

了解早期断奶仔猪的生理应激

Understanding the Biological Stress of Early Weaned Piglets

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主要内容

Presentation Outline

- 断奶期间的应激源 Stressors during weaning
- 断奶与采食量 Feed intake and weaning
- 断奶与肠道结构和功能的变化 Structure and Functional changes of intestine and weaning
- 断奶相关的炎症反应 Inflammation associated with weaning
- 总结/结论 Summary/Conclusions

断奶应激源

Weaning Stressors

- 断奶是猪一生中最大的应激期之一 Weaning is one of the most stressful periods in a pig's life
- 猪舍、营养、健康和管理是减少断奶应激采用的方法 Housing, nutrition, health, and management are technologies used to reduce effects of weaning
- 在断奶时仔猪面临极大的生理、环境和社会的挑战 Pigs experience significant physiological, environmental, and social challenges around weaning
- 应激源导致猪后期发生疾病，生长性能、采食量、发病率和死亡率等生产损失 Stressors result in predisposition to subsequent disease and other production losses in growth, intake, morbidity and mortality

断奶

Weaning

离开母猪和同窝仔猪
Removal from sow and littermates

打架和确定群中地位

Fighting and establishment
of social hierarchy

环境改变

Change in
environment

病原体接触增加

Increased exposure
to pathogens

运输应激

Transportation
stress

突然的日粮转变

Abrupt transition in diet



断奶阶段

The Weaning Phase

- 断奶阶段的特点 The weaning period is characterized by:

- 不同窝仔猪的混群
Co-mingling pigs from different litters
- 过渡到干饲料
Transition to dry feed
- 采食量降低
Reduced feed intake
- 失重
Loss of body weight
- 严重的腹泻
Severe diarrhea
- 死亡
Mortality



断奶是一个应激事件

Weaning is a Stressful Event

- 降低采食量和生长 Reduced feed intake and growth
- 增加腹泻 Increased scours
- 断奶引发炎症 Weaning induces inflammation
- 断奶引发肠道受损 Weaning induces intestinal breakdown
- 早期炎症影响猪后期生长性
Early inflammation impact's subsequent pig performance



断奶与采食量

Feed intake and weaning

- 断奶后，仔猪必须适应饲料的改变
When weaned, the piglet must adapt to abrupt changes in diet
- 断奶初期采食量常常减少 Often feed intake is reduced initially after weaning
- 仔猪营养不良和生长速度降低
The pig becomes malnourished and suffers from reduced growth

断奶与代谢能的摄入量

Metabolizable Energy intake and weaning

- 断奶后第一周代谢能摄入量减少到断奶前的60-70% Metabolizable energy is reduced by 60-70% of pre-weaning intake by the end for the 1st wk
- 大约断奶后2周代谢能摄入量恢复 Approximately 2 wks post-weaning to recover ME intake levels

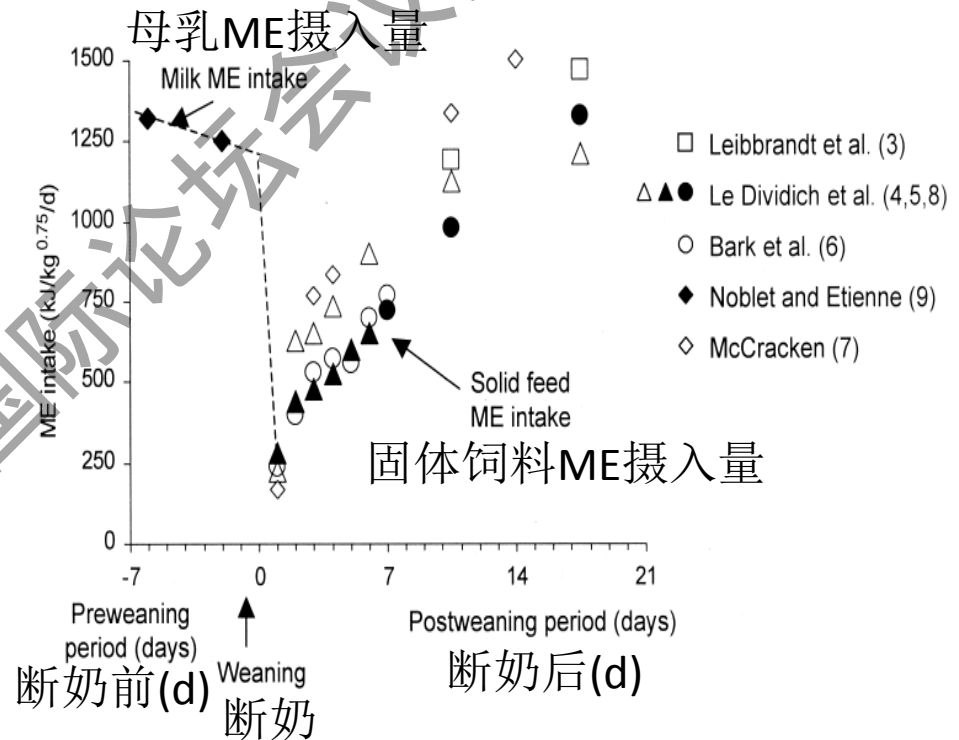


图1. 3和4周龄断奶对仔猪代谢能摄入量的影响

Fig 1. Effect of weaning between 3 and 4 weeks of age on voluntary metabolizable energy intake in piglets. (adapted from Le Dividich and Seve DAE 19:63)

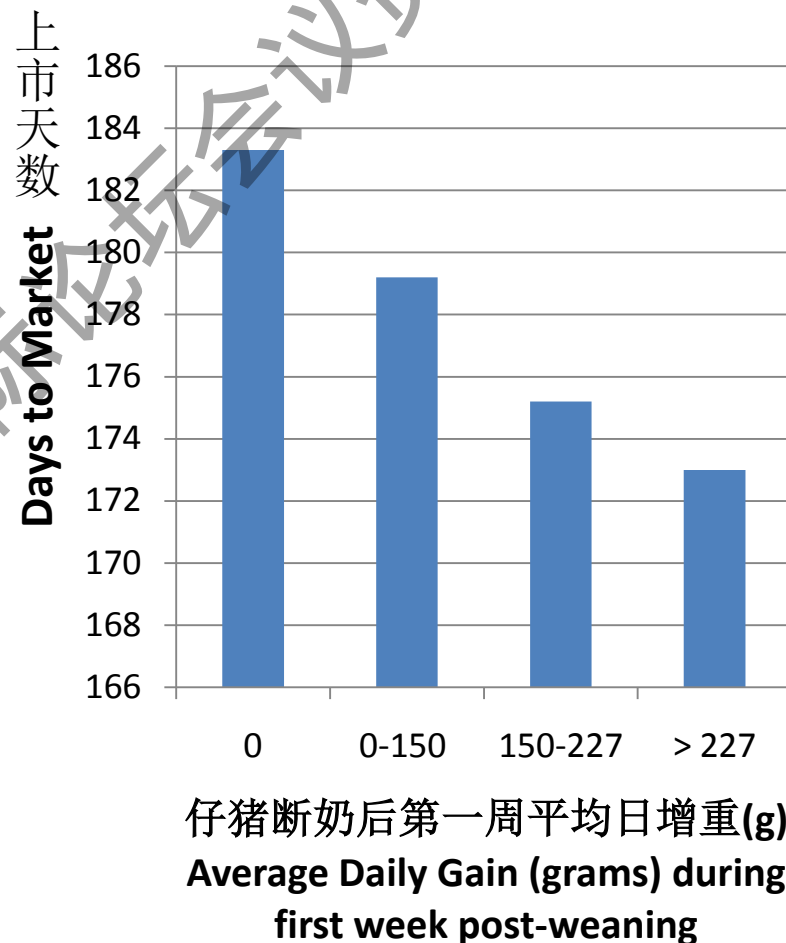
断奶后第一周增重对生产性能的影响

Weight gain in first week impacts performance

- 断奶后第一天仔猪损失100-250 g体重 Pigs lose about 100-250 g BW the first day after weaning.

- 断奶后第一周增重影响仔猪后期上市天数 Weight gain the first week impacts subsequent days to market (Tokach et al.,1992)

- 养猪者可利用饲料原料或添加剂来增加采食量 Producers can utilize feed ingredients or additives to increase feed intake



断奶与肠道结构和功能的变化

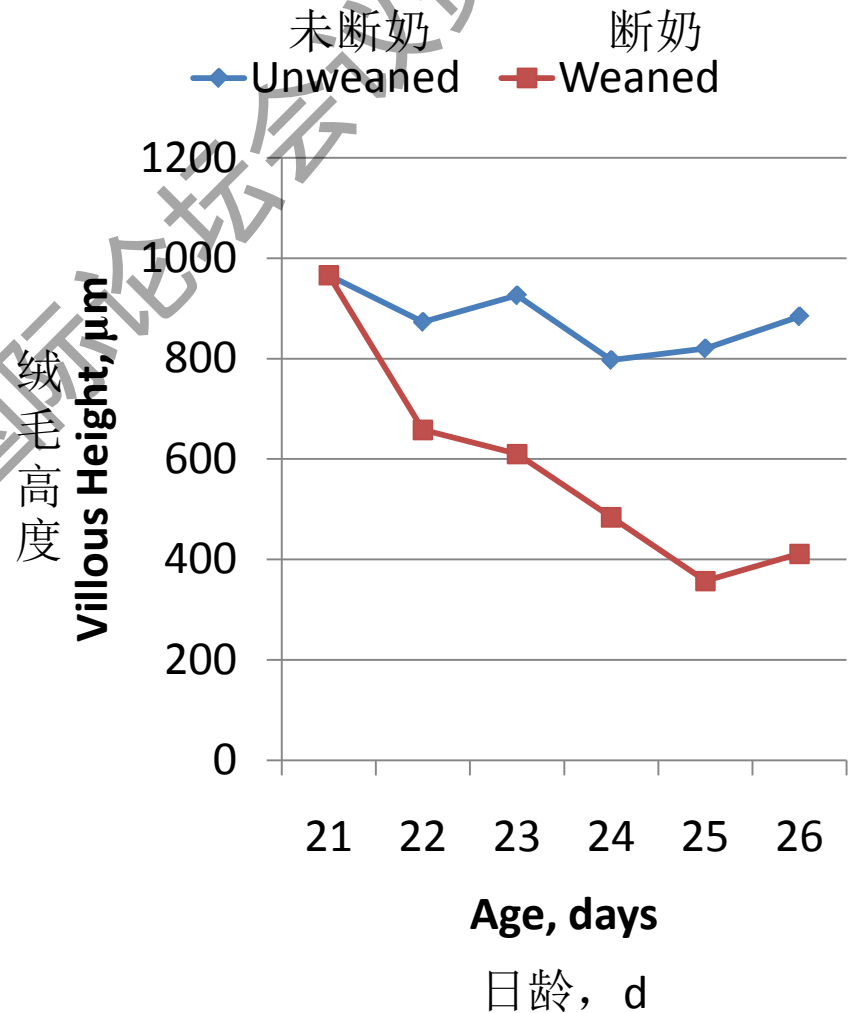
Structure and Functional changes of intestine and weaning

- 肠道吸收营养物质帮助猪生长 The intestine aids in the absorption of nutrients to help pigs grow
- 断奶后肠道发生结构和功能等生理学变化
Physiological changes in structure and function of the intestine occur during weaning
 - 酶活、吸收和分泌 Enzyme activities, absorption, and secretion
- 吸收能力受到影响，就会影响饲料转化率
Absorptive capacity is affected and can influence feed efficiency (Pluske et al., 1997)

断奶与肠绒毛结构变化

Structure Changes at Weaning

- 在21日龄断奶后的前24小时绒毛高度快速减少约25-35%
- Villous height rapidly decreases about 25-35% within the first 24 hours of weaning at 21 d of age.



断奶与消化酶的变化

Digestive Enzyme changes at Weaning

- 消化和胰脏分泌的变化影响肠道消化、吸收和分泌能力，最后影响屏障功能
- Changes in digestive and pancreatic secretions can impact the intestine's digestive, absorptive and secretive capacity and finally barrier function

消化酶活性 Digestive Enzyme specific activities	断奶后天数 Time post-weaning		
天数 Days	2	8	15
乳糖酶 Lactose	-19	-71	-80
麦芽糖酶 Maltase	-12	+2	+2
氨基肽酶 Amino-peptidase N	-49	-39	-39
胰脏Pancreas			
胰蛋白酶活性 Trypsin activity	+27	-6	+65
淀粉酶活性 Amylase activity	-8	-7	+23
脂肪酶活性 Lipase activity	+35	-59	-61

与断奶有关的炎症反应

Inflammation associated with weaning

- 当肠道屏障被破坏，其结果是引起炎症

When the intestinal barrier is compromised, it can result in inflammation

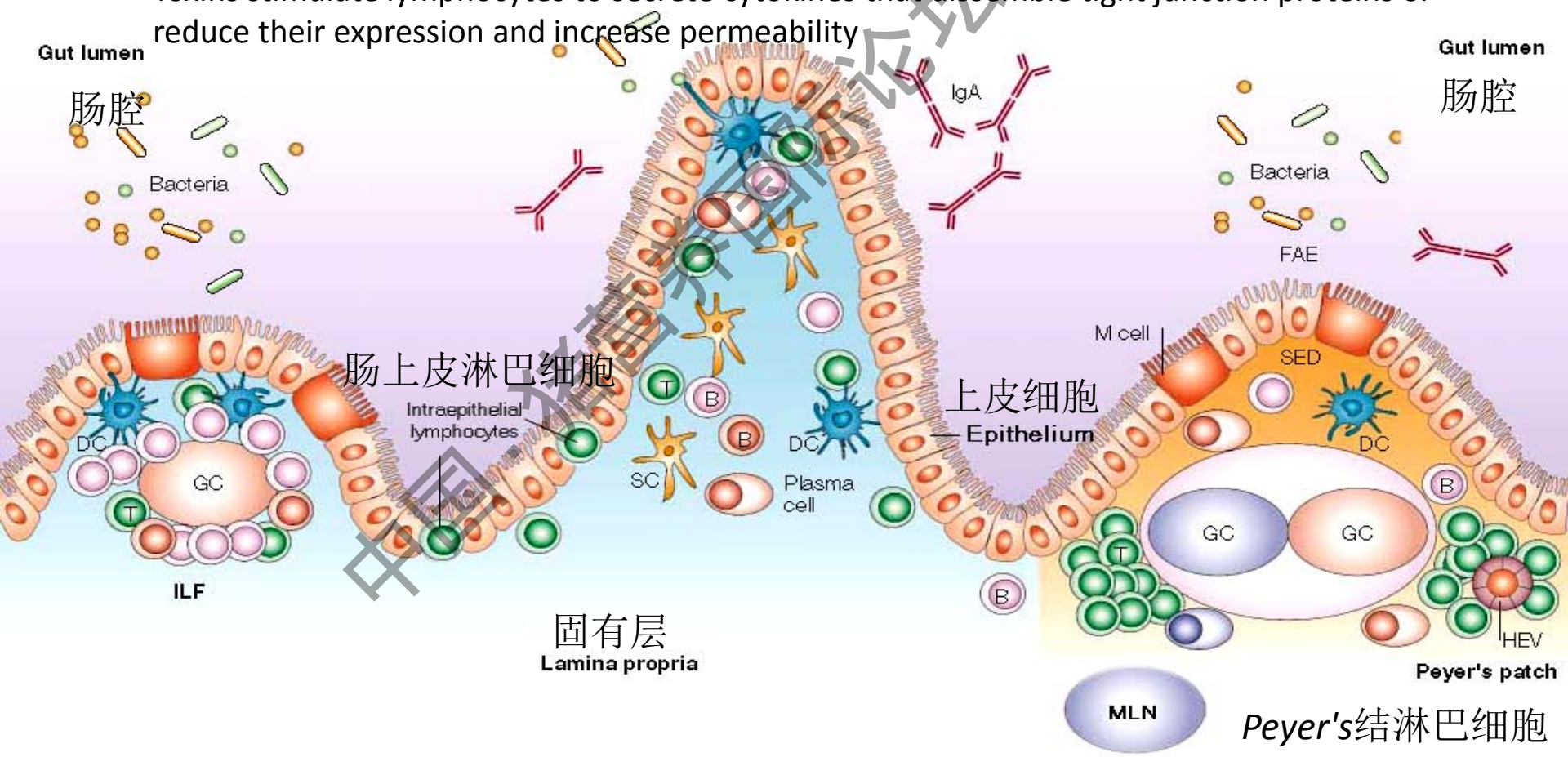
- 断奶降低肠道屏障功能

Consequences of weaning also result in reduced intestinal barrier function (Spreeuwenberg et al., 2001; Boudry et al., 2004; Moeser et al., 2007)

炎症与肠道屏障功能

Inflammation and Gut Barrier Function

- 肠道炎症降低屏障功能和营养物质的吸收 Intestinal Inflammation reduces barrier function and absorption of nutrients
- 毒素刺激淋巴细胞分泌细胞因子，掩盖紧密连接蛋白或者减少它们的表达和增加肠道通透性
- Toxins stimulate lymphocytes to secrete cytokines that disassemble tight junction proteins or reduce their expression and increase permeability



肠道屏障损坏

Breakdown in the Intestinal Barrier

应激诱导肠道功能紊乱

Stress-induced GI dysfunction



紧密连接蛋白破裂

Breakdown of tight junctions



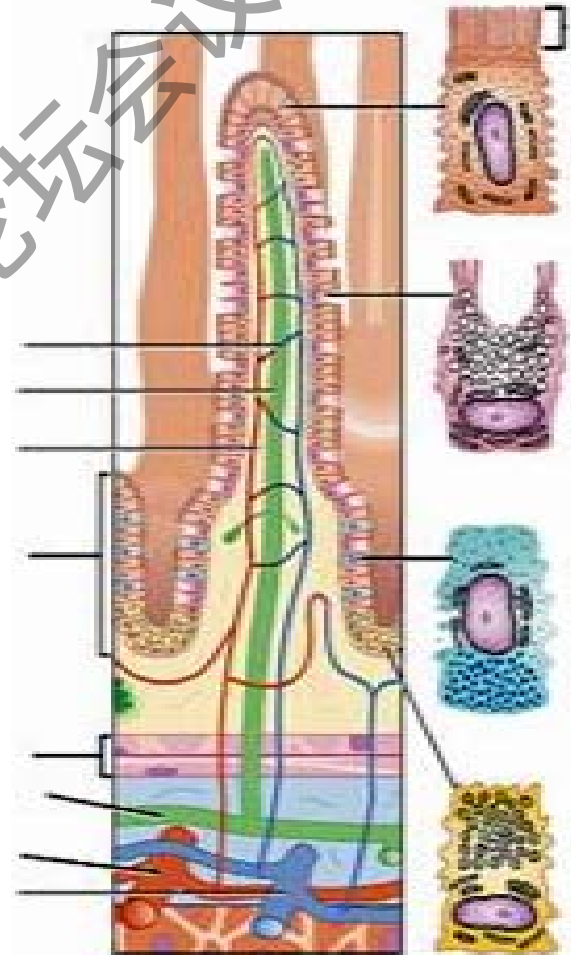
增加肠道通透性和炎症

Increased intestinal permeability
and inflammation



由于腹泻、低增重、生病和死亡从
而生产损失增加

Increased production loss due to
scours, low weight gain, sickness
and death.



断奶仔猪的净吸收减少

Net absorption is reduced in weaned pigs

- 与未断奶的仔猪相比，断奶仔猪对液体、钠和氯离子净吸收减少

Weaned pigs had less net absorption of fluid, sodium, and chloride compared to unweaned littermates.

- 与未断奶仔猪相比，断奶仔猪大肠杆菌感染部分降低了吸收 E. coli infected segments of weaned pigs had reduced absorption compared to infected unweaned pigs

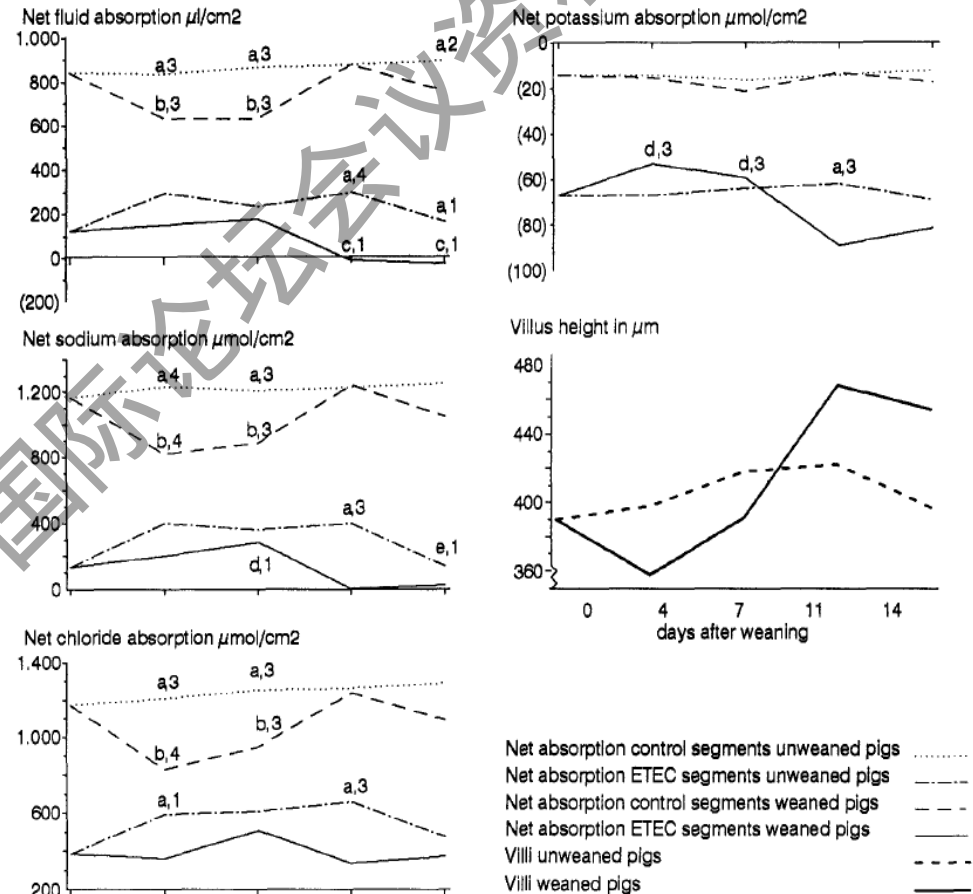


图 2. 未断奶仔猪和断奶仔猪在ETEC感染或未感染情况下液体、钠/氯/钾离子平均净吸收量

Mean net absorption of fluid, sodium, chloride, and potassium in uninfected and ETEC-infected segments of unweaned and weaned pigs (adapted from Nabuurs et al., 1994 56:379)

肠道屏障功能的测定：使用室内腔技术

Measurement of the Intestinal Barrier:

Ussing chamber technique

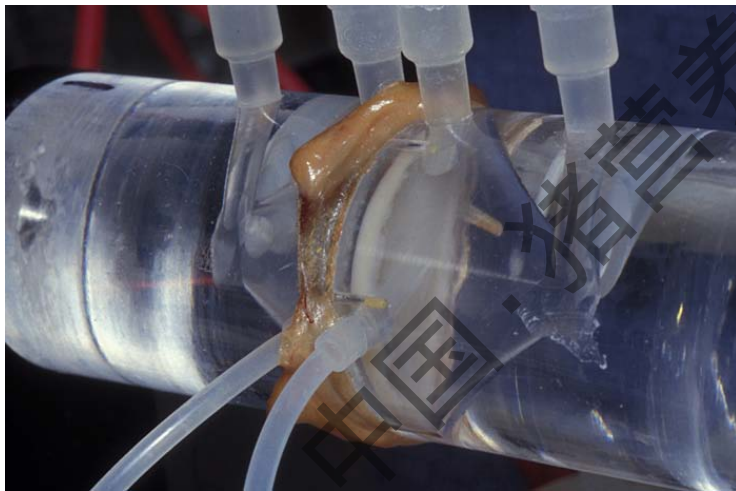
跨膜电阻抗

Transepithelial

Electrical Resistance (TER)

Ohm's Law:

$$R=V/I$$



High TER = Good - intact epithelial barrier

Low TER = Bad - leaky epithelial barrier

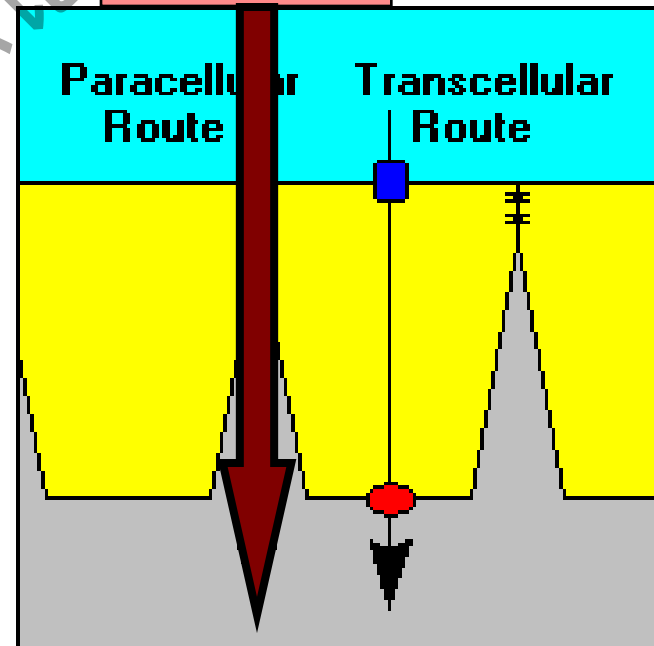
高TER = 好的 - 完整的肠上皮屏障

低TER = 差的 - 缺失的肠上皮屏障

放射性探针旁通量

Paracellular flux of
radiolabeled probe

³H-Mannitol



Low flux rate = Good - intact epithelial barrier

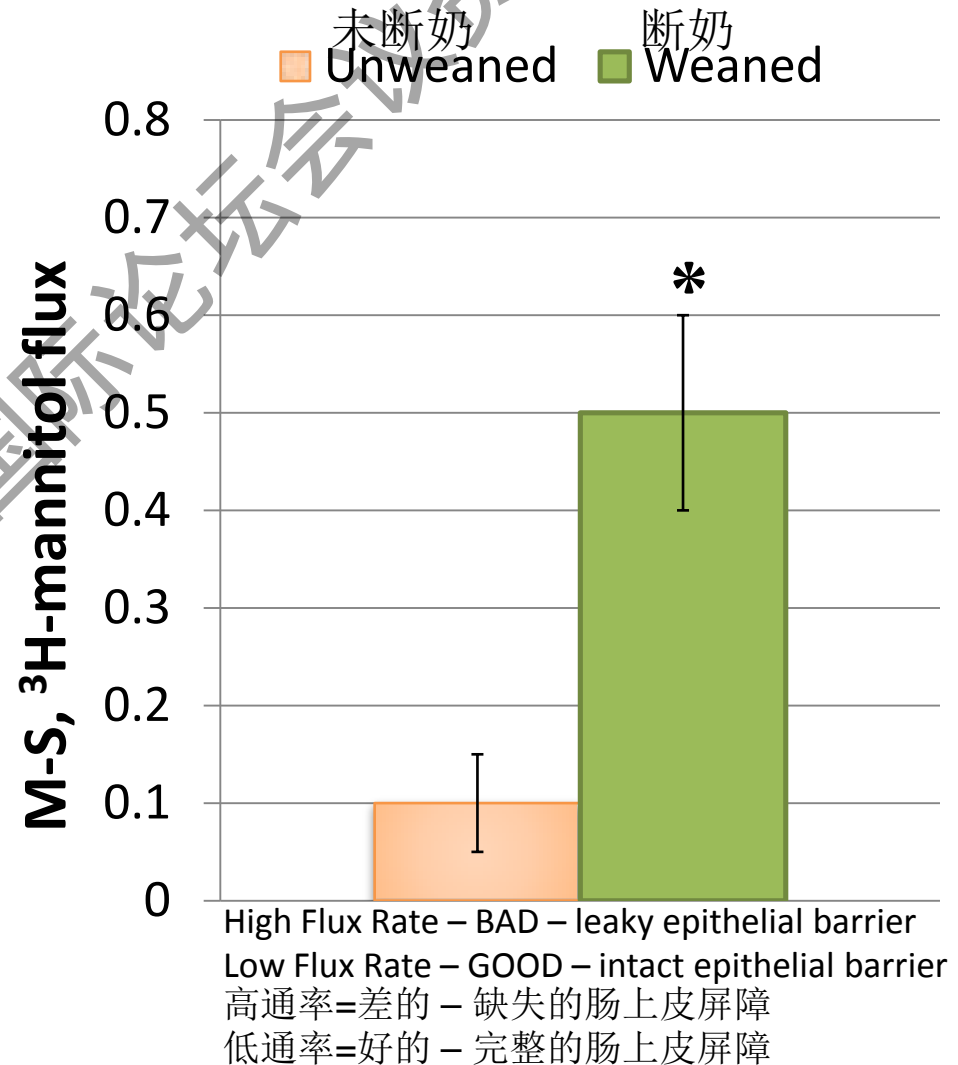
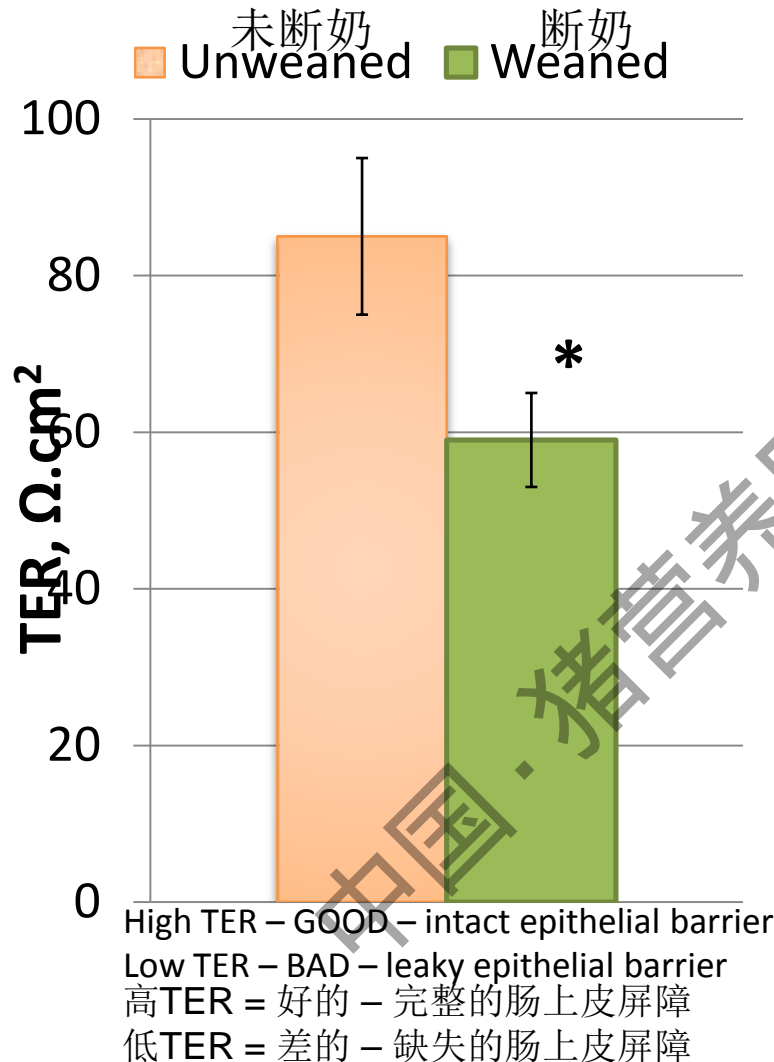
High flux rate = Bad - leaky epithelial barrier

低通率=好的 - 完整的肠上皮屏障

高通率=差的 - 缺失的肠上皮屏障

断奶引发仔猪肠道屏障功能下降

Weaning induces breakdown of the intestinal barrier in piglets

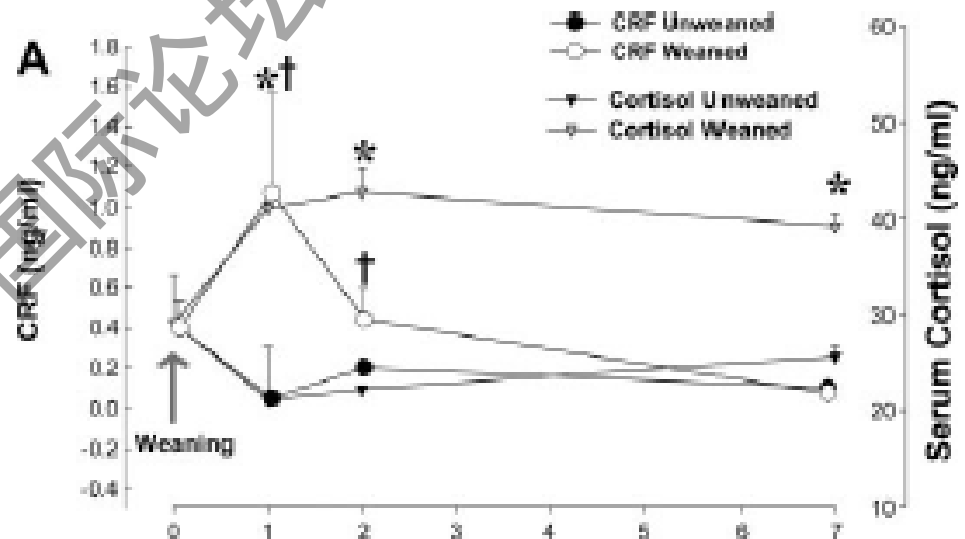


断奶诱导应激激素的释放

Weaning induces stress hormones

- 与未断奶仔猪相比，断奶后24 h，断奶引起的血清促肾上腺皮质激素释放因子达到114%和皮质醇为95% Weaning induced both serum corticotrophin-releasing factor (CRF) by 114% and cortisol by 95% compared to unweaned controls 24 h post-weaning

- 应激通路的激活可能介导肠道功能紊乱 Activated stress pathways may mediate intestinal dysfunction



断奶诱导肠道功能紊乱

Weaning induced intestinal dysfunction

- 通过TER和与血清CRF水平相关的分泌活性测定断奶诱导肠道功能紊乱

Weaning induced intestinal dysfunction as measure by TER and secretory activity is correlated with serum CRF levels.

- 断奶降低肠道屏障功能
Weaning results in reduced intestinal barrier function

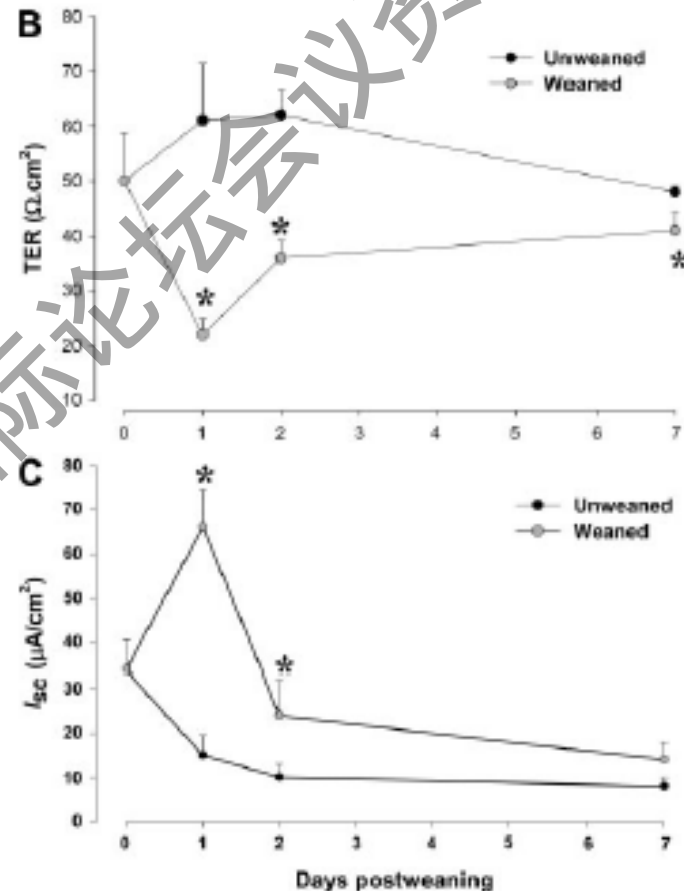


Fig 5 B,C. 肠道屏障功能的长期变化

Long term changes in intestinal barrier function. Values represent means \pm SE, $n = 6$ animals (adapted from Moeser et al., 2007, 292:G173)

断奶日龄影响肠道屏障功能

Weaning age impacts intestinal barrier function

- 随着断奶日龄的增加，肠道TER提高且通透性降低，因而肠道屏障功能改善

As weaning age is increased, intestinal barrier function is improved as indicated by improved TER and lower

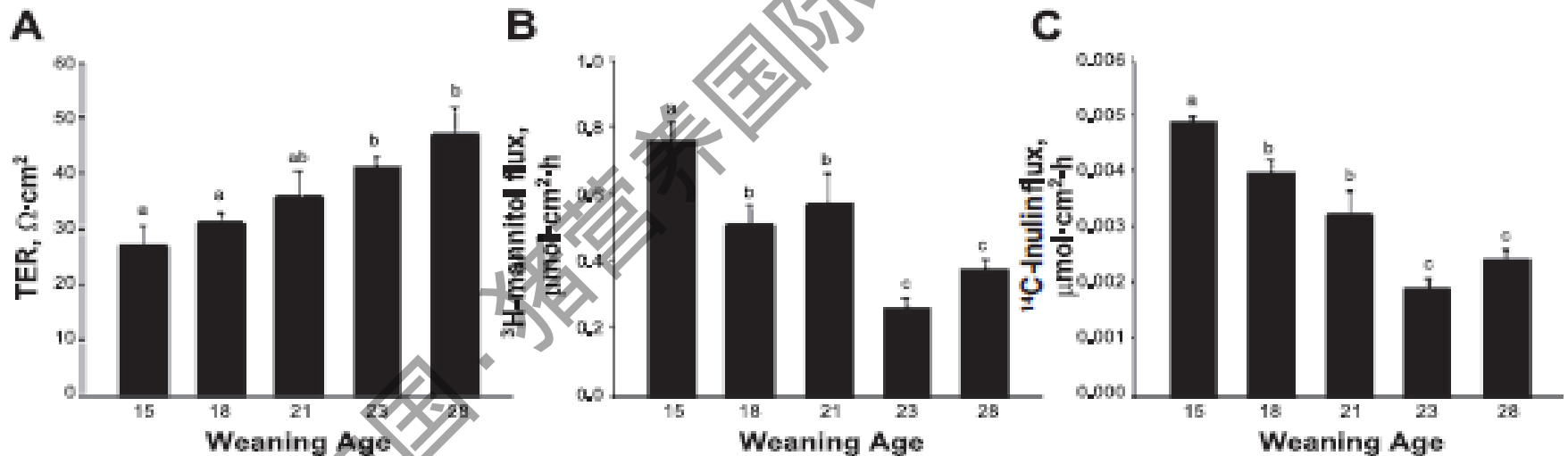


Fig 1. 断奶日龄对断奶猪空肠屏障功能的影响。值表示为平均数 \pm 标准误，每个处理选6头仔猪

Effects of weaning age on post-weaning barrier function in porcine jejunum. Values are means \pm SE, n = 6 pigs per weaning age treatment (adapted from Smith et al., 2010, 298:G352)

断奶对长期屏障功能的影响

Weaning impacts long term barrier function

- 仔猪断奶日龄为15或者28d，评估到9周龄

Weaning age of 15 or 28 d were evaluated after 9 wks of age.

- 仔猪早期断奶会降低其肠道黏膜屏障功能和增加肠道通透性 Earlier weaned pigs had reduced mucosal barrier function and increased permeability

- 因此，断奶破坏肠道屏障功能，而且有长期影响

Thus, weaning induces breakdown of intestinal barrier function and can impact longer term effects

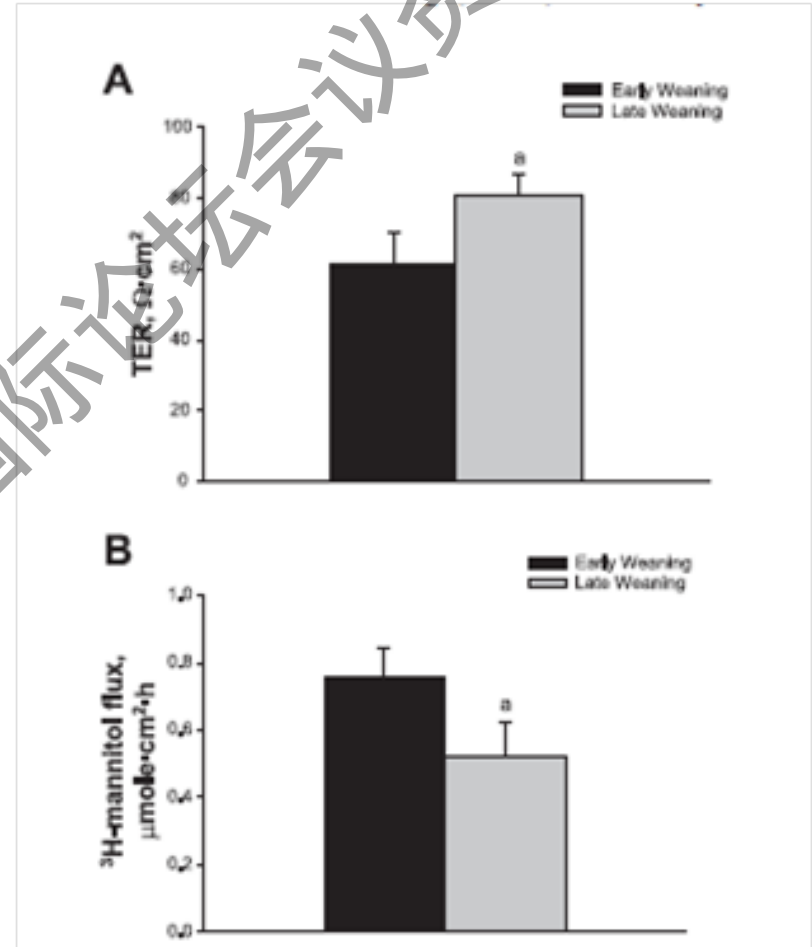


图3. 断奶日龄对仔猪(9周龄)空肠长期黏膜屏障功能的影响
Fig 3. Effects of weaning age and long-term mucosal barrier function in porcine jejunum harvested from 9 wk old pigs (from Smith et al., 2009, 298:G352)

断奶增加仔猪肠道中的TNF- α

Weaning is associated with increased TNF- α in the intestine of piglets

这些结果表明仔猪断奶后肠道会立即或短暂性地出现炎症细胞因子基因表达反应

“These results demonstrate that weaning in piglets is associated with an early and transient response in gene expression of inflammatory cytokines in the gut.”

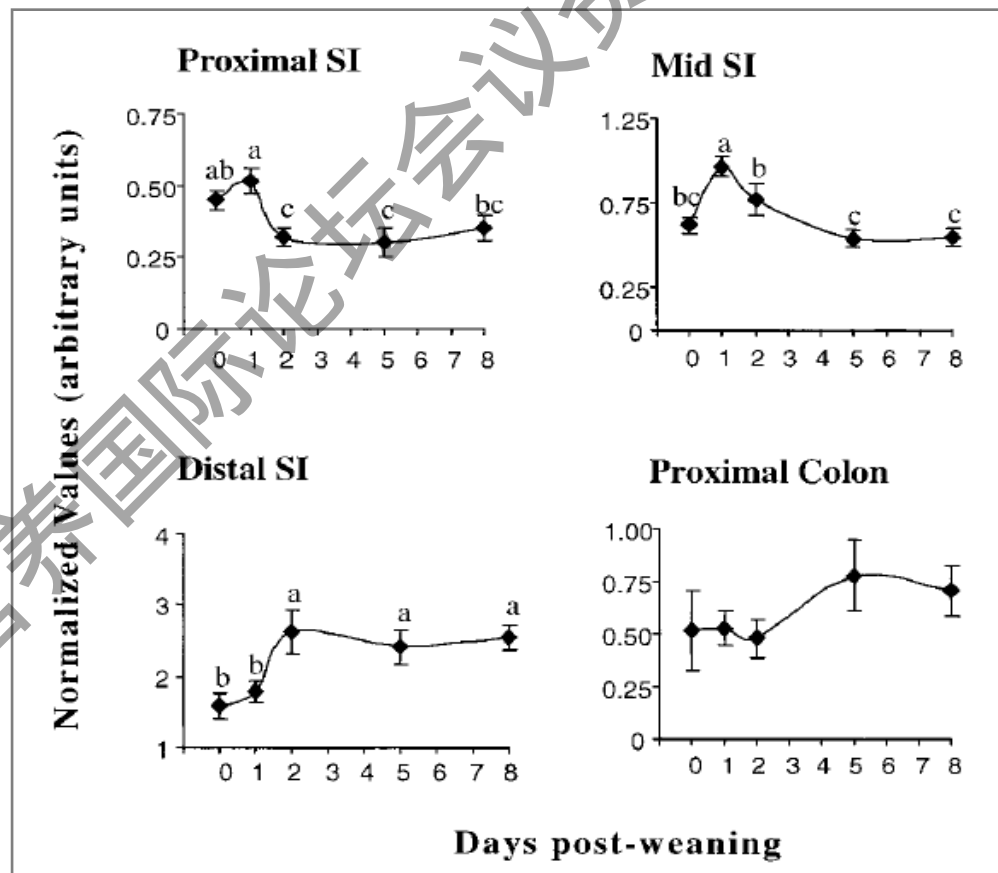


图 1. 断奶后不同天数仔猪小肠近端、中端和远端及结肠近端TNF- α mRNA 表达模式

Pattern of TNF- α mRNA expression in the proximal, mid-, and distal SI in the proximal colon of the intestine of piglets on the day of weaning (d 0) and on d 1, 2, 5, and 8 post-weaning. (Adapted from Pie et al., 2004, J. Nutr. 134:641).

免疫刺激

Immune Stimulation

- 免疫刺激的结果是产生促炎症细胞因子来调节中间代谢，从而导致动物生长性能降低，这是因为能量和养分被免疫途径所利用了

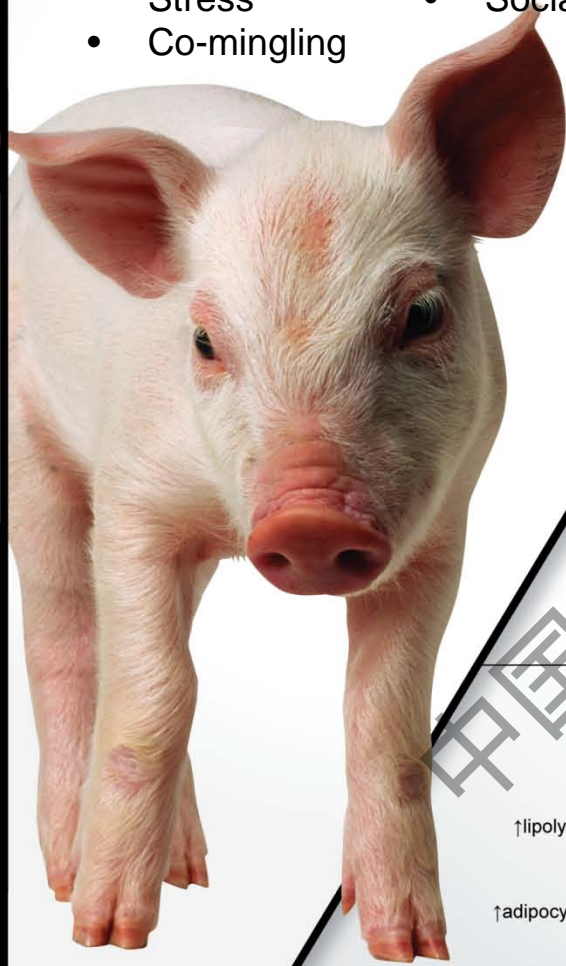
(Johnson, 1997; Spurlock, 1997)

Immune stimulation results in production of pro-inflammatory cytokines, which modulates intermediary metabolism leading to reduced growth of the animal because energy and nutrients are shifted to immune pathways.

(Johnson, 1997; Spurlock, 1997)

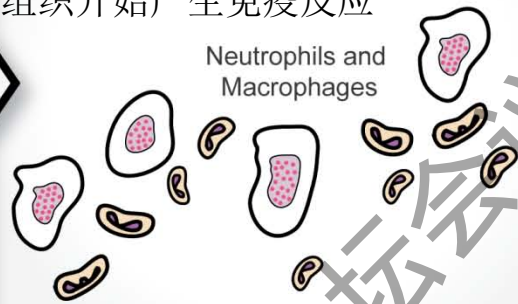
应激源Stressors:

- 日粮过渡
- 运输应激
- 混群
- Dietary Transitions
- Transportation Stress
- Co-mingling
- 接触致病菌
- 断奶
- 社会 Pathogen exposure
- Weaning
- Social



The immune response begins at local tissue sites with recruitment of inflammatory cells.

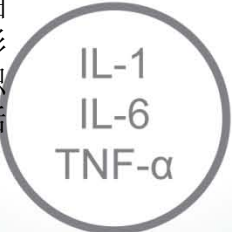
随着炎症细胞的增加，局部组织开始产生免疫反应



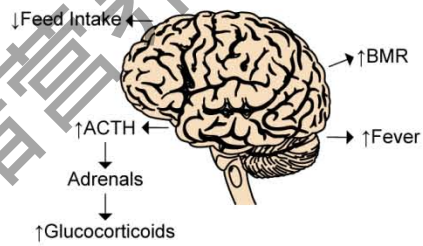
嗜中性粒细胞和巨噬细胞

These stimulated cells produce pro-inflammatory cytokines, affecting multiple tissue cells including the brain, the HPA axis, the liver, adipose tissue, muscle and bone.

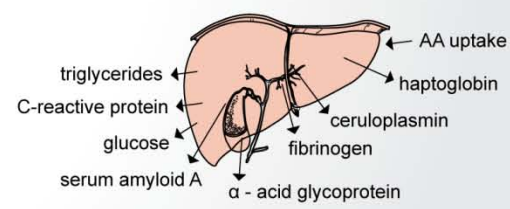
刺激细胞产生促炎症细胞因子，影响多个组织细胞，包括脑、HPA轴、肝脏、脂肪组织、肌肉和骨骼



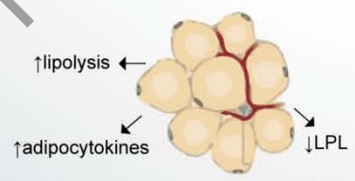
下丘脑-垂体肾上腺轴 Hypothalamic-Pituitary-Adrenal Axis



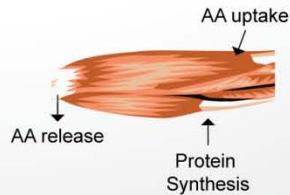
刺激急性期蛋白反应 Stimulation of the Acute Phase Protein Response



脂肪组织 Adipose Tissue



骨骼肌 Skeletal Muscle

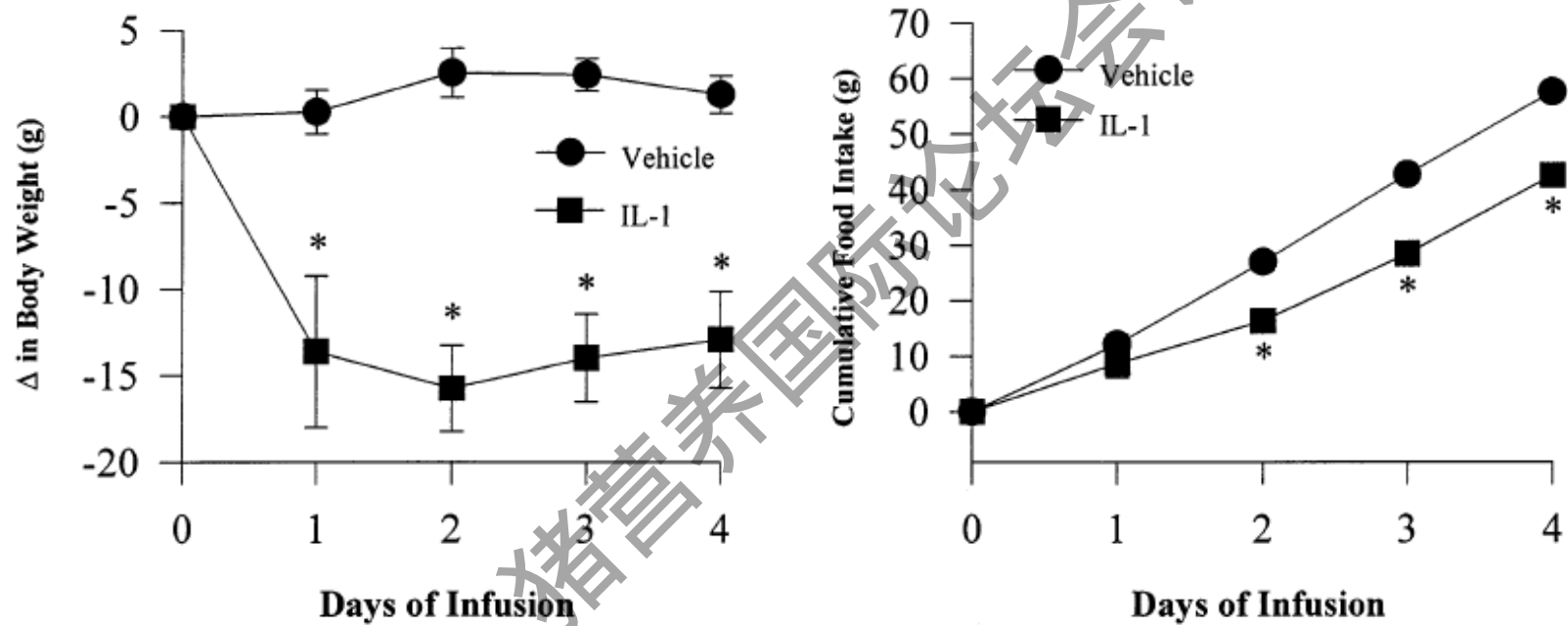


骨骼 Bone



慢性灌注IL-1会降低采食量和体重

Chronic infusion of IL-1 results in decreased food intake and body weight



从大鼠侧脑室慢性灌注重组白介素-1 β (IL-1, 1.56 ng/hr)会降低采食量和体重。在灌注的4天末，灌注IL-1的鼠比对照组的采食量和体重分别少18 g和15 g。

Chronic intracerebroventricular infusion of recombinant interleukin-1 β (IL-1, 1.56 ng/hr) decreased food intake and body weight of rats. At the end of the 4-d infusion period, rats receiving IL-1 had eaten 18 g less food and weighed approximately 15 g less than the vehicle-infused controls. (adapted from Johnson, 1998, DAE 15:309)

免疫系统激活对6-27 kg体重仔猪的影响

Effect of Immune System Activation in Pigs fed from 6 to 27 kg BW

免疫系统激活 Immune System Activation	低 Low	高 High	百分比变化 Percent Change
标准赖氨酸水平 Criterion and Lysine level	1.5% 赖氨酸 Lysine		
末重, kg Final BW, kg	27.6	26.6	-3.62
日采食量, g Daily Feed, g	1,002	911	-9.08
日增重, g Daily Gain, g	663	504	-23.98
增重/耗料, g/kg Gain/Feed, g/kg	662	565	-14.65
蛋白质: 油脂(瘦肉程 度) Protein:lipid (Leanness)	1.41	1.13	-19.86

断奶影响热休克蛋白的表达

Weaning impacts expression of heat shock proteins

- 21和28日龄仔猪断奶后热休克蛋白出现短暂性的增加
In 21 and 28 d old pigs, heat shock proteins were transiently increased after weaning (David et al., 2002)
- 热休克蛋白可以减轻断奶和促炎症细胞因子激活带来的负面影响，它可能通过抑制促炎症细胞因子和细胞增殖来发挥细胞保护作用。
Heat shock proteins may play a role in mitigating the negative effects associated with weaning and pro-inflammatory cytokine activation due to their cytoprotection mechanism by inhibiting pro-inflammatory cytokines and cellular proliferation (Malago et al., 2002).
- 了解热休克蛋白在肠道中的调节功能及有益作用还需要进一步研究
Further research is needed to understand heat shock protein modulation and beneficial effects in the intestinal tract.

结论 Conclusions

- 断奶会立即或随后引起代谢、免疫系统和肠道功能的生物学变化 Biological alterations in metabolism, immune system, and intestinal functions occur during and immediately after weaning
- 这些变化会对猪后期的生长和健康具有短期和长期的影响 These alterations are both short and long-term impacting the pig's growth and health.
- 对养猪生产者而言，至关重要的是利用合理的健康、营养和管理策略，将断奶应激引起的负面影响最小化，从而提高猪的生产性能。 It is critical for swine producers to utilize appropriate health, nutrition, and management strategies to minimize adverse effects of weaning stress and improve swine productivity

问题/意见

Questions/Comments

