Response of Growing Pigs to Environmental and Health Stress Adjustments in Dietary Nutrient Profile and Content

N. LE FLOC’H¹, P.H.R.F. CAMPOS², E. MERLOT¹

¹INRA PEGASE, SAINT GILLES 35590 France
²Universidade Federal dos Vales do Jequitinhonha e Mucuri, Diamantina, Brazil
Preserving health status: a major issue for pig production

- **Healthy (HEALTH)**
  - Economy (ECONOMY)
    - Productivity
    - Efficiency
    - Cost of medication
  - Environment (ENVIRONMENT)
    - Manure production
    - Pathogen excretion
    - Drug residues
  - Animal welfare (ANIMAL WELFARE)
    - Public perception
  - Public health (PUBLIC HEALTH)
    - Zoonosis
    - Food safety
    - Antibiotic resistance

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LE FLOC'H/ Shanghai
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健康养殖是养猪产业的主要问题

Preserving health status: a major issue for pig production

- **Health**: 药物保健 Medication

- **Economy**: 生产率 Productivity, 效率 Efficiency

- **Environment**: 环境控制少 Environment less controlled

- **Animal Welfare**: 用药少 Fewer medications

- **Public Health**: 食品安全 Food safety

- **Intensive farming**

- **Alternative farming**

- **Drug residues**

- **Antibiotic and medication use**

- **Antibiotic resistance**
WHO 1948: Definition of HEALTH

- Human
  - A state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity.

- Animal
  - The conceptualisation of health and disease in livestock
    - Health as normality
    - Health as biology
    - Health as a dynamic balance
    - Health as a state of physical and psychological well-being
    - Health as productivity including reproduction

- Animal Health
  - Level of functional and metabolic efficiency of a living organism: no disease, no stress, good productivity (maximum animal potential?)

- Major Infectious diseases are not in the scope of my lecture
Feed and nutrition are major components of multifactorial production diseases.

- Housing conditions
- Feed
- Temperature
- Virus
- Bacteria
- Fungi
- Dust
- Genetics
- Age
- Physiological status
- Nutritional status
- Animal
What is expected from Feed and Nutrition?

- To contribute to health preservation in a context where medication should be reduced

- To limit the consequences of health disturbances on performance
Feed, Nutrition and health are interconnected

A good health status is necessary to maintain feed efficiency, growth rate and to limit feed cost.

Ex. Chronic respiratory disease in pig:

- Feed conversion ratio + 0.3
- Duration of growing phase + 7-28 d

Source: http://www.thepigsite.com/pighealth/article/33/the-costs-of-disease/
Feed, Nutrition and health are interconnected

- 良好性能和饲料利用率
  Good performance & feed efficiency

- 生理
  Regulations & physiology

- 代谢
  Metabolism

- 消化
  Digestion

- 肌肉生长
  Muscle growth

- 骨骼发育
  Bone development

- 肠道发育与菌群
  Gut development & microbiote

- 免疫系统
  Immune system

- 粘膜完整性
  Mucosal integrity

- 良好健康状况
  Good health
目录 Outlines

• 猪应对健康受损的生理和代谢基础
  Physiological and metabolic basis of the pig response to health disturbances

• 猪应对健康受损能力的影响因素
  Factors impacting the pig ability to cope with health disturbances

• 为维持猪健康需要做哪些营养调整？
  Which nutritional adjustments to support pig health？
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- 猪应对健康受损的生理和代谢基础
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- Which nutritional adjustments to support pig health?
Effect of health disturbances on feed intake and growth - meta-analysis 122 studies -

Pastorelli et al., 2012

应激和研究之间的可变性
Variability between challenges and studies
- 不同强度
  Various intensities
  \[ \Delta ADG \geq \Delta ADFI \]
  (-30% à -10%) ≥ (-23% à -4%)
- 不同机制
  Various mechanisms

采食量 feed intake
消化紊乱 digestive disturbances
代谢调整 metabolic adaptations
A systemic inflammation caused by bacterial endotoxin (LPS) injection modifies nutrient utilization.

Merlot et al, 2013 EAAP

High Energy demand

Increase in protein breakdown
A systemic inflammation caused by bacterial endotoxin injection decreases insulin sensitivity

*Insulin is a hormone that allows the body (muscle, adipose tissue and liver) to use nutrients

Blood plasma Insulin, μU/mL  
Blood plasma Glucose, mg/L

→ Lower nutrient utilization by the muscle?
Experimental evidences showing that amino acid utilization is impacted by health disturbances

Plasma postprandial kinetics of AA in control and co-infected pigs (Mycoplasma and H1N1): respiratory disease

*禁食24h后（感染支原体23天，H1N1 3天）饲喂相同量的饲料(200g),测定血浆氨基酸水平
Plasma AA were measured after pigs were fed the same amount of feed (200 g) after being fasted overnight (23d post Mycoplasma and 3d post H1N1)

苏氨酸
Threonine, μM

精氨酸
Arginine, μM

苏氨酸参与到了免疫蛋白吗？
Threonine incorporation into immune proteins?

精氨酸用于合成一氧化氮利用率？
Arginine utilization for nitric oxide synthesis?
总结：健康受损影响所有代谢过程

To summarize: all metabolisms are affected by health disturbances

单核细胞Monocytes, 巨噬细胞macrophages...

IL1 - TNF- IL6

糖皮质激素 Glucocorticoids

糖异生 neogluconeogenesis,
蛋白质分解代谢 protein catabolism

甘油三酯TG

葡萄糖Glucose

尿素Urea

急性期蛋白APP

脂肪组织 Adipose tissue

瘦素 leptin

脂蛋白酶活性 Lipoprotein lipase activity

肌肉 Muscle

免疫细胞 Immune cells

氨基酸AA

氨基酸摄入 AA uptake

蛋白质降解 protein degradation

ACTH

病态行为（发热、食欲减退、冷漠）
sickness behavior (fever, anorexia, apathy...)

TG合成 TG synthesis

糖原分解-糖异生 Glycogenolysis-neogluconeogenesis

APP 合成 APP synthesis

氮排泄 Nitrogen excretion

2016 中国 猪业国际论坛
A focus on protein metabolism disturbances caused by immune system activation.

- **Hormones**
  - Cortisol
  - Insulin

- **Cytokines**
  - TNF-α
  - IL-1β
  - IL-6
  - INF-γ

- **Protein synthesis**
  - Energy production
  - Protein breakdown

- **Changes in AA partitioning**

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**October, 20th 2016**
目录 Outlines

- Physiological and metabolic basis of the pig response to health disturbances

✔ 猪应对健康受损能力的影响因素

(some) Factors impacting the pig ability to cope with health disturbances

- 外因：温度、卫生 External factors: temperature, hygiene
- 内因：基因型、性别 Internal factors: genotype, sexual type
High temperatures is an issue for pig production worldwide

**Background Context**

- Increased pig production in developing countries - tropical and subtropical areas
- Global warming

**Consequences on pig production?**

- Reduced feed intake and performance
- High temperatures favor pathogen dissemination

**Effect of high temperatures on pig ability to cope with a health challenge is unknown?**
Effects of high ambient temperature on inflammatory response induced by endotoxin

- 30 pigs fitted with a jugular catheter ≈ 50 kg
- 2 thermal conditions:
  - Thermo-neutrality (TN): 16 pigs; 24°C
  - High temperature: 14 pigs; 30°C

- 2 experimental periods
  - Period 1: day -7 to -1; before inflammatory challenge
  - Period 2: day 1 to 10; during inflammatory challenge
High ambient temperature alleviates inflammatory response and growth depression in pigs challenged with endotoxin.
High ambient temperature alleviates inflammatory response and growth depression in pigs challenged with endotoxin


Lower inflammatory response in pigs previously acclimated to high ambient temperature. Growth and protein deposition are less affected.
Influence of genotype

Animals genetically selected for high productive traits would be more susceptible and affected by production diseases.

Selection against immune capacity?
Reduced ability to use nutrients for health maintenance?
本研究目的  Objectives of the study

为了评估 To assess:

- 应对差环境卫生条件引起的免疫挑战的能力
  Ability to cope with an immune challenge caused by poor hygiene housing conditions

- 挑战应激后恢复能力
  Ability to recover after the challenge

根据残余采食量（RFI，测定饲料利用效率的一种指标）选择两条生产线的生长猪

...of two lines of growing pigs selected on their residual feed intake or RFI (a measure of feed efficiency)
试验设计 Experimental Design

→ 160头生长育肥猪，自由采食，单独饲喂
A total of 160 growing – finishing pigs fed ad libitum/individual pens

→ 4个试验组（每组40头猪）
4 Experimental groups (40 pigs per group)

生产线Line (L) × 环境Environment (E)

Low RFI (LRFI) → 效率高：采食比预期少
More efficient: eat less than predicted

High RFI (HRFI) → 效率低：采食比预期高
Less efficient: eat more than predicted

→ 12周，30-115kg，2阶段
12 Weeks (W) 30-115kg, 2 periods:

- 阶段1：挑战期(0-6周) 50%清洁/50%脏乱
  Period 1 or challenge (W0 - W6) 50% clean E / 50% dirty E
- 阶段2：恢复期(6-12周) 100%清洁
  Period 2 or recovery (W6 - W12) 100% clean E

Chatelet et al, ICPD 2016

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PROHEALTH
SEVENTH FRAMEWORK PROGRAMME
Europe
• Poor hygiene reduced growth rate: greater effect for the less efficient line (HRFI)
• No reduction of feed intake !!!!

Chatelet et al, ICPD 2016
炎症状特征 Inflammatory Response

结合珠蛋白 Haptoglobin (mg/L)

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L** + 97%
H*** + 117%
L x H + 71%

Chatelet et al, ICPD 2016

选择高饲料利用率对健康无负面影响
Selection for high feed efficiency has no negative impact on health

差卫生挑战导致系统炎症反应，且引起肺炎：低效率品系
Poor hygiene induced a systemic inflammation and caused pneumonia: for the less efficient line
目录 Outlines

- Physiological and metabolic basis of the pig response to health disturbances
- Factors impacting the pig ability to cope with health disturbances
- 为维持猪健康需要做哪些营养调整？
  - 重点关注氨基酸
- Which nutritional adjustments to support pig health ?
  A focus on Amino Acids
A focus on protein metabolism disturbances caused by immune system activation.

- Immune stimulation
- Inflammation
- Feed intake
- Metabolic changes
- Growth and protein deposition
- Growth
- Competition for AA utilization
- Body defenses
Some AA are specifically involved in metabolic processes associated with health maintenance.

- **合成特定蛋白**
  Incorporation into specific proteins
  Mucins, immunoglobulins, APP ...

- **氨基酸是肝脏、免疫细胞和肠细胞的营养成分**
  AA are nutrients for the liver, immune and intestinal cells
  - 糖原合成 neogluconeogenesis
  - 细胞增殖 cell proliferation

- **氨基酸是活性分子合成的前体**
  AA are precursors for the synthesis of active molecules
  - 细胞毒性物质 cytotoxic compounds
  - 抗氧化物 antioxidant compounds

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**苏氨酸**，**色氨酸**，**缬氨酸**
Thr, Trp, Val

**色氨酸**，**谷氨酰胺**
Trp, Gln ...

**半胱氨酸**，**精氨酸**
Cys, Arg
慢性肺炎对色氨酸代谢的影响
Effect of a chronic lung inflammation on TRP metabolism

通过弗氏佐剂注射诱导肺炎
Lung inflammation induced by Complete Freund's adjuvant injection

血浆TRP浓度
Plasma TRP concentrations

血浆色氨酸 plasma[TRP]

血浆中色氨酸消失
TRP disappearance from plasma

色氨酸分解代谢增加
Increased Trp Catabolism

合成富含TRP的蛋白
Incorporation into TRP rich-proteins ➔ 急性期蛋白 APP

IDO活性增加
Greater IDO activity

结合珠蛋白浓度增加
Greater haptoglobin concentration

Melchior et al 2004, 2005
TRP supply alleviates the effect of lung inflammation

Lung inflammation induced by Complete Freund’s adjuvant injection

Pigs fed with the high TRP diet had lower plasma [haptoglobin] and were healthier.

Antioxidant
Control of inflammatory response

TRP supply above recommendations maintains TRP plasma concentrations and limits the inflammation.
补充日粮色氨酸对相关健康参数的影响
Impact of TRP dietary supply on health parameters

- 上述剂量TRP（0.30 vs 0.18%）降低由注射diquat*造成的仔猪氧化应激
  TRP above recommendations (0.30 vs 0.18%) alleviates oxidative stress induced by diquat* injection in piglets:
  - 肝脏SOD* and GPx* 血浆MDA*
  - antioxidant SOD* and GPx* in the liver and plasma MDA*
  - 血浆尿素 plasma urea
  - 没有减弱氧化应激对生长性能的影响
did not attenuate the effect of oxidative stress on growth performance

  * Diquat : an herbicide known for inducing oxidative stress; SOD and GPx are antioxidative enzymes and MDA is a biomarker of oxidative stress.

- 上述剂量TRP（0.24 vs 0.74%）降低断奶仔猪应激
  TRP above recommendations (0.24 vs 0.74%) reduced the impact of weaning stress:
  - 唾液皮质醇反应 salivary cortisol response
  - 维持肠道形态 maintains gut morphology
  - 对生长性能无影响 no effect on growth performance

- 胃灌TRP减少由葡聚糖硫酸钠造成的新生仔猪结肠炎病变
  TRP supplied intragastrically reduced colitis lesions caused by DSS* in neonatal piglets

  * Koopmans et al 2006

- 胃灌TRP减少由葡聚糖硫酸钠造成的新生仔猪结肠炎病变
  TRP supplied intragastrically reduced colitis lesions caused by DSS* in neonatal piglets

  * Kim et al J 2010
The improvement of growth by additional tryptophan is greater in animals with moderate inflammation.
结论Conclusions (1)

维护农场动物健康：期望从饲料和营养中得到什么？
Preserving health of farm animals: What is expected from feed and nutrition?

降低用药的同时维护健康的策略
a strategy for health preservation with less medication
  ➔ 功能性营养成分Functional nutrients

降低较差健康状况对性能和营养利用率影响的策略
a strategy for limiting the consequences of poor health status on performance and efficiency of nutrient utilization
  ➔ 调整营养配方Modification of nutrient profile
从研究角度来看 From a research perspective

✓ 饲料和健康紧密相连，多样性和复杂性
   The interactions between feed and health are numerous, diverse and complex

✓ 仍需要有新的知识 New knowledge are still necessary
   ➢ 肠道微生物的作用 Role of digestive microbiota
   ➢ 超出生长性能以外的相关营养功能 Knowledge on nutrient functions beyond performance

✓ 下一步：超越概念认证 The next step: to go beyond the proof of concept
   ➢ 生理反应 physiologic response
   ➢ 菌群变化 changes in the microflora profile
   ➢ 基因表达 gene expression ...
结论 Conclusions (3)

从农场角度来看 From an on-farm use perspective

✓ 仍有很多限制因素需克服
   Some limitations are still to overcome

✓ 当调整饲料配方和饲喂方式来维持健康和性能时
   When feed formulation and feeding practices could be adapted to preserve both health and performance

   ➢ 以预防为目的 ➔ 鉴别限制性营养组分
      in a preventive way ➔ identification of sub limiting nutrients

   ➢ 以治疗为目的 ➔ 采食量低的问题
      in a curative way ➔ problem of low feed intake

   ➢ 补偿性增长 ➔ to sustain compensatory performance
从农场角度来看 From an on-farm use perspective

- 如何调整饲料配方和饲喂方式来维护健康和性能
  How feed formulation and feeding practices could be adapted to preserve both health and performance

- 以个体为群体（关键阶段） VS 群体中的个体
  group of individuals (critical phase) vs individual in a group
From an on-farm use perspective

How feed formulation and feeding practices could be adapted to preserve both health and performance

- group of individuals (critical phase) vs individual within a group

What could be expected from Precision Livestock Farming:

- the challenge of (early) detection of health disturbances: cough and lameness detection (Berkmans 2014),
  changes in feeding behavior (Maselyne et al 2015),
  drinking behavior (Cornoué et al 2013)
- Feed the group or the individual through precision feeding (Andretta et al 2014)
从农场角度来看 From an on-farm use perspective

- 如何调整饲料配方和饲喂方式来维护健康和性能
  How feed formulation and feeding practices could be adapted to preserve both health and performance

  - 以个体为群体（关键阶段）VS 群体中的个体
  - group of individuals (critical phase) vs individual within a group

- 可以从精细化养殖得到什么
  What could be expected from Precision Livestock Farming:

  - 早期检测健康问题带来的挑战：the challenge of (early) detection of health disturbances:
    - 咳嗽及腿病检测 cough and lameness detection (Berkmans 2014),
    - 采食行为的变化 changes in feeding behavior (Maselyne et al 2015),
    - 饮水行为 drinking behavior (Cornou et al 2013)

  - 通过精细化养殖饲喂群体或个体
    Feed the group or the individual through precision feeding (Andretta et al 2014)

- 日粮需要与其他饲养管理措施结合 Feed should be associated to other management strategies
What is ongoing? An example

An European project dedicated to production diseases* in intensive pig and poultry production systems

项目负责人：纽卡斯尔大学
22个参与者 2013-108
Leader: University of Newcastle (I Kyriazakis)
22 partners - 2013-2018

生产性疾病*: 遗传、环境（畜舍、营养、管理）和病原菌相互作用产生的多因素疾病
Production diseases*: multifactorial diseases in which genetics, environment (housing, nutrition, management) and pathogenic challenge show complex interactions

- 掌握基因型（骨骼健康，炎症反应，消化功能紊乱）与畜舍条件（母猪）交互作用的基础生理代谢
  To with the genotype (bone health, inflammatory response, digestive develop our understanding of the underlying physiological and metabolic mechanisms in interaction e disorders) and housing conditions (sows)
- 验证营养方案能够克服这些疾病的影响
  To test nutritional strategies to overcome the impact of these diseases
Any questions?

http://www6.rennes.inra.fr/pegase_eng/

Contact: nathalie.lefloch@inra.fr