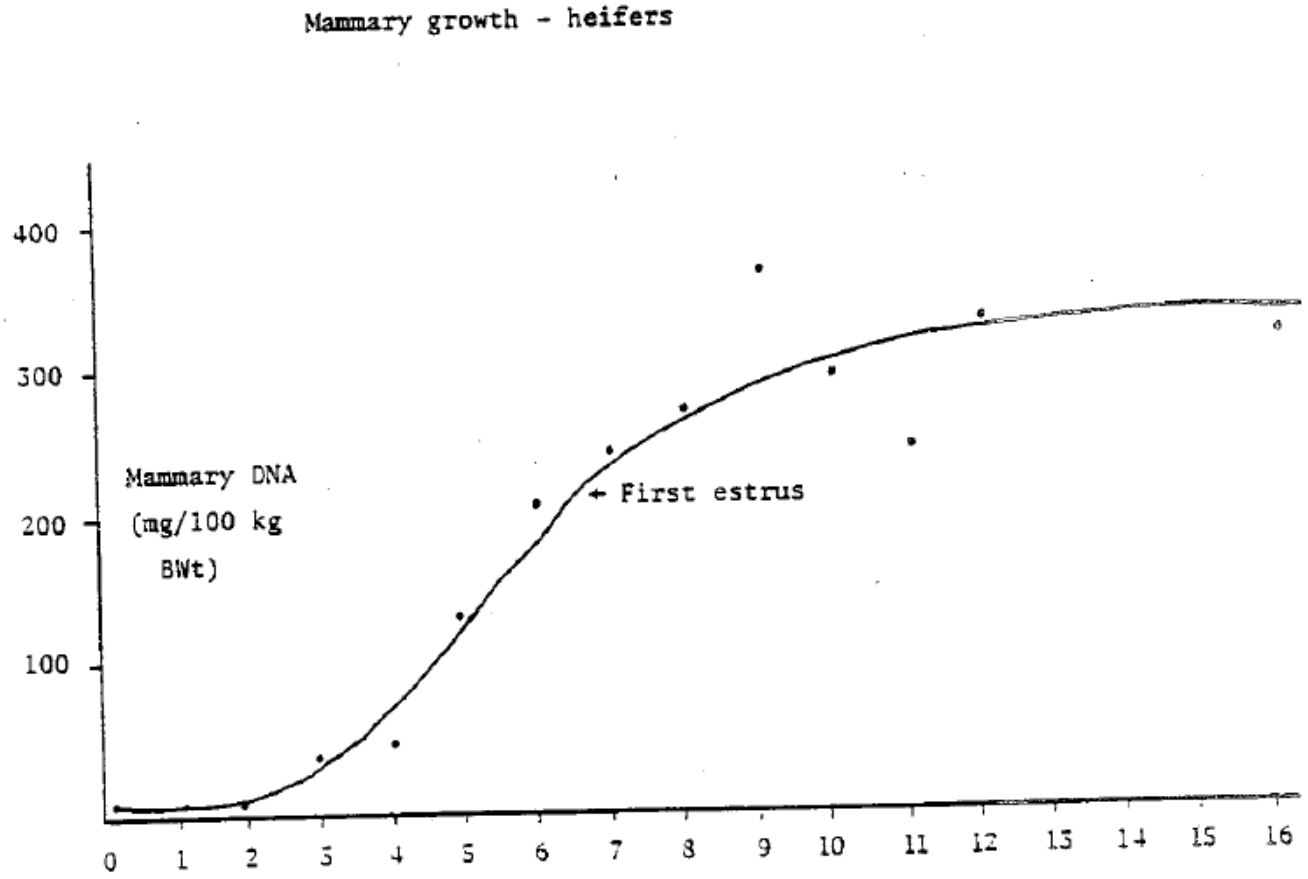


Fig. 1.11. Mammary gland growth is characterized by duct growth from a single duct (*1*), to branching (*2*), to more complex branching (*3*), to compound branching (*4*). End buds form on ends of ducts (*5*) and continue to enlarge in response to hormonal stimuli (stages *6* and *7*).

Birth to Puberty

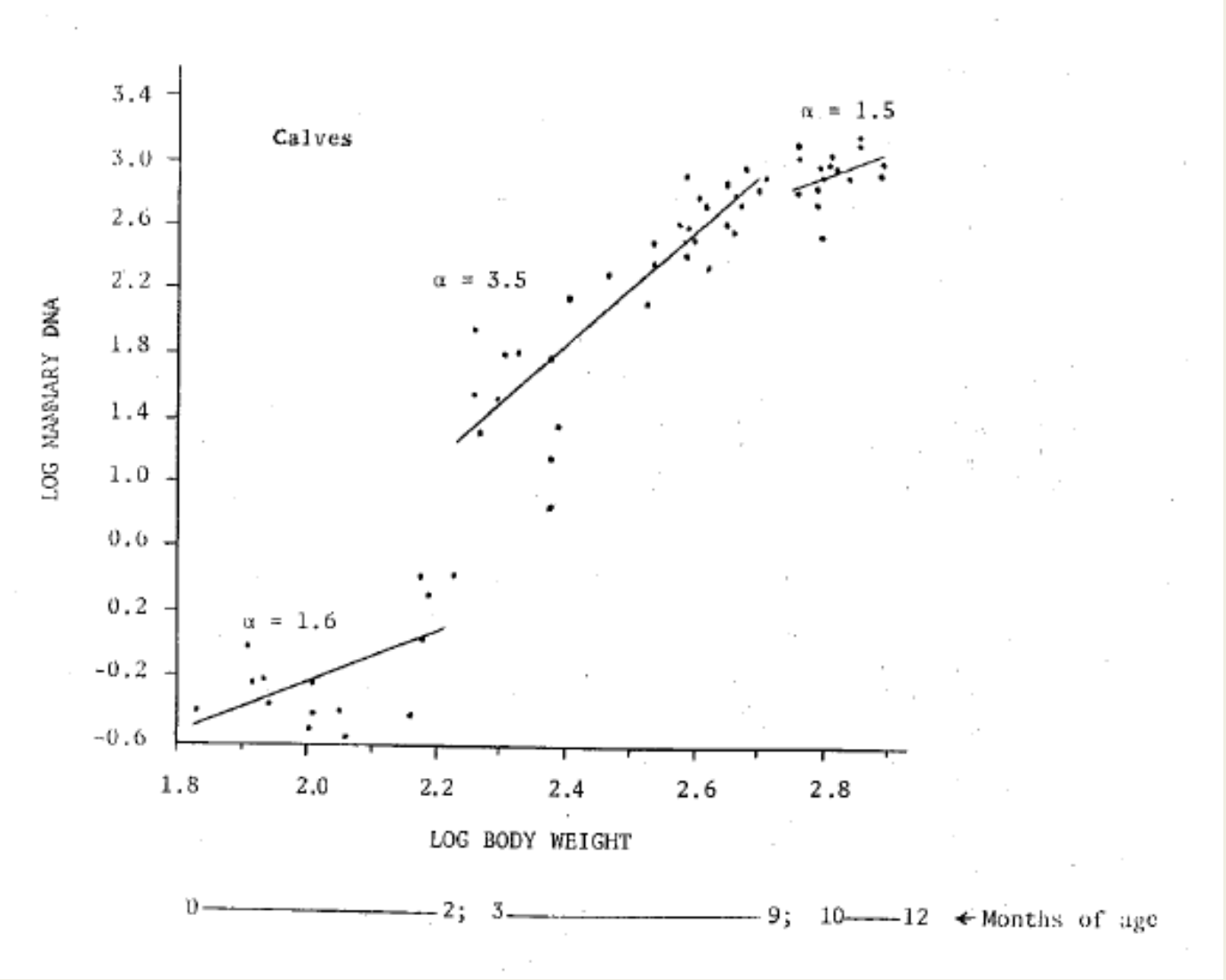
- DNA increases
  - Increased mammary cell numbers
- Birth to three months: isometric growth
  - DNA content parallels growth of other tissues
- Three months to puberty: allometric growth
  - Increase in DNA content greater than in other tissues

Birth to Puberty



Taken from Sinha and Tucker (J. Dairy Sci., 1969).

Birth to Puberty



Recurring Estrous Cycles

- After puberty, each recurring estrous cycle furthers mammary gland development
- Hormones
  - Estrogen influences duct growth
  - Progesterone influences secretary tissue development
- Terminal end buds (at end of ducts) develop into alveoli

Pregnancy

- Marked increase in mammary gland growth
  - In cattle, exponential growth throughout gestation
- Most of the duct growth occurs during 1st part of pregnancy
- Lobuloalveolar system forms during mid- to late-pregnancy
- Large growth occurs during pregnancy but regresses after peak lactation
- Cycle repeats itself with each pregnancy and lactation

Pregnancy

- Gland cistern increases in 5^{th} and 6^{th} months
- 4^{th} to 7^{th} months
  - Glandular proliferation increase near large ducts entering the gland cistern
- Further branching of small ducts
- Formation of end buds
- Secretary tissue replaces adipose tissue and forms small lobules
- Alveoli differentiate at the end of terminal ducts (smallest ducts)

Pregnancy

- 6^{th} to 9^{th} months
  - Marked increase in growth of duct secretary tissue, vascular system, and lymphatic system
- 9th month
  - Alveoli initiate some secretary activity
- Epithelial cells become distended
- Fat droplets are present in lumen of alveoli

Mammary Growth During Lactation

- Some additional growth occurs after parturition, except in sheep
- 65% increase in mammary DNA between 10 days prepartum and 10 days postpartum
- Mammary DNA maximized at peak lactation (~45 days)
- Cells per alveolus double at time of parturition
- After peak
  - Very little cellular proliferation
  - Cells destroyed and lost through milk
    - Not replaced by mitosis through declining stages of lactation

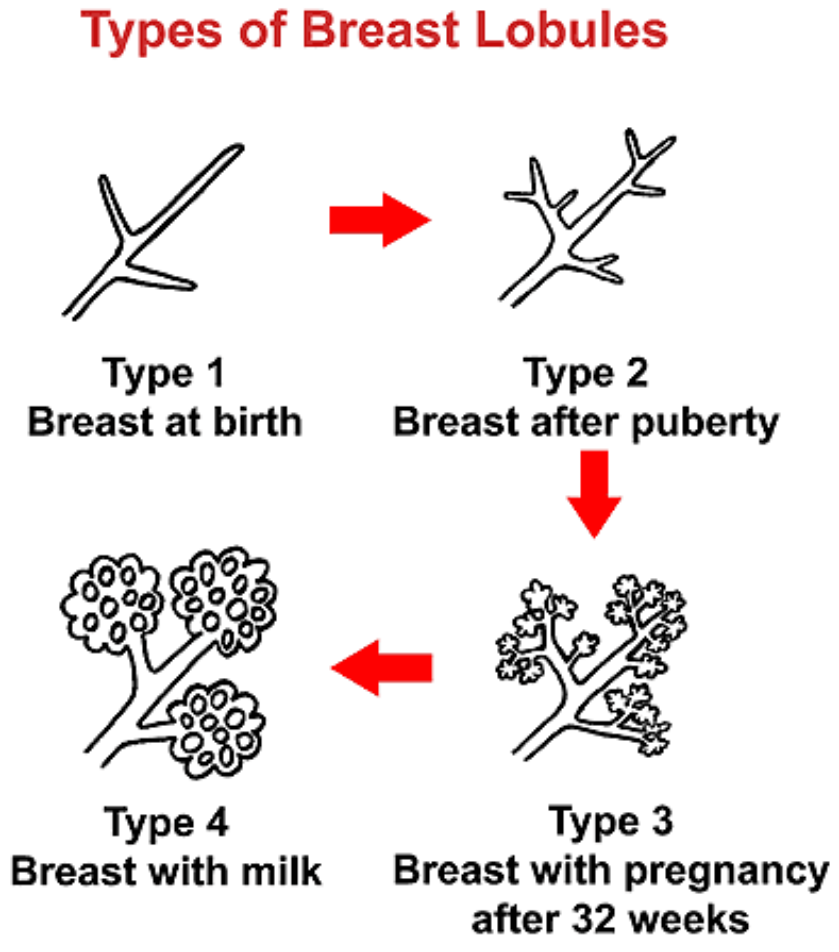
Species Differences

Percentage of mammary growth occurring at different phases of the life cycle

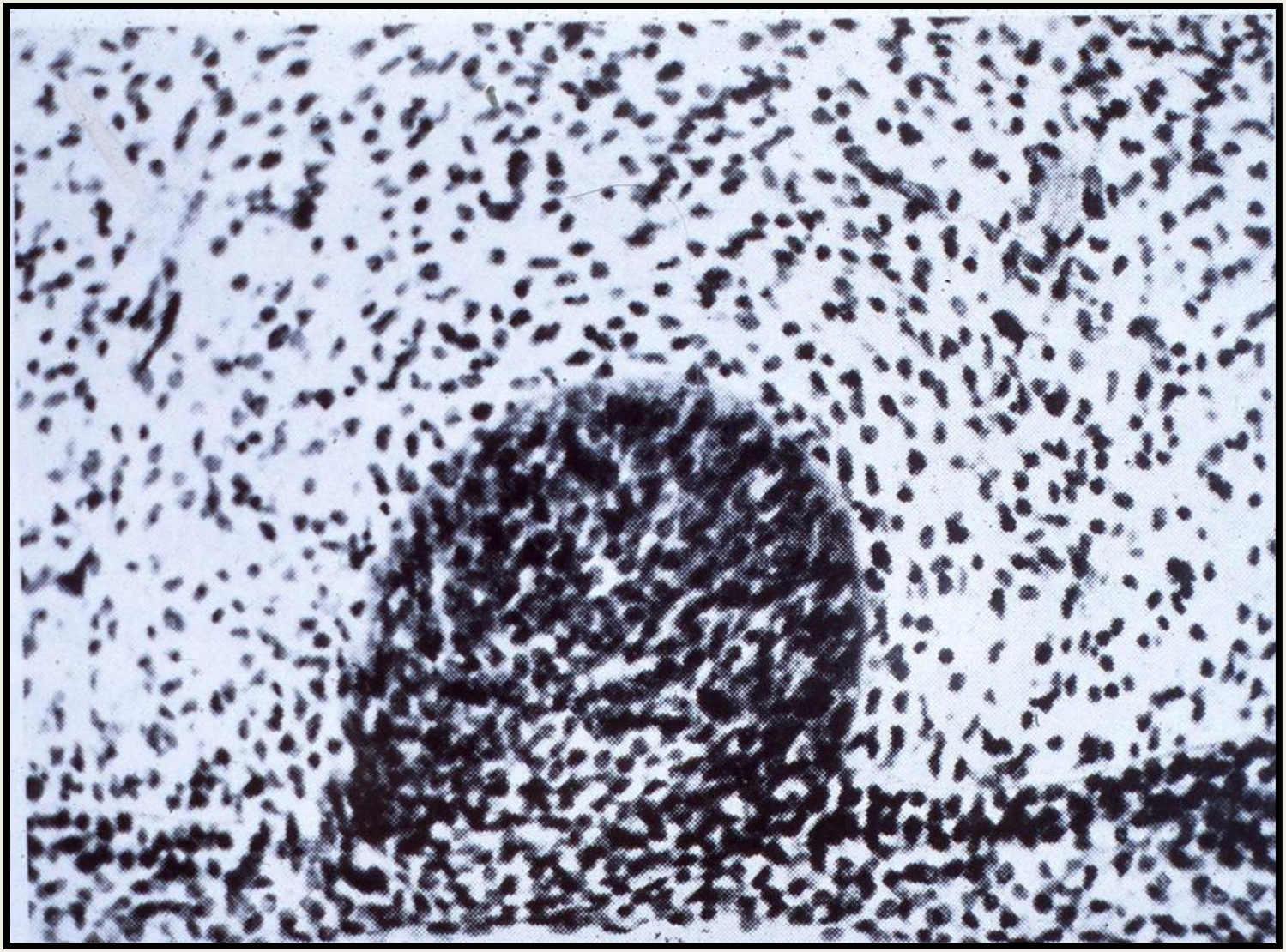
Species	% Mammary growth Birth to first Conception	During first Pregnancy	During first Lactation
Rat	10	50	40
Hamster	20	75	5
Rabbit	20	50	30
Sheep	20	78	2
Marsupial	5	5	90

Similar Developmental Process in Other Species

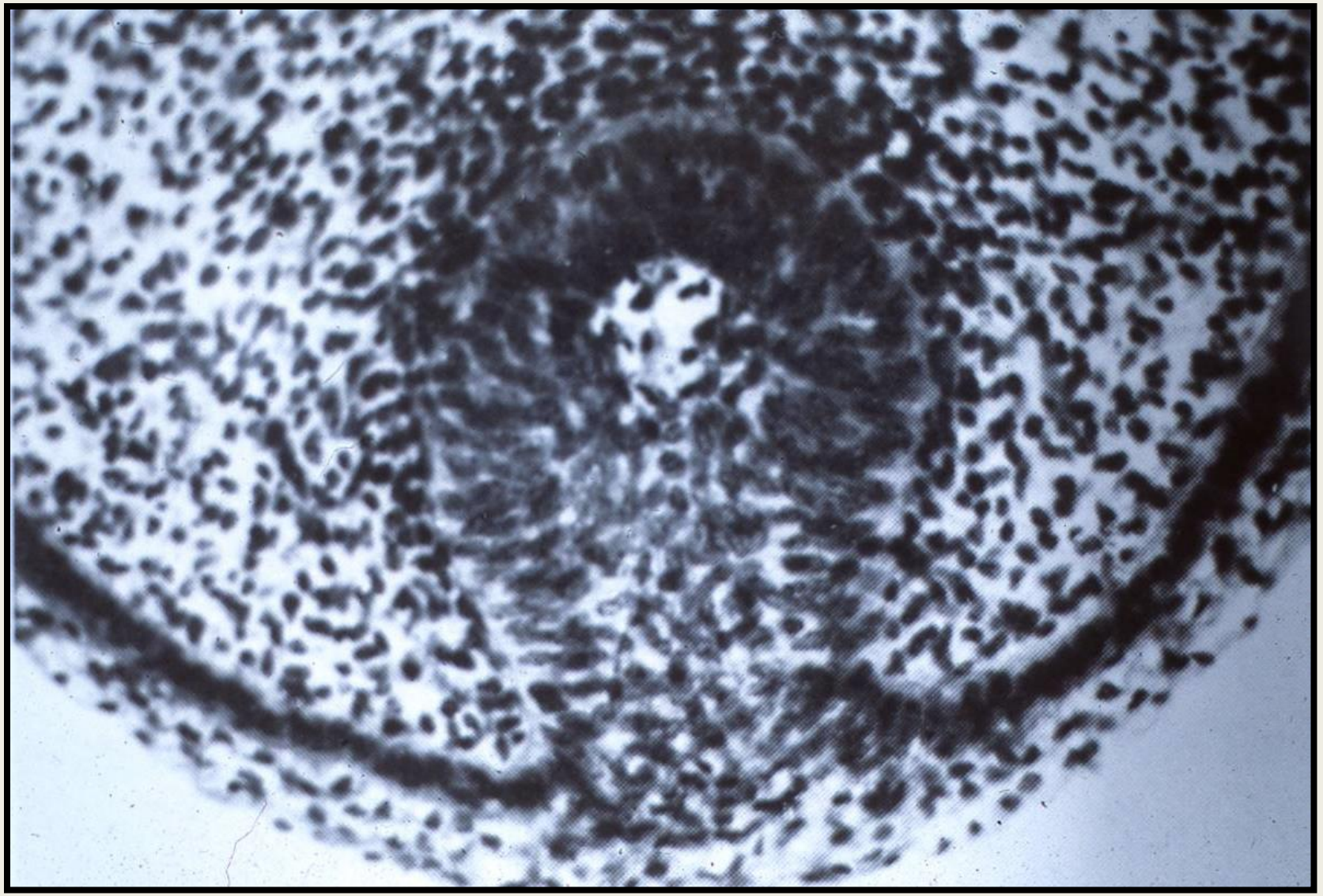
- Humans:



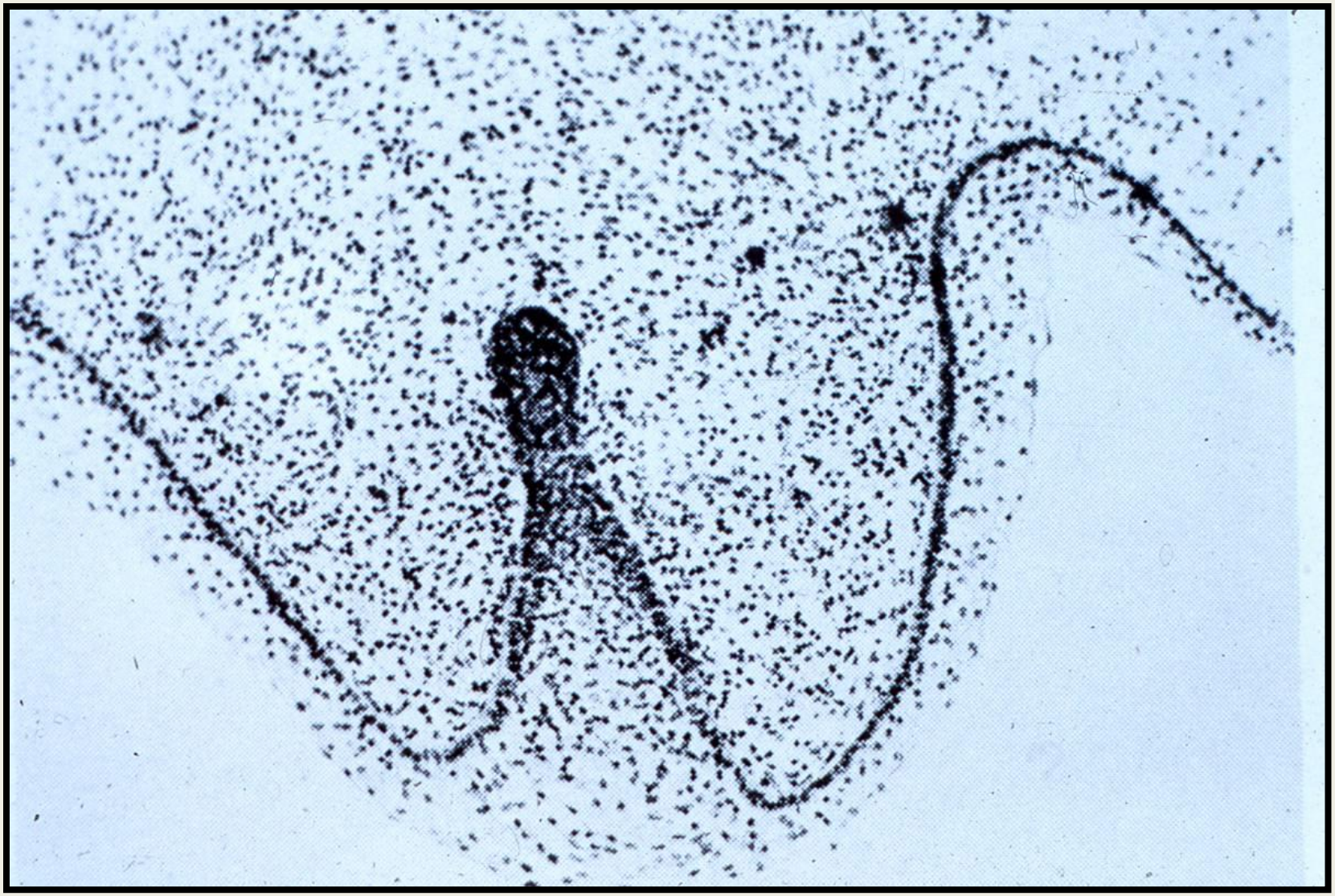
Bud



Bud



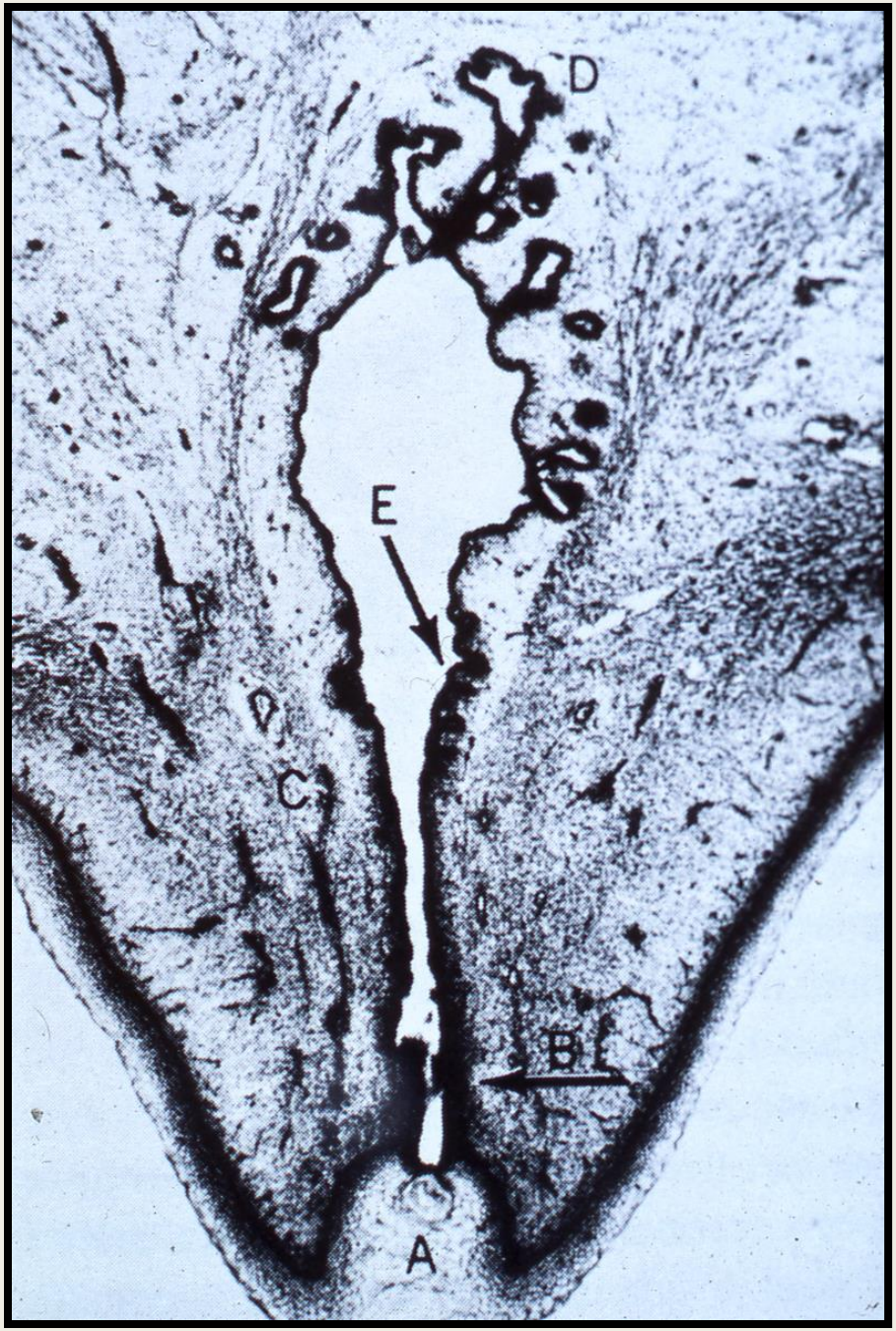
Primary sprout



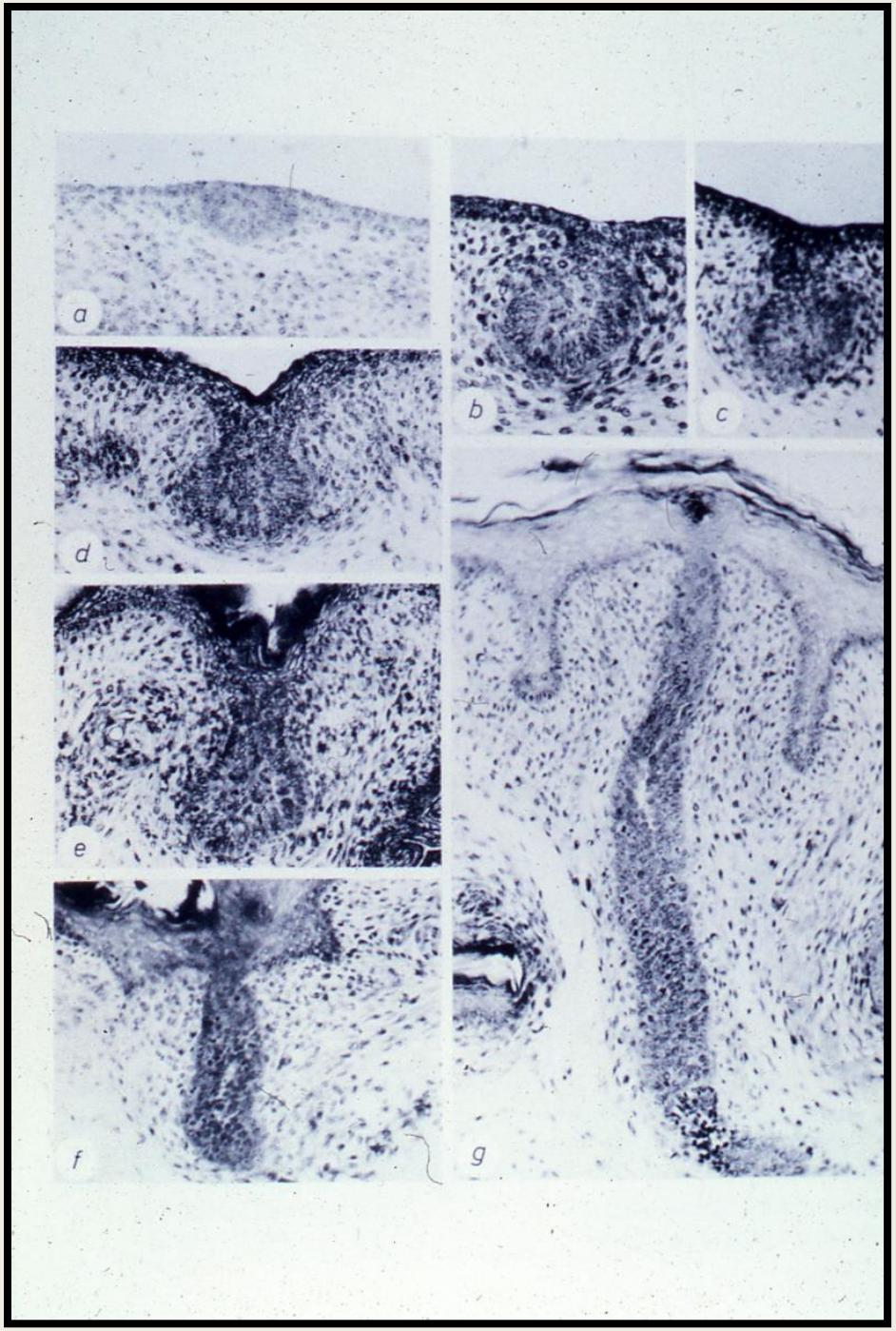
Primary sprout

Epidermal cone

Canalization



Fetal stages



Development during estrous cycle

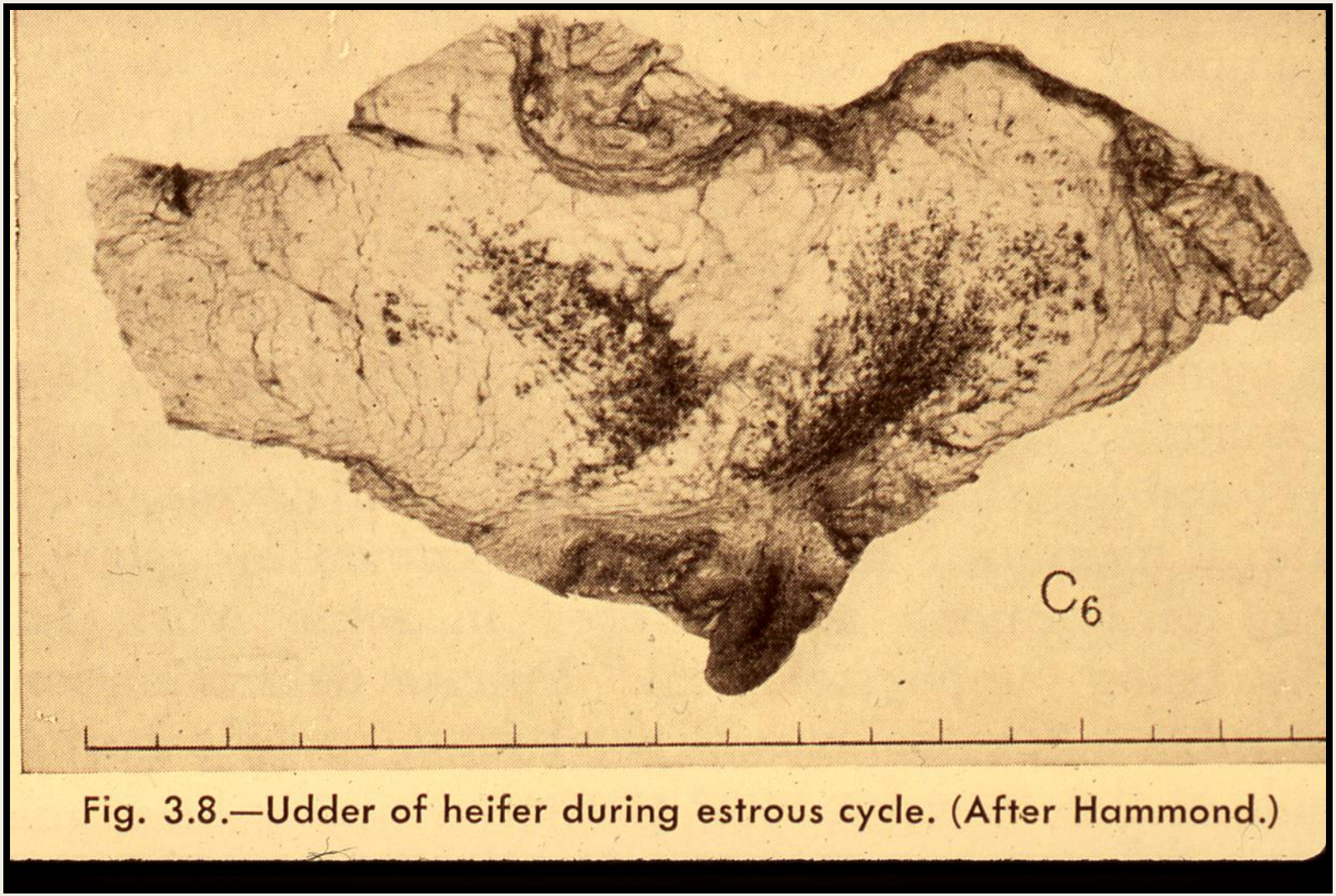


Fig. 3.8.—Udder of heifer during estrous cycle. (After Hammond.)

Development during pregnancy

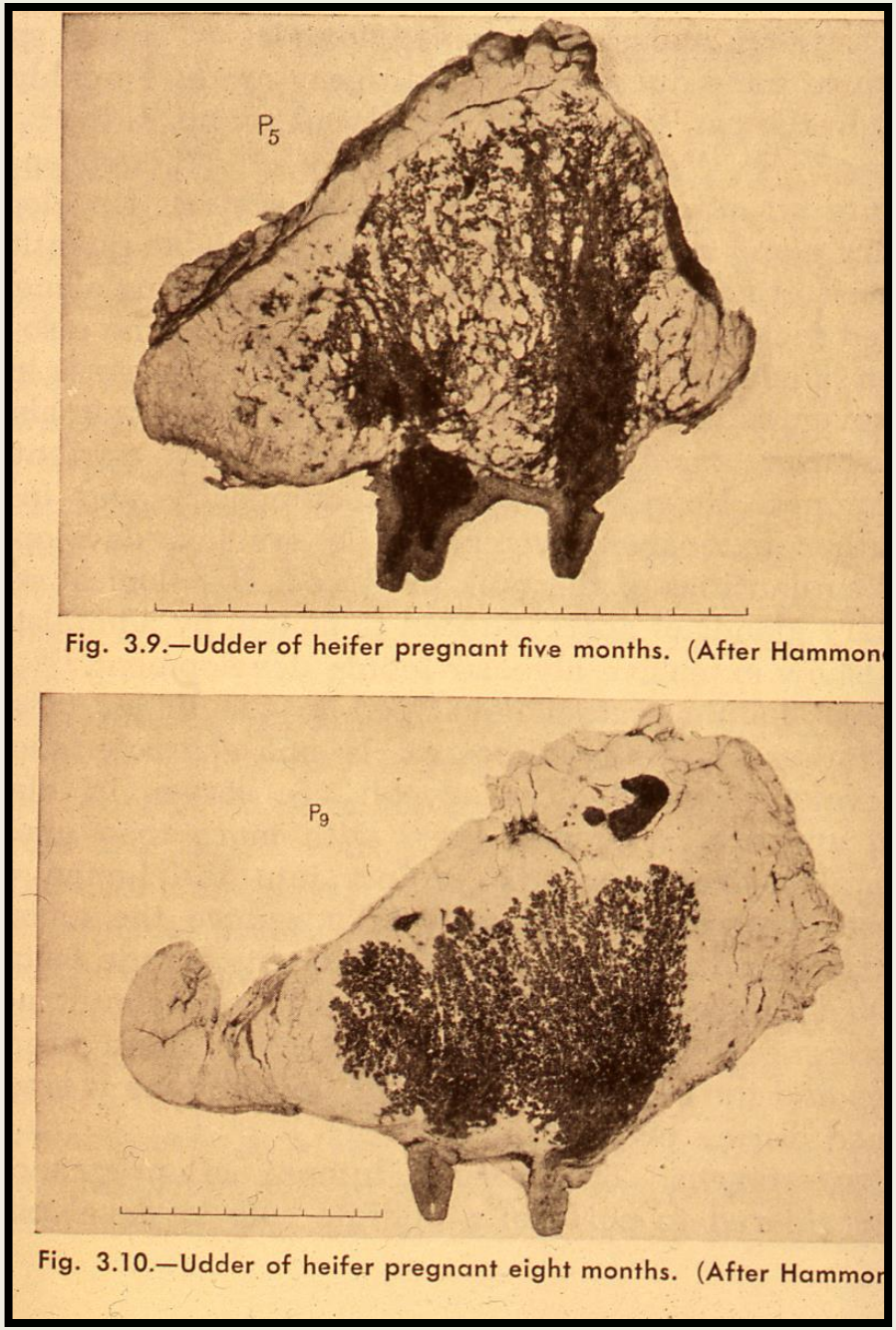


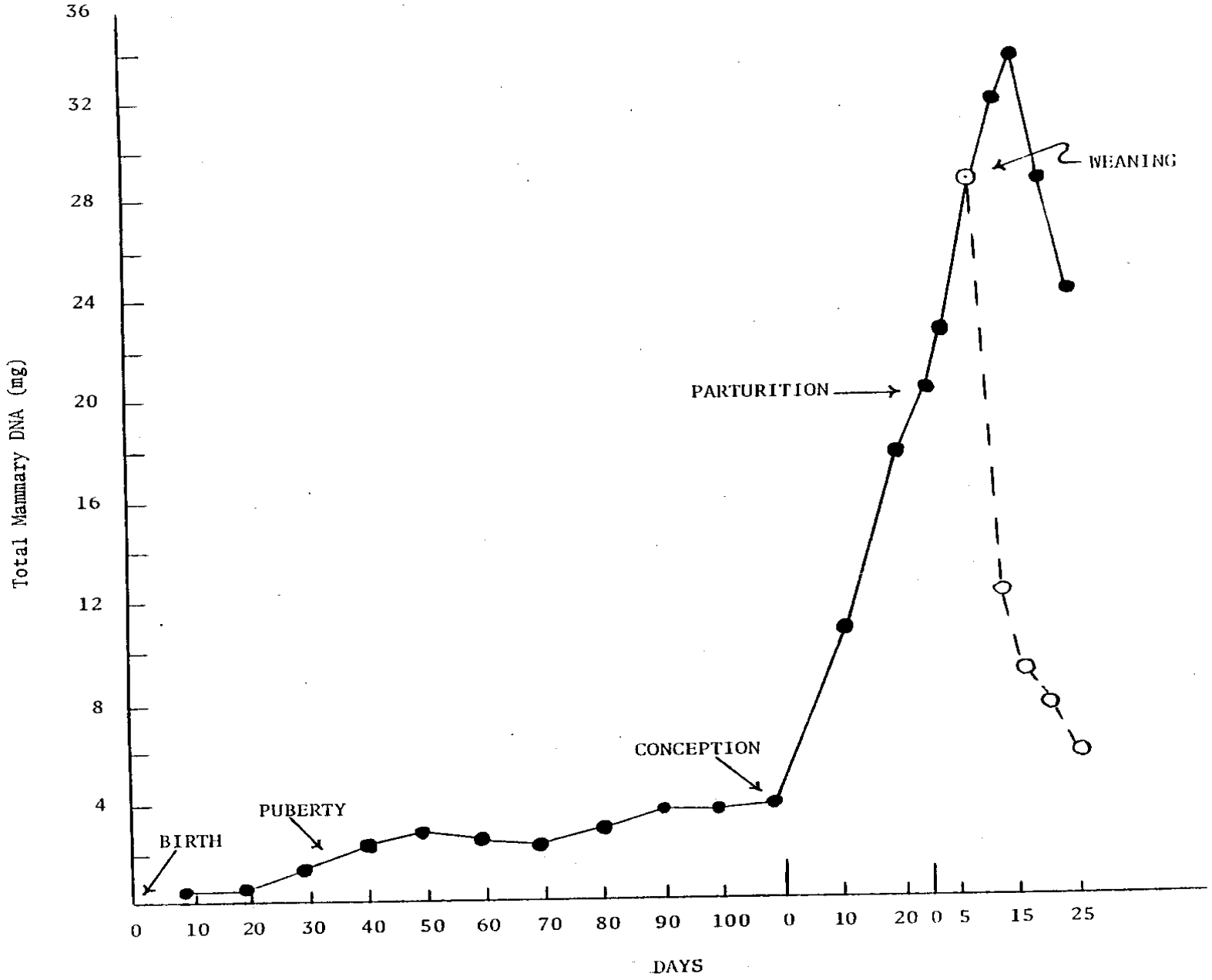
Fig. 3.9.—Udder of heifer pregnant five months. (After Hammon

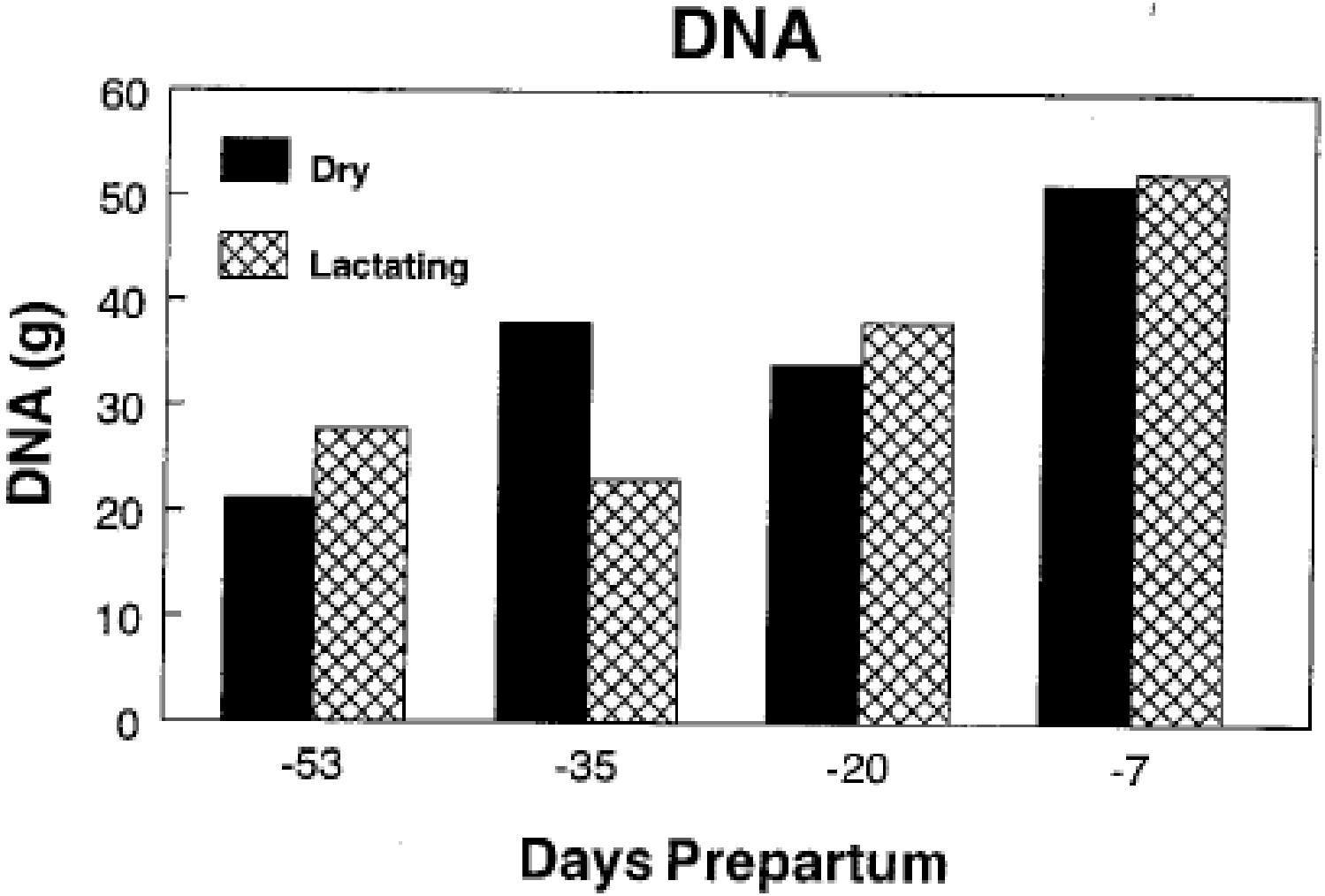
Fig. 3.10.—Udder of heifer pregnant eight months. (After Hammon

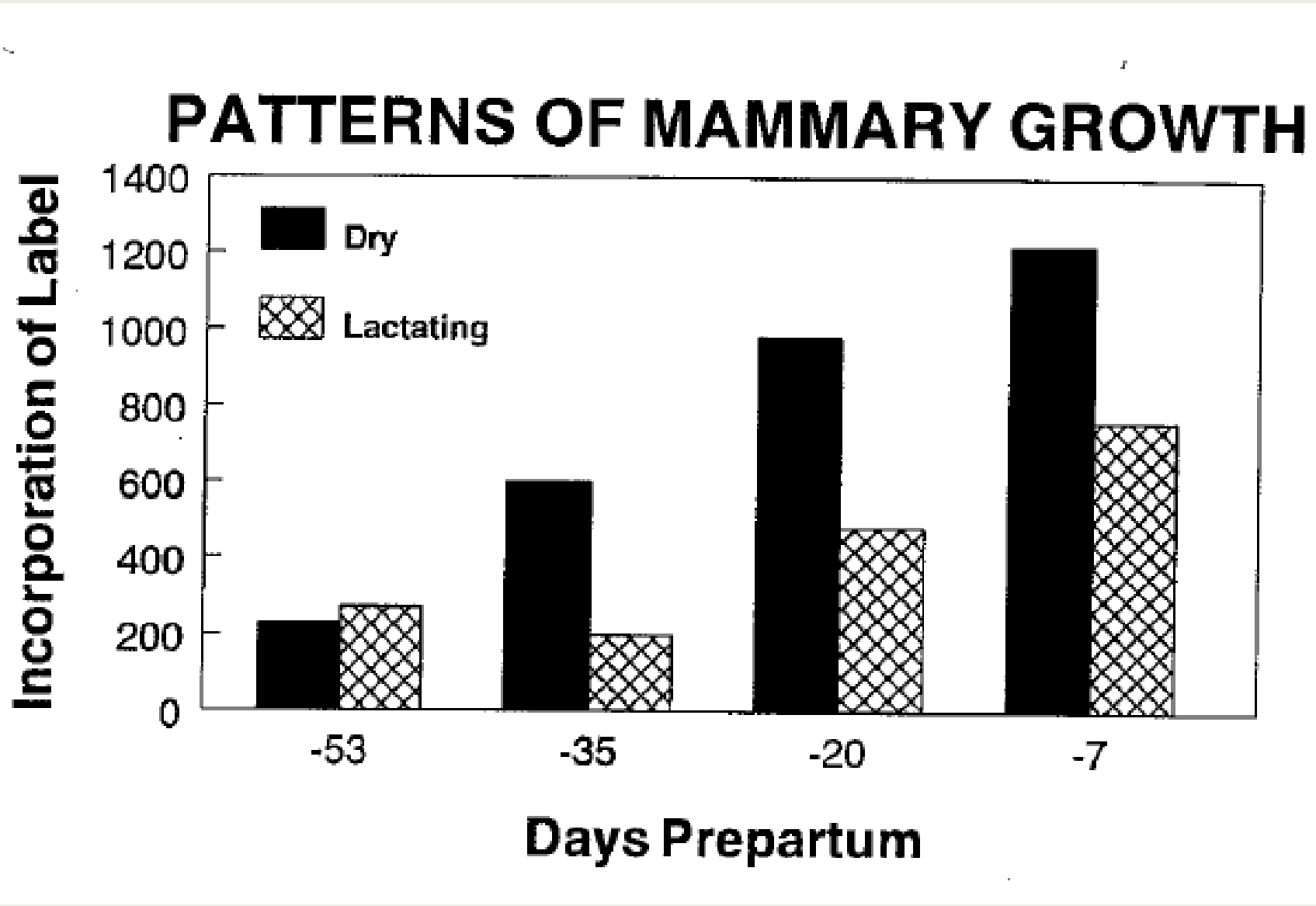
12 Month Old Heifer

6 Month Pregnant Heifer

Primigravid Heifer


Total Mammary DNA (mg)
36
32
28
24
20
16
12
8
4
BIRTH
PUBERTY
CONCEPTION
PARTURITION
WEANING
0
10
20
30
40
50
60
70
80
90
100
0
10
20
0
5
15
25
DAYS

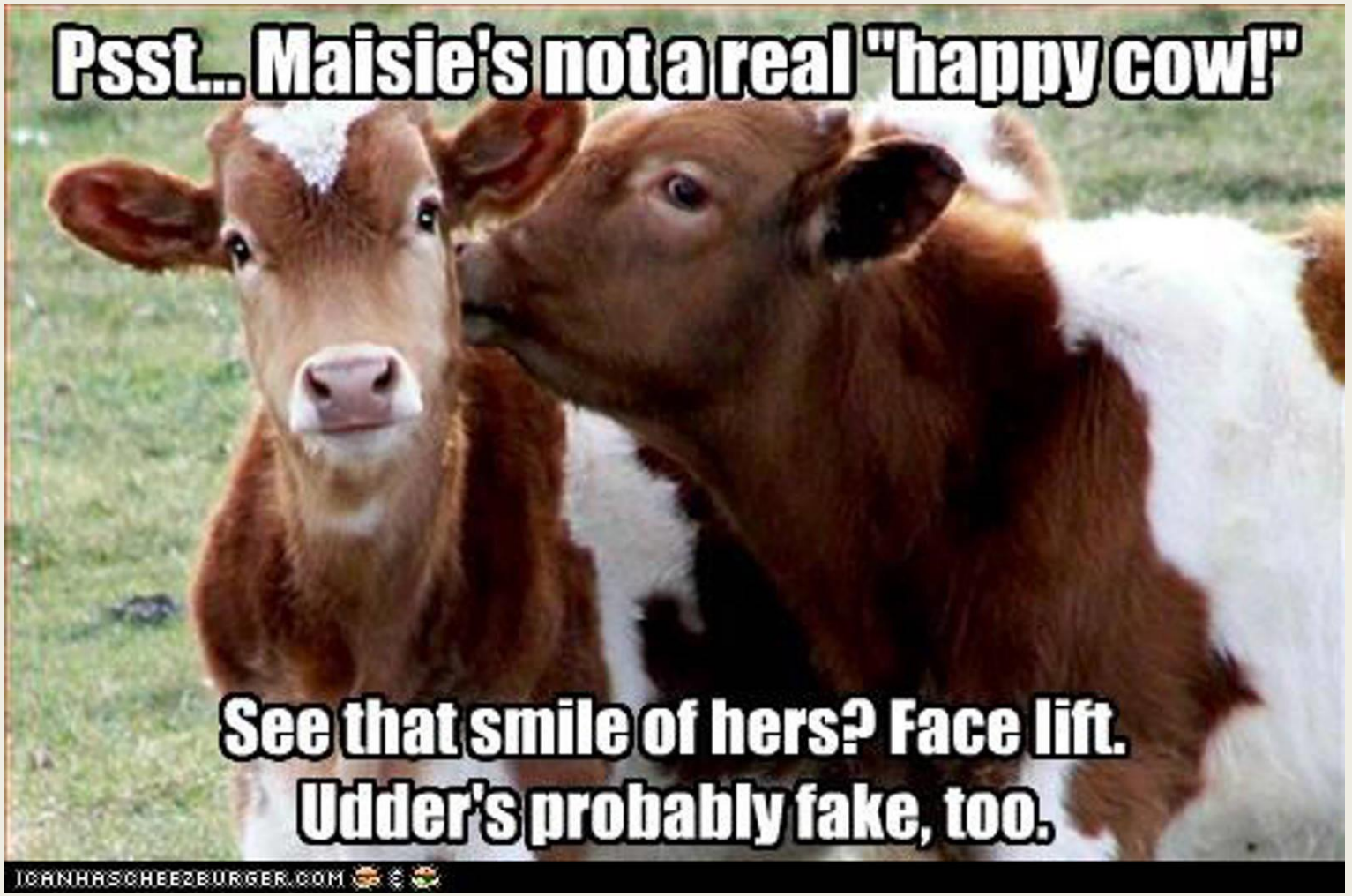

DNA
60
50
40
30
20
10
0
DNA (g)
Dry
Lactating
-53
-35
-20
-7
Days Prepartum


PATTERNS OF MAMMARY GROWTH
Incorporation of Label
1400
1200
1000
800
600
400
200
0
Dry
Lactating
-53
-35
-20
-7
Days Prepartum

Lactogenesis

- Initiation of lactation
- Process of functional differentiation that mammary tissue undergoes when changing from a non-lactating to a lactating state
- Normally associated with end of pregnancy and time of parturition

Questions?


Psst... Maisie's not a real "happy cow!"
See that smile of hers? Face lift.
Udder's probably fake, too.
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