SINDER 信得 HILE 海利

SINDER 信得

猪消化道疾病国际研讨会
International Pig Digestive Diseases Symposium

致病性猪大肠杆菌的流行趋势和防控现状

Trends in the Epidemiology of Pathogenic Escherichia coli in Swine and Current Status of Prevention and Control

报告人：陈家锃 博士/产品总监

Speaker: Chen Jiazeng Doctor/Product Director

Tel：15066253812

Tel：15066253812

河南. 南阳

Nanyang, Henan

山东信得科技股份有限公司

Shandong Xinde Technology Co., Ltd.

&山东海利生物制品有限公司

& Shandong Haili Bioproducts Co., Ltd.

2024年4月10日

April 10, 2024

猪消化道疾病国际研讨会

SINDER 信得 HILE 海利

SINDER 信得

猪消化道疾病国际研讨会
International Pig Digestive Diseases Symposium

目 录

contents

contents

01. 大肠杆菌病的流行现状
01. Current Epidemiology of Escherichia coli Infection

02. 大肠杆菌病的防控措施
02. Measures for Prevention and Control of Escherichia coli Infection

03. 大肠杆菌防控技术储备
03. Technical Stockpile for Prevention and Control of Escherichia coli

猪消化道疾病国际研讨会

一、大肠杆菌病原的流行现状
I. Current Epidemiology of Escherichia coli Pathogens

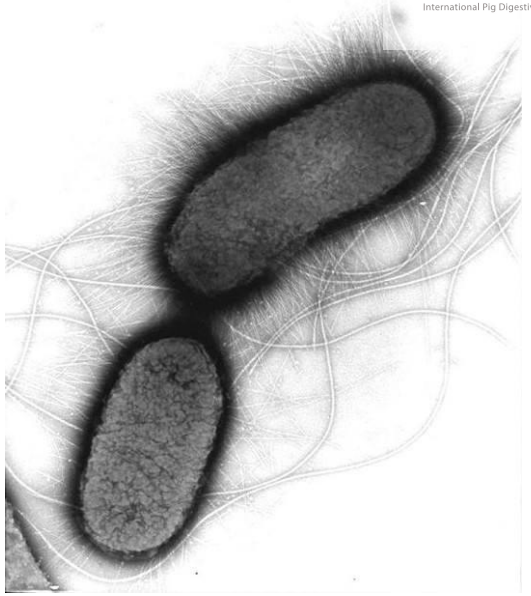
猪消化道疾病国际研讨会

1. 致病大肠杆菌病：猪场常在菌，超60%健康猪携带

1. Pathogenic Escherichia coli Disease: Common in pig farms, with over 60% of healthy pigs carrying it

- 猪大肠杆菌病：可导致初生仔猪腹泻（习惯称仔猪黄白痢）、断奶仔猪腹泻或水肿病、全身性感染、大肠杆菌性乳房炎及泌尿系统感染；可在不同品种的猪群，全工段发生：

  Porcine Escherichia coli Disease: Can lead to diarrhea in neonatal piglets (commonly referred to as yellow-white scours), post-weaning piglet diarrhea or edema disease, systemic infections, Escherichia coli mastitis, and urinary system infections; can occur throughout the production cycle in pig populations of different breeds.



- 母猪群：子宫炎、乳房炎、无乳综合征

  Sow herd: Metritis, mastitis, agalactia syndrome

- 产房仔猪：黄痢、白痢、水肿病（少）

  Farrowing piglets: Yellow scour, white scour, edema disease (less common)

- 断奶仔猪：水肿病、断奶后仔猪腹泻

  Weaned piglets: Edema disease, diarrhea in piglets after weaning

猪消化道疾病国际研讨会

1. 仔猪黄白痢：受母抗和环境影响，多发生于头胎母猪及后代

1. Neonatal Yellow-White Scours: Influenced by maternal antibodies and environmental factors. it mainly occurs in first-parity sows and their offspring

- 仔猪黄痢：多发生于产房内10日龄仔猪，死亡率高，病程快

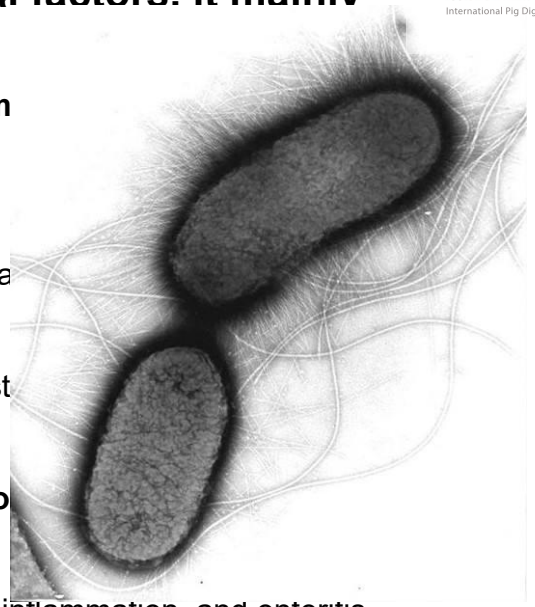
  Neonatal Piglet Yellow Scours: Often occurs in piglets around 10 days old in the farrowing house, with a high m progression.

有呕吐物，黄色稀便或水泻，并发脱水症状，腹肌松弛、无力；

Symptoms include vomiting, yellowish loose stools or diarrhea, accompanied by dehydration, relaxed abdominal muscles, a

小肠扩张，肠壁变薄，充血，肠系膜淋巴结肿大、充血、出血；

The small intestine is dilated, the intestinal wall becomes thin, congested, mesenteric lymph nodes swell, become congest



- 仔猪白痢：多发生于10~ 30日龄仔猪，发病率高，死亡率低

  Neonatal Piglet White Scours: Often occurs in piglets aged 10 to 30 days, with a high incidence rate and low mo

病猪体温不高，乳白色或灰白色稀粪，胃肠卡他性炎症，肠炎；

Affected pigs have normal body temperature, with milky white or grayish-white loose stools, gastric and intestinal catarrhal inflammation, and enteritis.

猪消化道疾病国际研讨会

3. 大肠杆菌病：水肿病散发，近年发病率有所抬头

3. Escherichia coli Disease: Edema disease is sporadic, and in recent years, the incidence rate has shown an upward trend.

- 猪水肿病：主要发生于断奶后两周的仔猪群，急性死亡，愈后易反复

Edema Disease in Pigs: Primarily occurs in groups of piglets two weeks post-weaning, resulting in acute death with a tend

散发或小范围暴发，发病前猪群多出现腹泻症状，死亡率较高；

It sporadically occurs or erupts in small outbreaks. Before the onset of the disease, the pig population often exhibits symptom high mortality rate.

表现出神经症状，突然瘫痪，精神萎靡，呼吸困难，侧卧划水；

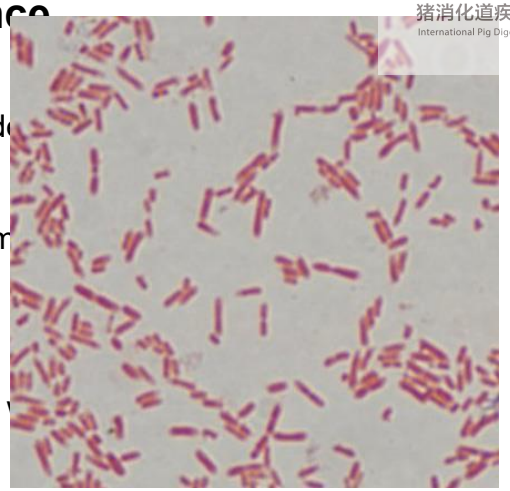
Affected pigs show neurological symptoms such as sudden paralysis, depression, difficulty breathing, and swimming motion

体温不高，全身性水肿，眼结膜、结肠肠系膜水肿，呈胶冻样；

Affected pigs exhibit low body temperature, systemic edema, edema of the conjunctiva and mesentery of the colon, appearing gelatinous.

断奶后生长较快的仔猪多发，育肥猪亦可发生，导致生长缓慢。

This condition is more common in rapidly growing post-weaning piglets and can also occur in growing-finishing pigs, leading to slow growth.



猪消化道疾病国际研讨会

4. 黄白痢/腹泻致病机理：仅需要繁殖即可致病，应激易导致发病

4. Pathogenic Mechanism of Yellow-White Scours/Diarrhea: Pathogenesis only requires colonization to cause disease, and stress can easily trigger the onset of the disease.

- 致病机理：粘附→大量增殖（必要条件）→释放肠毒素→影响电解质平衡→分泌性腹泻和脱水→ 代谢性酸中毒→死亡

  Pathogenesis: Adhesion → extensive proliferation (necessary condition) → release of enterotoxins → disruption of electrolyte balance → secretory diarrhea and dehydration → metabolic acidosis → death

- 致病条件：ETEC属于非侵蚀性大肠杆菌，只需要黏附、菌群增殖释放肠毒素即可致病，因此其发病率与自身抵抗力和环境密切相关

  Pathogenic Conditions: ETEC belongs to non-invasive Escherichia coli, requiring only adhesion, bacterial proliferation, and toxin release to cause disease. Therefore, its incidence is closely related to innate resistance and environment.

- 致病因素：潮湿的环境（致病菌易存活）

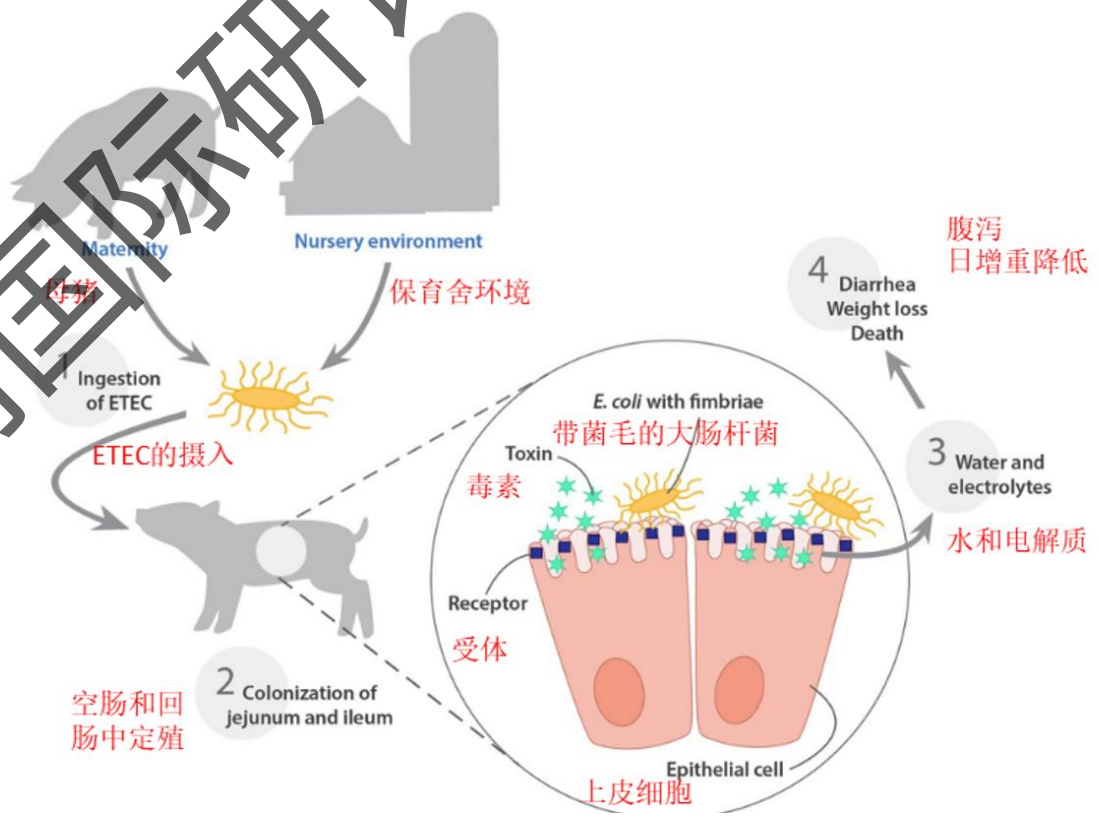
  Pathogenic Factors: Humid environment (favorable for pathogen survival)

  冷应激（导致猪群抵抗力差）

  Cold stress (leading to poor resistance in pig populations)

  母抗低（头胎次母仔易暴发）

  Low maternal antibody levels (first-parity sows and their offspring are more susceptible to outbreaks)



猪消化道疾病国际研讨会

5. 仔猪水肿病：病毒性腹泻后易继发水肿病

5. Piglet Edema Disease: Often occurs as a secondary condition after viral diarrhea

- 致病机理：病原菌侵入肠黏膜上皮→定植大量复制→分泌志贺毒素→侵入肠上皮细胞杀灭细胞→引起出血性结肠炎→毒素吸收引起肠道血管、脑血管（神经症状）→破坏血管壁→靶组织水肿

  Pathogenesis: Pathogenic bacteria invade the intestinal mucosal epithelium → colonize and replicate extensively → secrete Shiga toxins → **invasion of intestinal epithelial cells and cell lysis** → cause hemorrhagic colitis → toxin absorption leads to vascular damage in the intestine and brain (neurological symptoms) → destruction of vascular walls → tissue edema in target organs

- 致病条件：STEC为侵蚀性大肠杆菌，病原菌需侵入肠粘膜定植

  Pathogenic Conditions: STEC is an invasive Escherichia coli, requiring the pathogen to invade and colonize the intestinal mucosa.

- 致病因素：菌群紊乱/肠道紊乱（致病菌易定植）

  Pathogenic Factors: Disruption of gut microbiota/intestinal disorders (favorable for pathogen colonization).

  肠粘膜的损伤（易侵入肠粘膜致病）

  Damage to intestinal mucosa (facilitates pathogen invasion and pathogenesis)

  母源抗体低（与哺乳猪水肿病有关）

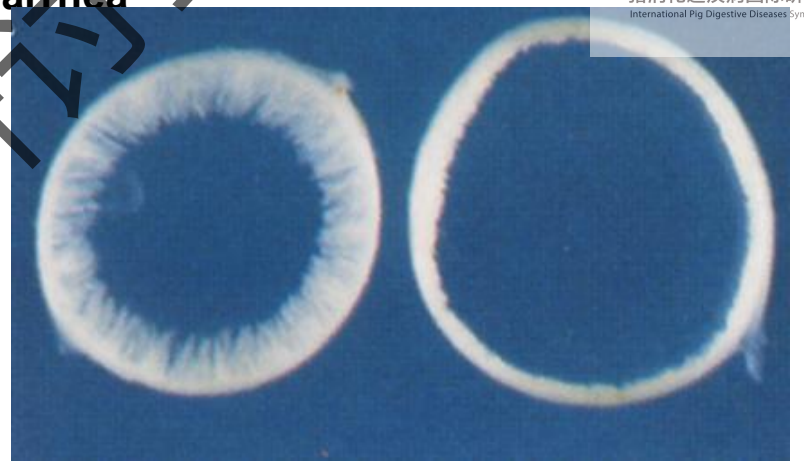
  Low maternal antibody levels (associated with porcine edema disease)

- 可导致肠粘膜损伤的疾病（病毒性腹泻如PED/轮状病毒）

  Diseases causing damage to intestinal mucosa (viral diarrhea such as PED/rotavirus)

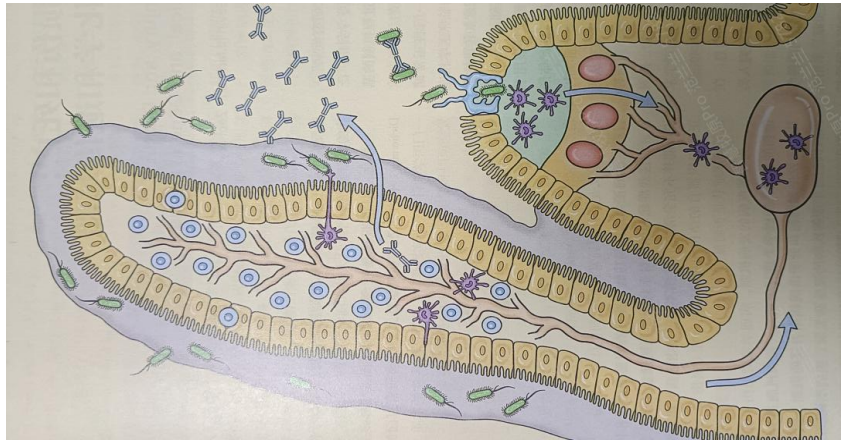
- 弱毒力的S-indel株的危害：可导致断奶仔猪与育肥猪

  Harm from low-virulence S-indel strains: Can lead to post-weaning piglets and growing-finishing



正常
Normal

PEDV引起的病变
Lesions caused by PEDV



轮状病毒引起肠绒毛萎缩导致大肠杆菌易侵入肠黏膜
Rotavirus-induced villous atrophy leading to increased susceptibility of Escherichia coli invasion of the intestinal mucosa

猪消化道疾病国际研讨会

6. 大肠杆菌流行现状：血清型多，多以致病性区分

6. Current Epidemiology of Escherichia coli: Varied serotypes, often distinguished by pathogenicity

- 按毒素分：产肠毒素（ETEC）、肠致病性（EPEC）、肠出血性（EHEC）、产志贺毒素大肠杆菌（STEC）、肠道外致病大肠杆菌（ExPEC）等，ETEC导致的腹泻和STEC导致的水肿病发病率最高；

  According to toxin classification: Enterotoxigenic Escherichia coli (ETEC), Enteropathogenic Escherichia coli (EPEC), Enterohemorrhagic Escherichia coli (EHEC), Shiga toxin-producing Escherichia coli (STEC), Extraintestinal pathogenic Escherichia coli (ExPEC), etc. Among them, ETEC is the most common cause of diarrhea and STEC is the most common cause of edema disease

- 按抗原分：荚膜抗原（K）、菌体抗原（O）、菌毛抗原（F）、鞭毛抗原（H）

  According to antigen classification: **Capsular antigen (K), Somatic antigen (O), Flagellar antigen (H)**

致病型 Pathogenic type	细菌细胞表面黏附素 Bacterial surface adhesins	毒素 Toxins	血清型 Serotypes	疾病 Diseases
产肠毒（ETEC） Enterotoxigenic Escherichia coli (ETEC)	F5 (K99)/F6 (/987P)/F41 F5 (K99)/F6 (/987P)/F41	STa STa	O8/O9/O20/O64/O101 O8/O9/O20/O64/O101	新生仔猪腹泻（黄白痢） Neonatal piglet diarrhea (yellow-white scours)
	F4（K88） F4（K88）	Sta/STb/LT/EAST-1/α-溶血素 Sta/STb/LT/EAST-1 /α-hemolysin	O8/O138/O141/O145/O147/O149/O157 O8/O138/O141/O145/O147/O149/O157	新生仔猪腹泻(黄白痢) Neonatal piglet diarrhea (yellow-white scours) 断奶后仔猪腹泻 Post-weaning piglet diarrhea
	F4（K88）/AIDA F4 (K88)/AIDA	Sta/STb/LT/EAST-1/α-溶血素 Sta/STb/LT/EAST-1/α-hemolysin	O8/O138/O139/O141/O147/O149/O157 O8/O138/O139/O141/O147/O149/O157	/ /
	F18/AIDA F18/AIDA	Sta/STb/LT/Stx/EAST-1 Sta/STb/LT/Stx/EAST-1	O8/O138/O139/O141/O147/O149/O157 O8/O138/O139/O141/O147/O149/O157	水肿病 Edema disease
肠出血性（EHEC） Enterohemorrhagic Escherichia coli (EHEC)	F5（K99）/F6（987P），F41、F4（K88）/Eae F5（K99）/F6（987P），F41、F4（K88）/Eae	STX2E/EAST1/α-溶血素 STX2E/EAST1/α-hemolysin AE因子 AE factor	O157/O26/O111 O157/O26/O111	/ /
肠致病性（EPEC） Enteropathogenic Escherichia coli (EPEC)	Eae（紧密黏附素） Eae (Intimin)		O45/O103 O45/O103	急性炎症反应 Acute inflammatory response
产类志贺毒素 (STEC) Shiga-like toxin-producing Escherichia coli (STEC)	F18/AIDA F18/AIDA	Stx2e/EAST-1/α-溶血素 Stx2e/EAST-1/α-hemolysin	O138/O139/O141/O147 O138/O139/O141/O147	便秘、水肿病 Constipation, edema disease
肠道外致病(ExPEC) Extraintestinal pathogenic E. coli (ExPEC)	P/S P/S	CNF CNF	O6/O8/O9/O11/O15/O17/O18/O20/O45/O60/O78/O83/O93/O101/O112/O115/O116 O6/O8/O9/O11/O15/O17/O18/O20/O45/O60/O78/O83/O93/O101/O112/O115/O116	大肠杆菌性败血症/多发性浆膜炎 Escherichia coli septicemia/polyserositis
	P/S	CNF	O1/O4/O6/O18	泌尿生殖感染

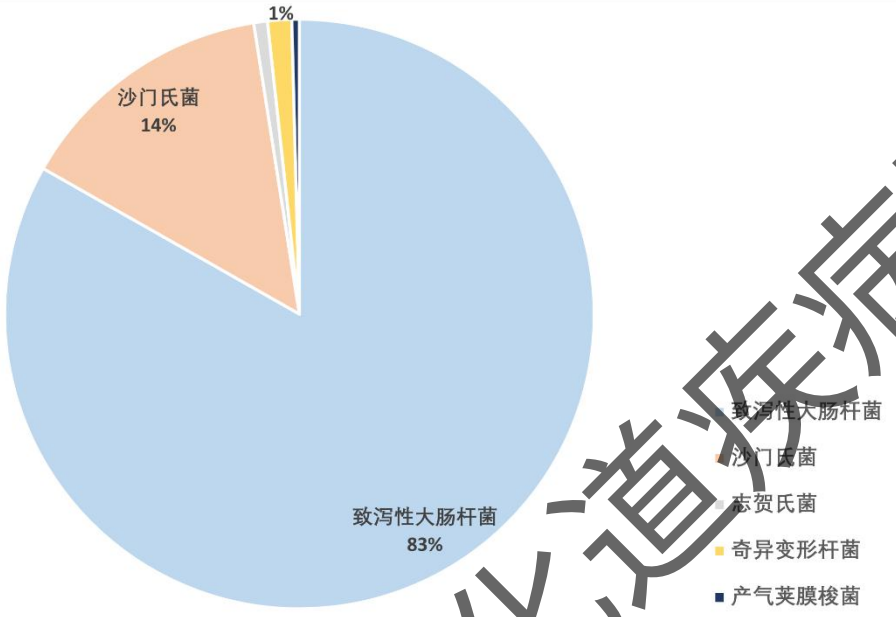
猪消化道疾病国际研讨会

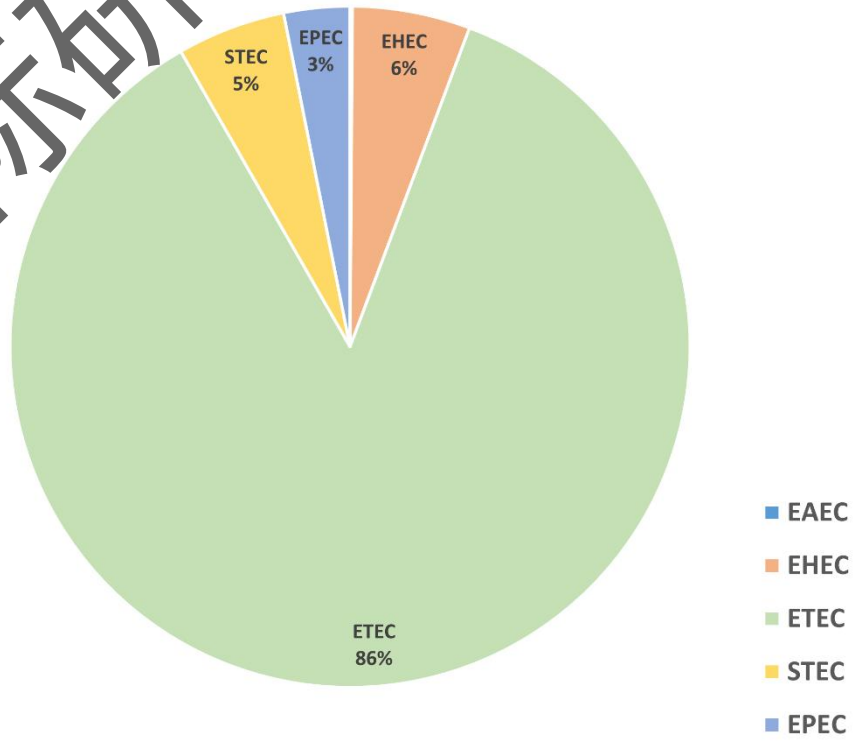
6. 大肠杆菌流行现状：致病大肠杆菌占比83%，其中ETEC占比86%

6. Current Epidemiology of Escherichia coli: Pathogenic Escherichia coli accounts for 83% of cases, with ETEC accounting for 86% of that proportion

数据来源：哈兽研动物细菌病创新团队张万江首席科学家（数据未公开）

Data source: Chief Scientist Zhang Wanjing from the Innovative Team for Animal Bacterial Diseases at Harbin Veterinary Research Institute (Data not publicly available)





EIEC：肠道侵袭性大肠埃希氏菌；EPEC：肠道致病性大肠埃希氏菌；ETEC：产肠毒素大肠埃希氏菌；STEC：产志贺毒素大肠埃希氏菌；

EIEC: Enteric Invasive Escherichia coli; EPEC: Enteropathogenic Escherichia coli; ETEC: Enterotoxin-producing Escherichia coli; STEC: Shiga Toxin-producing Escherichia coli;

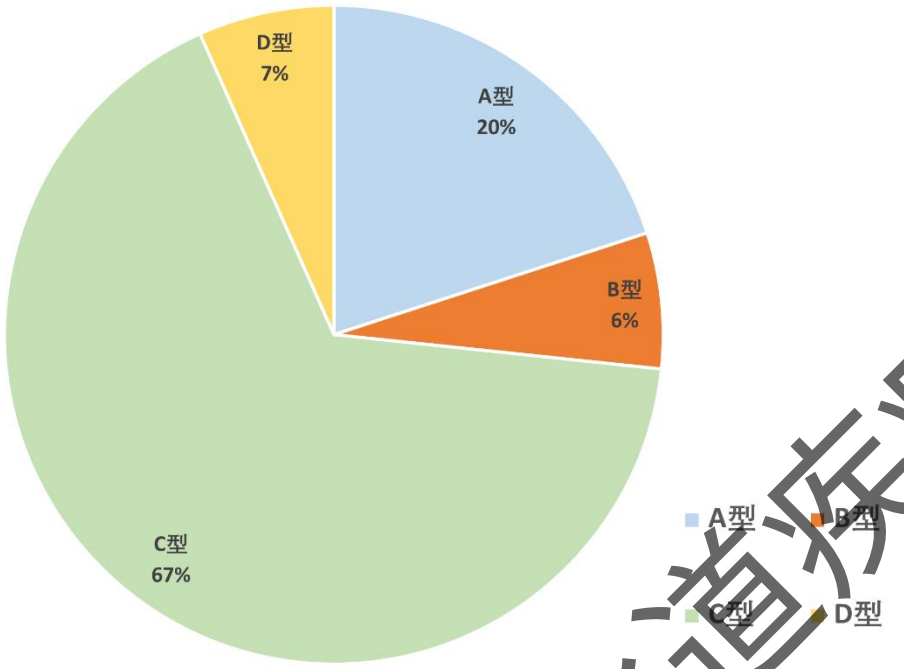
EHEC：肠道出血性大肠埃希氏菌；EAEC：肠道聚集性大肠埃希氏菌；

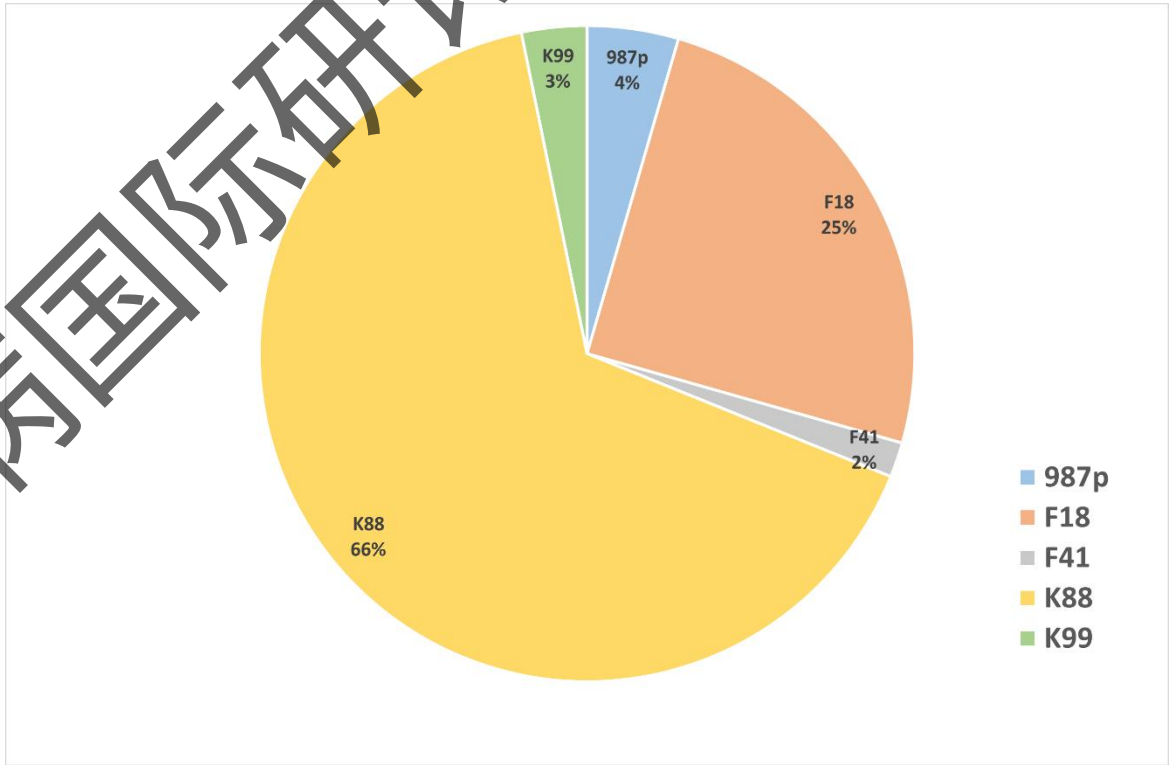
EHEC: Enterohemorrhagic Escherichia coli; EAEC: Enteroaggregative Escherichia coli;

猪消化道疾病国际研讨会

6. 大肠杆菌流行现状：C型占比67%，按抗原分型以K88和F18占比最高

6. Prevalence of E. coli: 67% of C-types, with K88 and F18 accounting for the highest percentage by antigenic typing





数据来源：哈兽研动物细菌病创新团队张万江首席科学家（数据未公开）

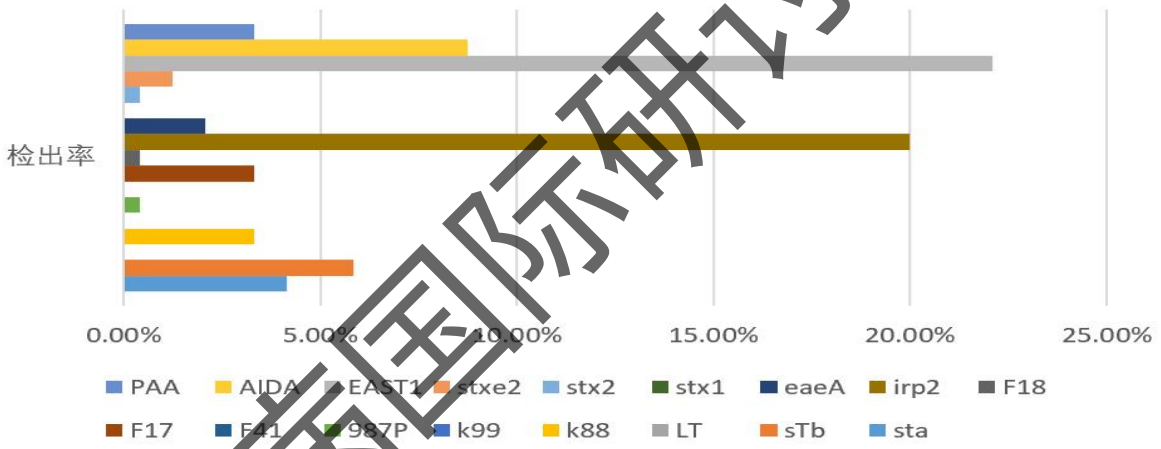
Data source: Chief Scientist Zhang Wanjing from the Innovative Team for Animal Bacterial Diseases at Harbin Veterinary Research Institute (Data not publicly available)

猪消化道疾病国际研讨会

6. 大肠杆菌病的流行病学：2023年信得共分离399株，鉴定242株的毒力基因

6. Epidemiology of Escherichia coli disease: a total of 399 strains were isolated and 242 strains were identified with virulence genes by Sinder in 2023

病料来源 Source of disease material	分离菌株数量（株） Number of strains isolated (strains)
山东某大学病料（山东、河北、河南区域） Disease material from a university in Shandong (Shandong, Hebei and Henan regions)	47 47
广东某集团 A group in Guangdong	41 41
屠宰场1 Slaughterhouse 1	8 8
屠宰场2 Slaughterhouse 2	18 18
浙江规模场 Zhejiang Scale Field	32 32
四川某集团养殖场1 Farm 1 of a group in Sichuan	38 38
四川某集团养殖场2 Farm 2 of a group in Sichuan	6 6
四川某集团场3 Farm 3 of a group in Sichuan	21 21
山东某集团场 A farm of a group in Shandong	3 3
福建某集团场1 Farm 1 of a group in Fujian	6 6
福建某集团场1 Farm 1 of a group in Fujian	5 5
山东聊城地区 Liaocheng prefecture in Shandong	26 26
四川某集团场4 Farm 4 of a group in Sichuan	15 15
潍坊区域 Weifang region	4 4
四川某集团养殖场5 Farm 5 of a group in Sichuan	5 5
四川某集团养殖场6 Farm 6 of a group in Sichuan	23 23
四川某集团养殖场7 Farm 7 of a group in Sichuan	5 5
福建某集团场8 Farm 8 of a group in Fujian	4 4
四川某集团养殖场8 Farm 8 of a group in Sichuan	2 2
江苏某集团 A group in Jiangsu	21 21
广西某集团 A group in Guangxi	69 69



毒力基因流行集中于携带EAST1、irp2、Sta/b、 AIDA这些毒力基因被K88、K99、F18、AIDA型所涵盖。
The prevalence of virulence genes is focused on virulence genes carrying EAST1, irp2, Sta/b, AIDA, which are covered by the K88, K99, F18, AIDA types.

毒力基因 Virulence gene	阳性菌株数量 Number of positive strains	毒力基因 Virulence gene	阳性菌株数量 Number of positive strains

数据来源：信得细菌病防控团队
Data source: Sinder Bacterial Disease Prevention and Control Team

猪消化道疾病国际研讨会

7. 流行现状：导致腹泻的菌株占比19.83%，以K88为主

7. Prevalence status: 19.83% of strains causing diarrhea, dominated by K88

菌株名 Strain names	携带毒力因子 Virulence factor carried	菌株名 Strain names	携带毒力因子 Virulence factor carried

03型仅在广西检出，08型仅在福建、四川有检出；07型在山东、四川检出较高。
Type O3 was detected only in Guangxi, and type O8 was detected only in Fujian and Sichuan; type O7 was detected at a higher level in Shandong and Sichuan.

血清型 Serotypes	数量 Number	百分比 Percentage
03 O3	1株 1	2.17% 2.17%
07 O7	24株 24	52.17% 52.17%
08 O8	6株 6	13.04% 13.04%
未定型菌株 Undetermined strains	15株 15	32.61% 32.61%

省份 Provinces	大肠菌株 Large intestine strains	腹泻菌株 Diarrhea strains	腹泻菌株分离率 Isolation rate of diarrhea strains
山东 Shandong	58 58	9 9	15.51% 15.51%
浙江 Zhejiang	10 10	3 3	30.00% 30.00%
福建 Fujian	21 21	5 5	23.80% 23.80%
广东 Guangdong	3 3	3 3	100% 100%
广西 Guangxi	18 18	2 2	11.11% 11.11%
四川 Sichuan	116 116	25 25	21.55% 21.55%
河北 Hebei	1 1	1 1	100% 100%

2023年冬季10-12月份细菌性腹泻病料数据分析
Analysis of bacterial diarrhea disease materials in October-December of winter 2023

- 腹泻型以 Stb、EAST1、AIDA（23.91%）和irp2、EAST1（13.04%）的毒力基因组合检出率高；
  The virulence gene combinations of Stb, EAST1, AIDA (23.91%) and irp2, EAST1 (13.04%) have a high detection rate in diarrhea type;
- 按抗原分腹泻病原以K88为主，血清型以07为主
  According to the antigen, the diarrhea pathogen is mainly K88, and the serotype is mainly 07

数据来源：信得细菌病防控团队
Data source: Sinder Bacterial Disease Prevention and Control Team

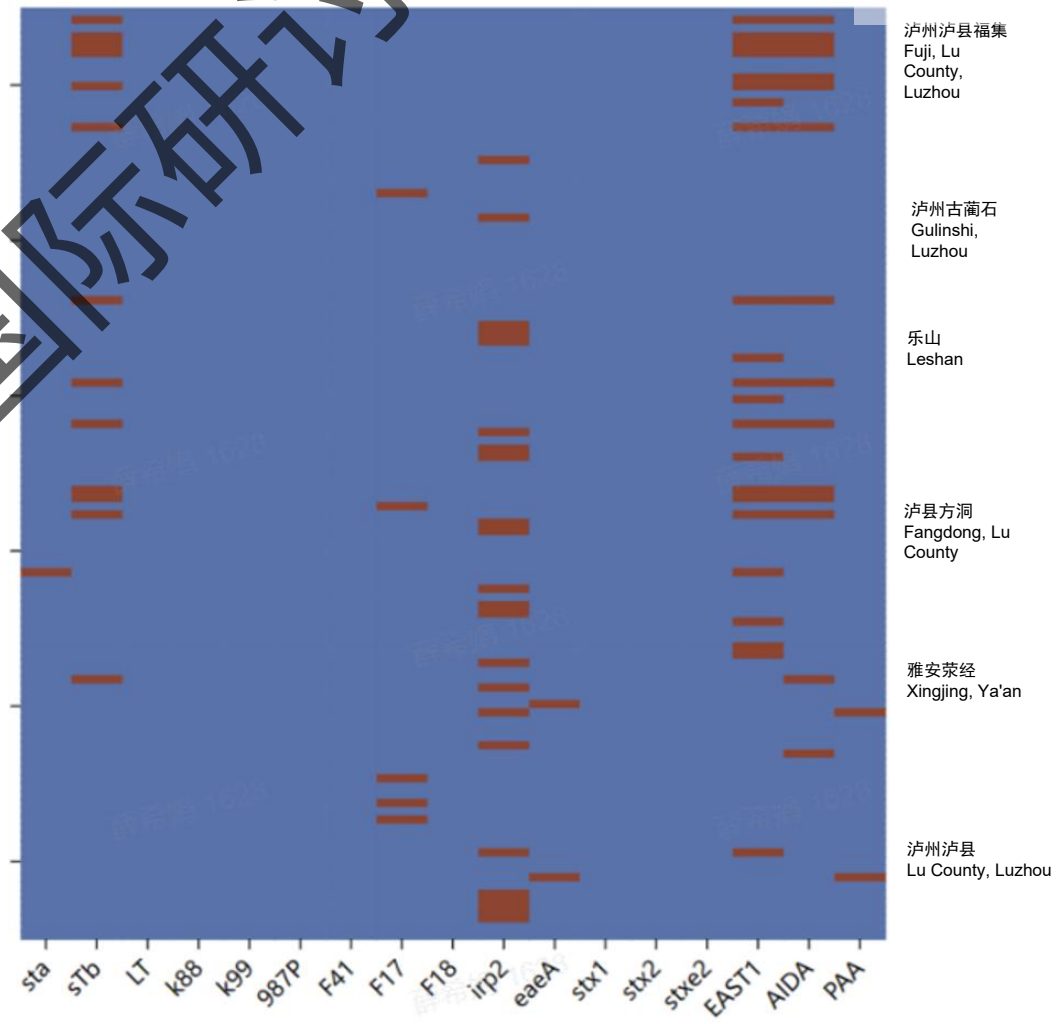
猪消化道疾病国际研讨会

8. 四川某集团流行病学调查：以携带STb、irp2、EAST1、AIDA
8. An epidemiological survey of a group in Sichuan: carrying STb, irp2, EAST1 and AIDA.

收样时间 Sample collection time	送检地址 Delivery address	病料数量 Number of disease material	大肠杆菌检出率 E. coli detection rate
23.10.26 23.10.26	**泸州泸县福集 **Fuji, Lu County, Luzhou	40份 40	95% 95%
23.10.27 23.10.27	**泸州古蔺石宝 **Shibao, Gulin, Luzhou	6份 6	100% 100%
23.10.27 23.10.27	**乐山** **Leshan**	18份 18	100% 100%
23.11.04 23.11.04	**乐山** **Leshan**	3份 3	100% 100%
23.11.10 23.11.10	**乐山** **Leshan**	2份 2	0% 0%
23.11.28 23.11.28	**泸州泸县方洞 **Fangdong, Lu County, Luzhou	15份 15	100% 100%
23.12.04 23.12.04	**雅安荥经县 **Xingjing County, Ya'an	9份 9	100% 100%
23.12.04 23.12.04	**泸州泸县 **Lu County, Luzhou	27份 27	88.89% 88.89%
23.12.16 23.12.16	**乐山** **Leshan**	5份 5	100% 100%

检测显示仔猪腹泻大肠杆菌主要携带STb、irp2、EAST1、AIDA组合型毒力因子导致仔猪腹泻，少部分菌株携带F17致使腹泻。

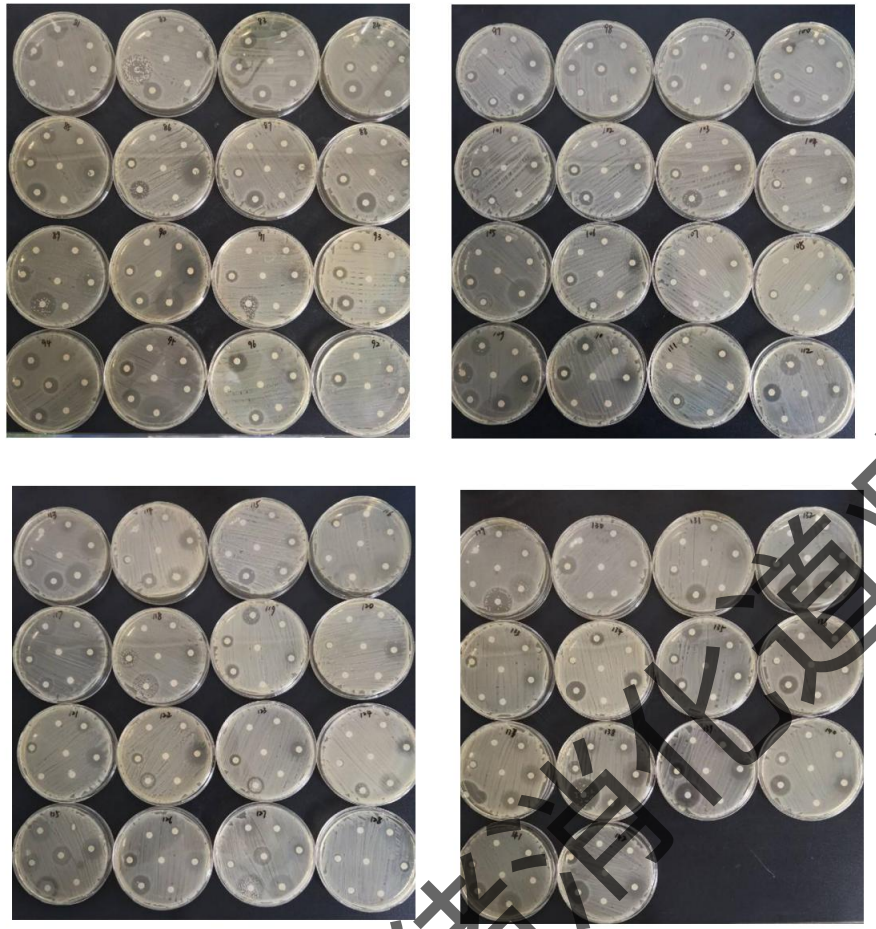
The test showed that piglet diarrhea E. coli mainly carries combined virulence factors including STb, irp2, EAST1 and AIDA, leading to piglet diarrhea, and a small number of strains carry F17 leading to diarrhea.



猪消化道疾病国际研讨会

9. 四川某集团大肠杆菌耐药性分析：对抗生素普遍不敏感，常用抗生素耐药

9. Drug resistance analysis of E. coli in a group in Sichuan: general insensitivity to antibiotics and resistance to commonly used antibiotics



对该集团的23年11月份的分离猪大肠杆菌菌株，集中进行耐药性检测，对抗生素普遍耐药

The group's isolates of swine E. coli strains on November 23 were centrally tested for resistance a

抗生素种类 Types of antibiotics	耐药 Drug-resistance	敏感 Sensitivity	耐药率 Drug-resistance rate
磺胺间甲氧嘧啶钠 Sulfamethoxypyrimidine sodium	54 54	8 8	87. 1% 87.1%
泰妙菌素 Tiamulin	43 43	19 19	69. 4% 69.4%
替米考星 Tilmicosin	61 61	1 1	98. 4% 98.4%
氟苯尼考 Florfenicol	49 49	13 13	79% 79%
多西环素 Doxycycline	40 40	22 22	64. 5% 64.5%
恩诺沙星 Enrofloxacin	29 29	33 33	**46. 8% 46.8%**
阿莫西林 Amoxicillin	60 60	2 2	96. 8% 96.8%

猪消化道疾病国际研讨会

四川省猪、鸡源大肠杆菌对抗生素耐药性研究

Study on antibiotic resistance of Escherichia coli from pig and chicken sources in Sichuan Province, China

四川省猪、鸡源大肠杆菌对抗生素耐药性研究

岳秀英[1]，葛　荣[1]，吴晓岚[1]，陆　强[1]，孙　吉[1]，宁宜宝[2]，邹立扣[3]

（1. 四川省兽药监察所，四川 成都 610041；2. 中国兽医药品监察所，北京 海淀 100081；
3. 四川农业大学，四川 都江堰 611830）

摘要：对四川省 2009－2014 年共 2 954 株猪、鸡源大肠杆菌进行 13 种抗生素耐药性测定，同时对耐头孢噻呋大肠杆菌及 O_{157} 菌株耐药基因进行检测。结果表明：大肠杆菌对抗生素耐药谱广，多重耐药严重。大肠杆菌对抗生素耐药率呈逐年波动下降趋势，猪源大肠杆菌对抗生素耐药率总体耐药率为 40.40% ~92.32%，抗生素耐药率依次为：TET（92.32%）> SIZ（91.96%）> AMP（91.25%）> SXT（87.56%）> DO（77.67%）> FFC（73.97%）> SH（69.91%）> EN（66.00%）> AMC（61.10%）> OFX（59.39%）> CN（57.82%）> PME（42.53%）> CEF（40.40%）。鸡源大肠杆菌对抗生素的总体耐药率为 9.17% －89.41%，抗生素耐药率依次为：SIZ（89.41%）> AMP（85.01%）> SXT（83.40%）> TET（83.01%）> EN（72.03%）> OFX（63.37%）> AMC（62.14%）> DO（58.90%）> FFC（55.10%）> SH（50.52%）> CEF（46.9%）> CN（33.91%）> PME（9.17%）。2009 年－2014 年猪源大肠杆菌耐药率总体高于鸡源大肠杆菌。研究表明，监测大肠杆菌的抗生素耐药性对动物的养殖、疾病的预防及耐药性的控制有着重要意义。

磺胺类（87. 56%～91. 96%）＞青霉素类（91. 25%）＞四环素类（77. 67%～92. 32%）＞氯霉素类（73. 97%）＞氟喹诺酮类 （59. 39%～66%）＞氨基糖苷类（57. 82%～69. 91%）＞加酶抑制剂类（61. 10%）＞多黏菌素类（42. 53%）＞头孢类（40. 40% ）。

Sulfonamides (87.56%-91.96%) > Penicillins (91.25%) > Tetracyclines (77.67%-92.32%) > Chloramphenicol (73.97%) > Fluoroquinolones (59.39%-66%) > Aminoglycosides (57.82%-69.91%) > Addition enzyme inhibitors (61.10%) > Polymyxins (42.53%) > Cephalosporins (40.40%) .

Table 1 Resistance of *Escherichia coli* isolates originating from faecal samples of healthy cattle and swine and clinical submissions collected from 2010 to 2015 in Estonia

Antimicrobial	Cut-off values for resistance (mg/L)*	Healthy animals				Diagnostic submissions			
		Dairy cattle (n = 171)		Swine (n = 120)		Dairy cattle (n = 63)		Swine (n = 143)	
		%	(95% CI)	%	(95% CI)	%	95% CI	%	95%
Ampicillin*H	> 8	3.5	*(0.8 to 6.3)*	21.5	*(14.3 to 29.1)*	58.7	(46.5 to 70.9)	53.9	(45.7 to 62.1)
Cephotaxime	> 0.5	1.2	(−0.4 to 2.8)	2.5	(−0.3 to 5.3)	7.9	(1.2 to 14.6)	4.2	(0.9 to 7.5)
Cephazidime	> 0.5	2.9	(0.4 to 5.4)	3.3	(0.1 to 6.5)	7.9	(1.2 to 14.6)	7.7	(3.3 to 12.1)
Streptomycin*H	> 16	7.0	*(3.2 to 10.8)*	*39.2*	*(30.5 to 40.8)*	63.5	(51.6 to 6.4)	54.6	(46.4 to 62.8)
Gentamycin*D	> 4	7.0	(3.2 to 10.8)	12.5	(6.6 to 18.4)	*20.6*	*(10.6 to 30.6)*	*5.6*	*(1.8 to 9.4)*
Kanamycin	> 16	8.8	(4.6 to 13.1)	10.0	(4.6 to 15.4)	0.0	NA	0.0	NA
Ciprofloxacin*H	> 0.06	*0.6*	*(−0.6 to 1.8)*	*5.8*	*(1.6 to 10.0)*	38.1	(26.1 to 50.1)	32.2	(24.5 to 39.9)
Nalidixic acid*D	> 16	0.6	(−0.6 to 1.8)	3.3	(0.1 to 6.5)	*17.5*	*(8.1 to 26.9)*	*32.2*	*(24.5 to 39.9)*
Tetracycline*H	> 8	*7.0*	*(3.2 to 10.8)*	*32.5*	*(24.1 to 40.9)*	58.5	(46.3 to 70.7)	60.2	(52.2 to 68.3)
Colistin*H	> 2	*2.4*	*(0.1 to 4.7)*	*11.6*	*(5.9 to 17.3)*	3.2	(−1.6 to 7.6)	5.6	(1.8 to 9.4)
Chloramphenicol	> 16	2.4	(0.1 to 4.7)	5.8	(1.6 to 10.0)	9.5	(2.3 to 16.7)	18.2	(11.9 to 24.5)
Florfenicol	> 16	0.0	NA	0.8	(−0.8 to 2.4)	0.0	NA	0.7	(−0.7 to 2.1)
Trimethoprim*H	> 2	*3.5*	*(0.8 to 6.3)*	*22.4*	*(14.9 to 29.9)*	55.6	(43.3 to 67.9)	53.9	(45.7 to 62.1)
Sulfamethoxazole*H	> 64	*4.7*	*(1.5 to 7.9)*	*30.0*	*(21.8 to 38.2)*	60.3	(48.2 to 70.4)	68.5	(60.1 to 76.1)

* Swedres-Svarm 2015. Consumption of antibiotics and occurrence of antibiotic resistance in Sweden. Solna/Uppsala ISSN 1650-6332, 117, Table 2.17

*H and *D Statistically significant difference (P < 0.05) between healthy dairy cattle and swine, and between dairy cattle's and swine's clinical submissions. Corresponding percentages are also presented in italic face

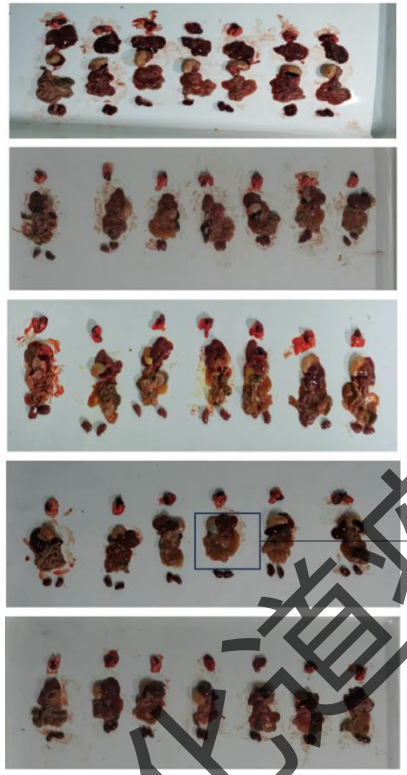
Escherichia coli isolates from clinical submission showed the most prevalent resistance against sulfameth oxazole (68.6%), tetracycline (60.2%), streptomycin (54.6%), ampicillin (53.9%) and trimethoprim (53.9%). E. coli isolates from cattle clinical submissions were also mainly resistant to streptomycin (63.5%), sulfamethoxa_x0002_zole (60.3%), tetracycline (58.8%), ampicillin (58.7%) and trimethoprim (55.6%) (Table 1).

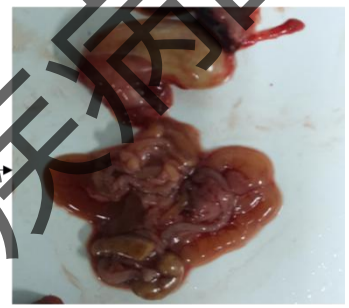
Escherichia coli isolates from clinical submission showed the most prevalent resistance against sulfameth oxazole (68.6%), tetracycline (60.2%), streptomycin (54.6%), ampicillin (53.9%) and trimethoprim (53.9%). E. coli isolates from cattle clinical submissions were also mainly resistant to streptomycin (63.5%), sulfamethoxa_x0002_zole (60.3%), tetracycline (58.8%), ampicillin (58.7%) and trimethoprim (55.6%) (Table 1).

猪消化道疾病国际研讨会

10. 四川某集团大肠杆毒力分析：毒力为中高等毒力

10. Virulence analysis of Escherichia coli from a group in Sichuan: The virulence is medium and high





菌株 Strains	半数致死量 Half lethal dose	毒力基因 Virulence gene
菌株1 Strain 1	1.338×10^{9}cfu 1.338×109cfu	Stb/EAST1/AIDA+ Stb/EAST1/AIDA+
菌株2 Strain 2	1.23×10^{9}cfu 1.23×109cfu	Stb/EAST1/AIDA+ Stb/EAST1/AIDA+
菌株3 Strain 3	8.91×10^{8}cfu 8.91×108cfu	F17+ F17+
菌株4 Strain 4	3.55×10^{9}cfu 3.55×109cfu	Stb/EAST1/AIDA+ Stb/EAST1/AIDA+
菌株5 Strain 5	3.16×10^{9}cfu 3.16×109cfu	Stb/EAST1/AIDA+ Stb/EAST1/AIDA+

选取部分四川地区分离仔猪腹泻菌株采用昆明小鼠，分组进行了动物实验评估毒力，死亡小鼠剖检可见肠壁变薄水肿透明，内有黄色粘液，并得出腹泻菌株的半数致死量。

Some strains of diarrhea isolated from piglets in Sichuan area were selected and animal experiments were conducted to assess the virulence using groups of Kunming mice, and autopsy of dead mice revealed a thin, oedematous and transparent intestinal wall with yellow mucus, and yielded an LD50 for the diarrhea strain.

猪消化道疾病国际研讨会

二、致病性大肠杆菌的防控措施
II. Prevention and control measures for pathogenic E. coli

猪消化道疾病国际研讨会

1. 致病大肠杆菌的防控措施

1. Preventive and control measures for pathogenic E. coli

- 降低传染源：受污染的水源和饲料、栏位的刷洗
  Reducing sources of infection: contaminated water and feed, pen brushing
- 避免冷应激：过高的体表风速、转群应激、高湿
  Avoid cold stress: excessive body surface wind speed, pig transfer stress, high humidity
- 消灭传染源：筛选噬菌体环境消杀或噬菌体治疗
  Elimi ening phage for environmental disinfection or phag
- 提高 猪免疫
  Impr on of sows (especially gilts) immunization of pigle

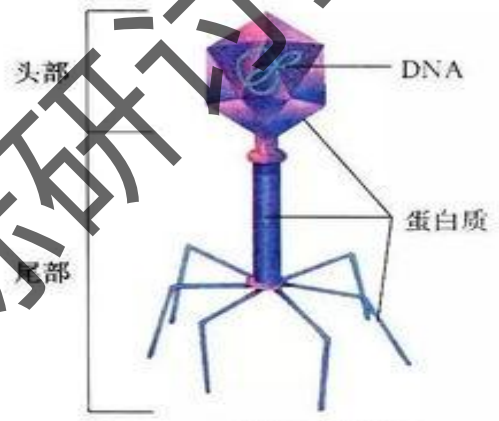
抗菌药物的使用
Use of antimicrobial drugs

多重耐药
Multi-drug resistance

治疗效果下降
Decline in treatment ness

食品安全要求
Food safety requirements

公共卫生安全
Public health security



无处不在的噬菌体
phage are everywhere

2015年，《遏制细菌耐药国家行动计划（2016-2020年）》
In 2015, National Action Plan to Curb Bacterial Resistance (2016-2020)

2017年，《全国遏制动物源细菌耐药性行动计划（2017-2020年）》
In 2017, National Action Plan to Curb Antimicrobial Resistance of Animal-derived Bacteria (2017-2020)

2018年，《农业农村部办公厅关于开展兽药抗菌药物减量化行动试点工作的通知》
In 2018, Notice of the General Office of the Ministry of Agriculture and Rural Affairs on Carrying out the Pilot Work of Reducing Antimicrobial Drugs for Veterinary Drugs

2019年，第194号公告，自2020年1月1日起，在养殖业中退出除中药外的所有促生长类药物饲料添加剂品种。
In 2019, Proclamation No. 194, as of January 1, 2020, all growth promoting drug feed additive varieties except traditional Chinese medicine would be withdrawn from the farming industry.

猪消化道疾病国际研讨会

2. 噬菌体技术路线：建立噬菌体库，从污水和病料中分离噬菌体

2.Phage technique route: establishing a phage bank and isolating phage from sewage and diseased material.

- 噬菌体：是一类感染细菌、放线菌、支原体、蓝细菌等微生物的细菌病毒的总称，又被称为细菌病毒。

Phage: a general term for a class of bacteriophages that infect microorganisms such as bacteria, actinomycetes, mycoplasmas, cyanobacteria, etc., also known as **bacteriophages**.

- 生物圈10^{30}~10^{32}个噬菌体；10^{23}个噬菌体感染细菌/s；

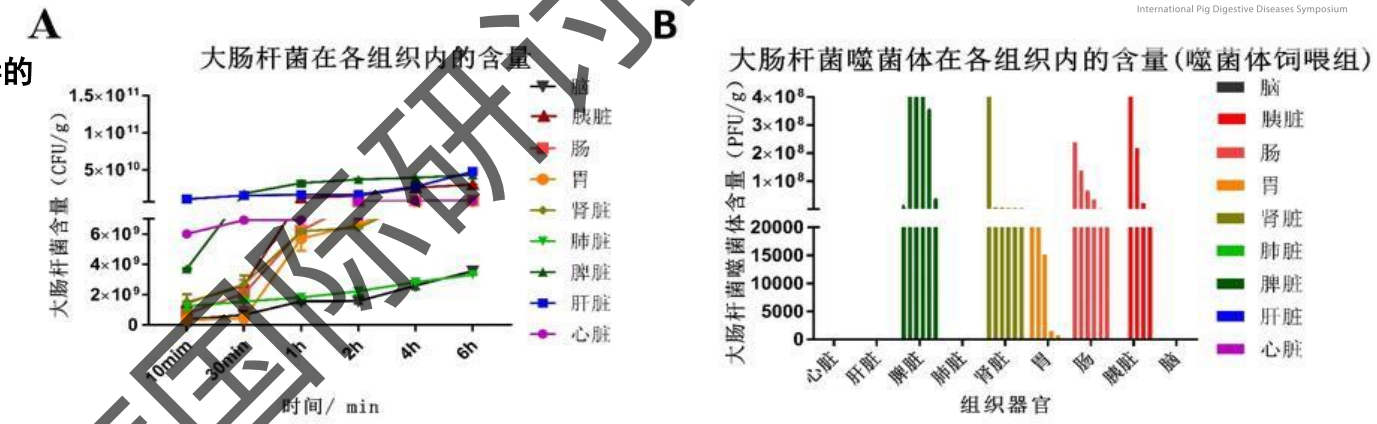
The biosphere contains 10^{30}~10^{32}phages；10^{23}phages infect bacteria per second.

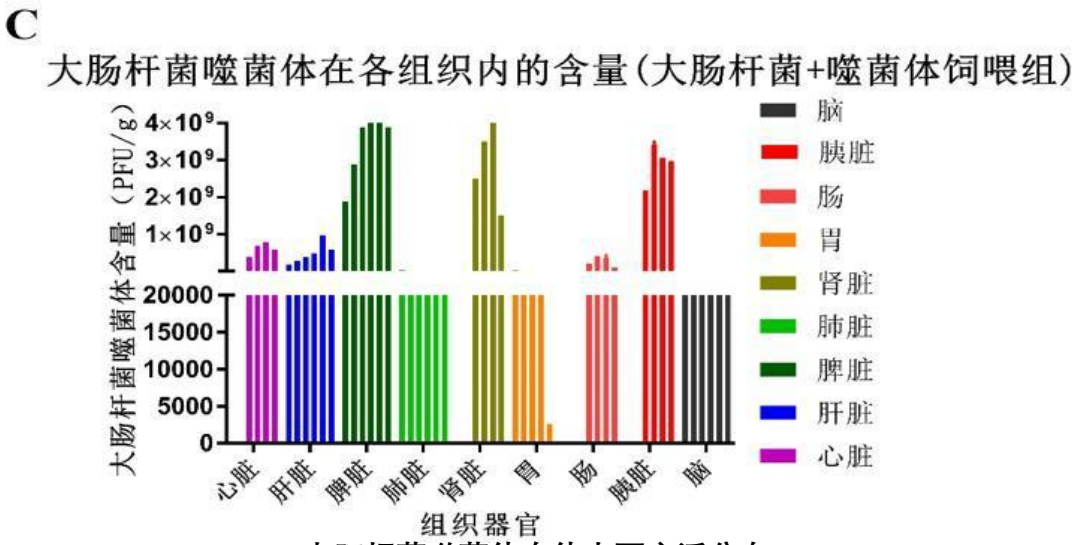
- 噬菌体吃掉全球一半的细菌/48h

phage consume half of the global bacteria per 48 hours.

- 噬菌体是细菌的“天敌”，噬菌体与抗生素具有协同作用（抗生素破坏细胞壁后有利于噬菌体裂解酶发挥裂解作用）

phage are the 'natural enemies' of bacteria, and they have a synergistic effect with antibiotics (the disruption of the cell wall by antibiotics





大肠杆菌噬菌体在体内可广泛分布

Coliphage can be widely distributed in the body

猪消化道疾病国际研讨会

2. 噬菌体技术路线：建立噬菌体库，可从污水和病料中分离噬菌体

2.Phage technique route: establishing a phage bank and isolating phage from sewage and diseased material.

噬菌体分类 Classification of phage	数量 Number	占比 Proportion
广谱噬菌体 Broad-spectrum phage	15 15	12. 39% 12.39%
＞10*9的噬菌体 ＞10*9 phage	51 51	42. 15% 42.15%
＞10*10的噬菌体 ＞10*10 phage	38 38	31. 40% 31.40%
＞10*8的噬菌体 >10*8 phage	17 17	14. 04% 14.04%

- 仔猪腹泻噬菌体121株，分离自山东、四川、福建的污水，对应覆盖其各省分离的病原菌。
  There are 121 strains of phage that cause diarrhea in piglets, isolated from sewage in Shandong, Sichuan, and Fujian, corresponding to the pathogenic bacteria isolated from each province.
- 交叉筛选验证覆盖目前腹泻菌株库存率为85. 30%。
  Cross-screening validation shows that the current inventory rate of diarrhea strains is 85.30%.
- 噬菌体筛选到生产周期短，1个月可完成：筛选→配型→生产→检验
  The entire process from phage screening to production is relatively short, and can be completed within one month: screening → matching → production → inspection.

猪消化道疾病国际研讨会

2. 噬菌体技术路线：环境消杀，噬菌体+抗生素

2.Technical route for phage therapy： environmental disinfection, the combination of phage +antibiotics

- 预防的使用方法：环境喷洒，超声雾化消杀

  Usage of prevention: spraying in the environment, ultrasonic atomization disinfection

- 治疗的使用方法：灌服，严重时添加抗生素

  Usage of treatment: oral gavage, antibiotics added in severe cases.

不同抗生素+噬菌体对某集团客户大肠杆菌MIC对比结果
Comparative results of different antibiotics and phage against E. coli MIC for a group of clients

菌株编号/药物 Strain Number/Drug	阿莫西林粉 Amoxicillin Powder	大观林可 Spectinomycin Hydrochloride and Lincomycin Hydrochloride	多西环素 Doxycycline	金霉素 Chloramphenicol	阿莫西林粉+噬菌体 Amoxicillin Powder+ bacteriophages	大观林可+噬菌体 Spectinomycin Hydrochloride+ Lincomycin Hydrochloride and bacteriophages	多西环素+噬菌体 Doxycycline + bacteriophages	金霉素+噬菌体 Chloramphenicol +bacteriophages

世界提高抗菌药物认识周
World Antimicrobial Awareness Week

人畜+病原菌+抗生素
=抗药性

处方：噬菌体+抗生素
→协同抗菌药理学
=降低抗药性

噬菌体协同抗生素遏制抗药性

山东省兽医抗药性监测网
山东农学会噬菌体专业委员会

噬菌体+抗生素，协同作用明显，MIC值提高10-100倍

The synergistic effect of bacteriophages and antibiotics is evident, resulting in a significant increase in MIC values by 10 to 100 times.

猪消化道疾病国际研讨会

3. 免疫技术路线：新建群/后备免疫，仔猪根据发病时间调整免疫程序

3.Immunization technique route: establishing new herd/reservoir immunization, adjusting the immunization program for piglets based on the time of disease outbreak

- 后备猪群免疫：驯化，降低头胎次的黄白痢的损失
  Immunization of gilt herds: domestication to reduce the loss of yellow and white scours in the first litter.
- 产房仔猪腹泻：母仔同免，提升母抗与仔猪保护率
  Piglet diarrhea in the farrowing house: simultaneous immunization of sows and piglets to enhance the protection rate of maternal antibodies and piglets.
- 断奶后水肿病：仔猪免疫，减少水肿病急性致死率
  Post-weaning edema disease: immunization of piglets to reduce the acute fatality rate of edema disease.
- 肠可净（仔猪大肠埃希氏菌病三价灭活疫苗）
  Escherichia Coli Trivalent Vaccine for Piglets，Inactivated
- 高母源抗体防止仔猪的黄白痢－含有K88、K99、987P纤毛抗原－医用级铝胶佐剂，抗体产生更快更高
  High levels of maternal antibodies prevent yellow and white scours in piglets - containing K88, K99, and 987P fimbrial antigens - medically graded aluminum hydroxide adjuvant for faster and higher antibody production.
- 效价高－用RIHA（反向间接血凝）测定抗原效价，K88及K99抗原≥40X，987P≥160X
  High potency - antigenic potency measured by RIHA (Reverse Indirect Haemagglutination), K88 and K99 antigens ≥40X, 987P ≥160X

猪消化道疾病国际研讨会

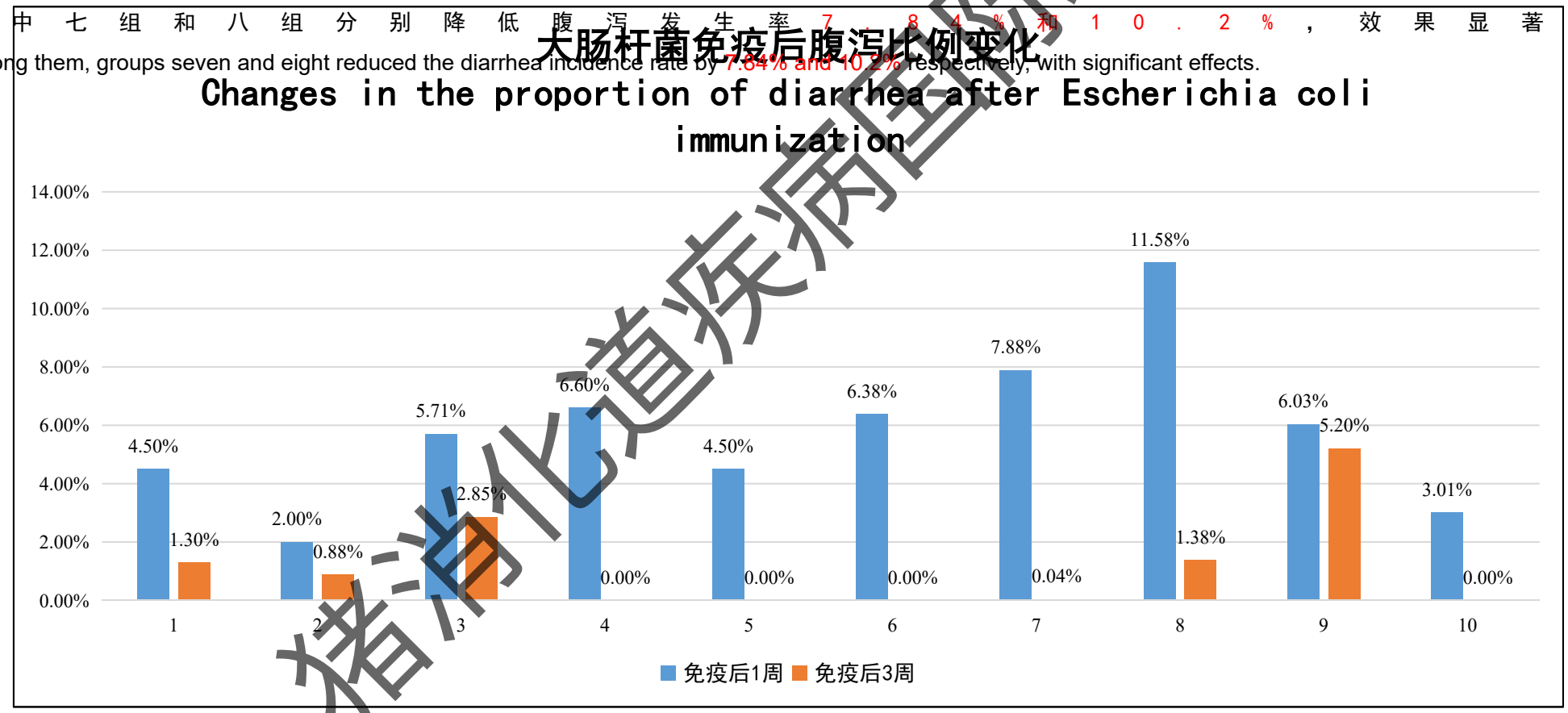
肠可净临床试验-保育猪
Clinical Trial of Escherichia Coli Trivalent Vaccine for Newborn Piglets, Inactivated - Nursery Pigs

- 疫苗免疫1周后，腹泻猪只为886头，腹泻发生率为7.15%，疫苗免疫3周后，腹泻猪只数量为155头，腹泻发生率为1.6%；疫苗免疫3周后比免疫1周后腹泻发生率降低为5.55%，疫苗免疫3周后对腹泻发生率的降低效果显著。

  One week after vaccine immunization, the number of pigs with diarrhea was 886, with a diarrhea incidence rate of 7.15%. Three weeks after vaccine immunization, the number of pigs with diarrhea decreased to 155, with a diarrhea incidence rate of 1.6%. Compared to one week after immunization, the diarrhea incidence rate decreased by 5.55% three weeks after immunization, indicating a significant effect of the vaccine in reducing the occurrence of diarrhea.

- 其中七组和八组分别降低腹泻发生率7.84%和10.2%，效果显著。

  Among them, groups seven and eight reduced the diarrhea incidence rate by 7.84% and 10.2% respectively, with significant effects.

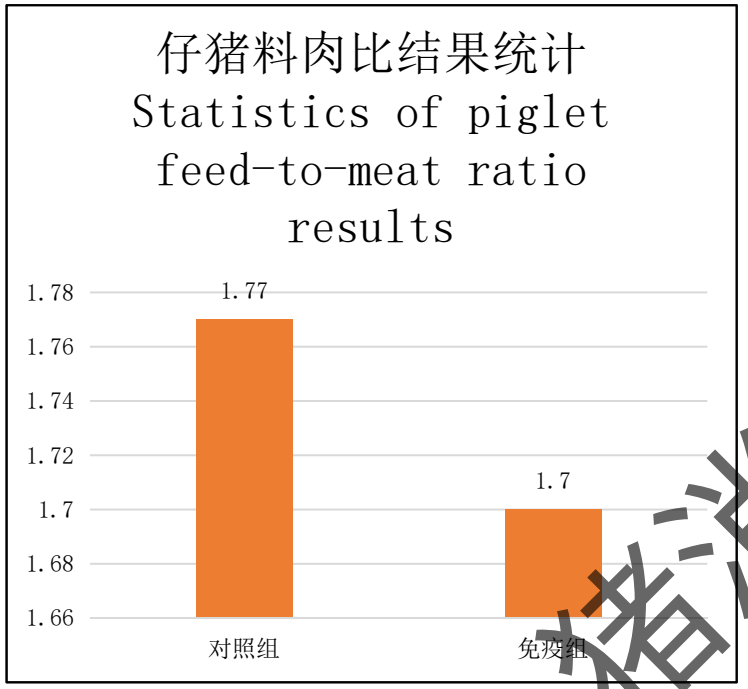


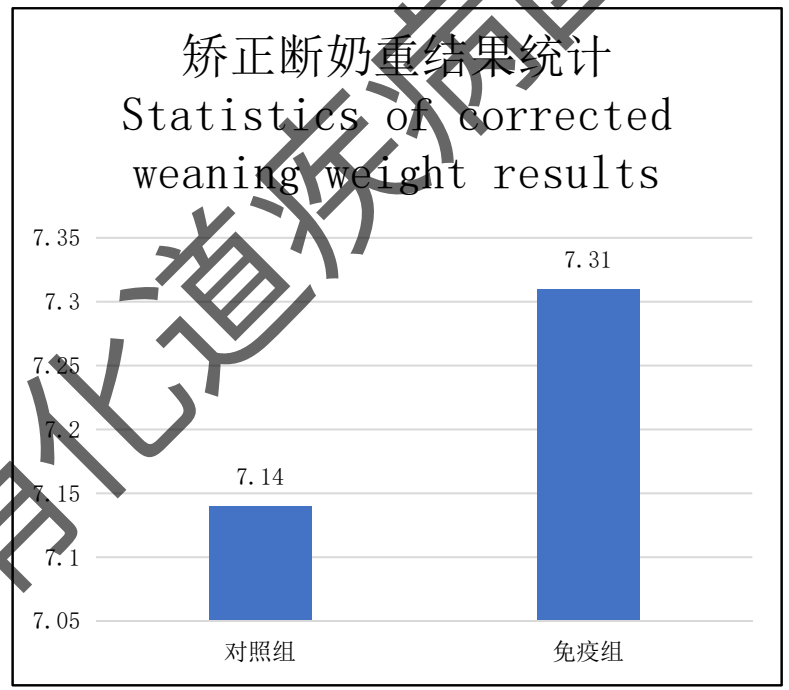
猪消化道疾病国际研讨会

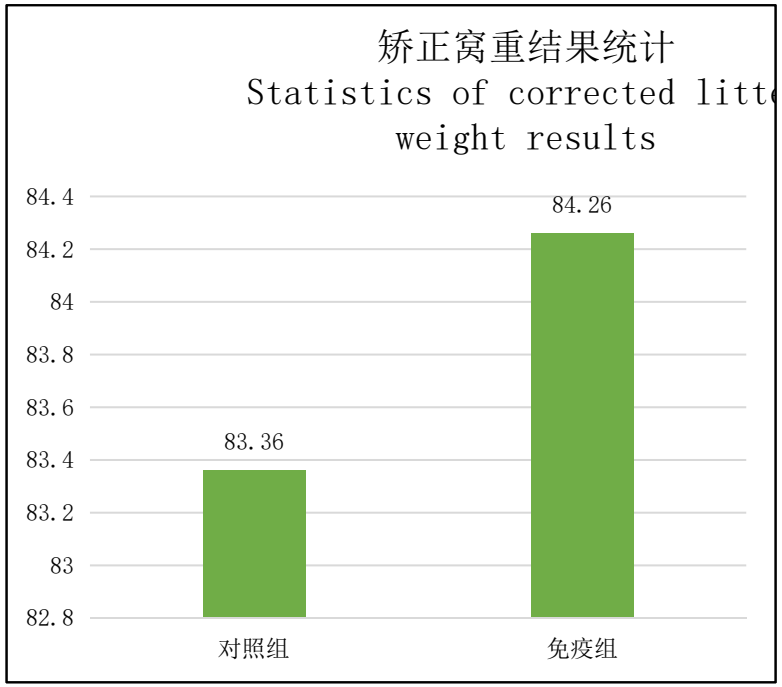
肠可净临床试验—哺乳仔猪
Clinical trial of Escherichia Coli Trivalent Vaccine for Newborn Piglets, Inactivated——lactating piglets

- 本次大肠杆菌免疫试验选择2个猪场共计7个批次，免疫程序为产前40d和产前20d免疫2针，免疫后观察仔猪出生后的临床效果，并统计各批次生产成绩，如下图。
  For this immune trial of Escherichia coli, a total of 7 batches from 2 pig farms were selected. The immunization program involved two shots, one at 40 days before birth and another at 20 days before birth. After immunization, the clinical effects on piglets after birth were observed, and the production performance of each batch was recorded, as shown in the following figure.

- 使用后腹泻率降低效果较好。统计批次结束成绩发现：仔猪料肉比降低约0.07，仔猪断奶矫正重提升0.17kg，仔猪断奶矫正窝重提升0.9kg。
  The use of the product has achieved good results in reducing diarrhea rates. According to the statistics of the batches' end results, it was found that the feed-to-meat ratio of piglets decreased by approximately 0.07, the corrected weaning weight of piglets increased by 0.17kg, and the corrected litter weight of piglets at weaning increased by 0.9kg.







猪消化道疾病国际研讨会

SINDER 信得 HILE 海利
猪消化道疾病国际研讨会
International Pig Digestive Diseases Symposium

三、大肠杆菌的防控的技术储备

三. Technical Stockpile for Prevention and Control of Escherichia coli

猪消化道疾病国际研讨会

1. 噬菌体的软硬件技术储备

1.Software and hardware technology stockpile for

畜禽致病菌及其噬菌体库	畜禽致病菌致病机理	噬菌体与宿主菌作用机制	噬菌体生物制品研发

噬菌体改造	生物信息学平台

- 动物致病性细菌的分离与鉴定，细菌病原菌库建设；
  Isolation and identification of animal pathogenic bacteria, and establishment of bacterial pathogen banks;
- 噬菌体分离鉴定及生物学特性研究，噬菌体库建设；
  Isolation, identification and biological characterisation of phage, phage bank construction;
- 对噬菌体分析和改造，拓宽其宿主谱，提升裂解率；
  Analyzing and modifying bacteriophages to broaden their host range and enhance lysis efficiency.
- 猪的菌种库与噬菌体库：
  Strain and phage banking in pigs:
- 猪大肠杆菌、梭菌、**猪巴氏杆菌、波氏杆菌、副猪嗜血杆菌、传染性胸膜放线杆菌、链球菌、猪葡萄球菌、沙门噬菌**
  Swine Escherichia coli, Clostridium, Pasteurella multocida, Bordetella bronchiseptica, Haemophilus parasuis, Actinobacillus pleuropneumoniae, Streptococcus, Staphylococcus hyicus, Salmonella

猪消化道疾病国际研讨会

信得-聊大噬菌体研究中心50多人团队
The Xinde-Liaocheng University Bacteriophage Research Center has a team of over 50 people.

2. 噬菌体生产条件：按GMP活菌疫苗线生产，避免污染风险

2. Production conditions for bacteriophages: manufactured according to the GMP live vaccine production line to avoid the risk of contamination.

- 全国最大的冻干车间性价比最优的冻干保护剂粉剂更稳定

  The largest freeze-drying workshop in the country offers the most cost-effective freeze-drying protectant powder for greater stability.

- 拥有50L、100L、200L、2T、10T不同发酵体系，满足不同菌株、不同客户的噬菌体发酵需求；在局部百级的洁净区灌装，保证产品无菌，保证噬菌体发酵效价>10^9PFU/ml

  We possess various fermentation systems ranging from 50L, 100L, 200L, 2T to 10T, meeting the needs of different strains and customers for bacteriophage fermentation. The filling is conducted in local clean zone with cleanliness class 100 to ensure sterility of the products and a bacteriophage fermentation titer greater than 109PFU/ml.

猪消化道疾病国际研讨会

猪消化道疾病国际研讨会
International Pig Digestive Diseases Symposium

3. 大肠杆菌疫苗生产工艺

3. Production process of Escherichia coli vaccine

1 种子细胞初级放大 Primary amplification of seed cells

2 种子细胞二级、三级放大 Secondary and tertiary amplification of seed cells

3 抗原液的制备 Preparation of antigen solution

4 抗原液离心 Centrifugation of antigen solution

5 抗原液二级过滤 Secondary filtration of antigen solution

种子细胞初级放大 种子细胞二级、三级放大 抗原液的制备 抗原液离心 抗原液二级过滤

6 抗原液超滤浓缩 Ultra-filtration concentration of antigenic solution

7 疫苗水相制备 Vaccine aqueous phase preparation

8 疫苗乳化工艺 Vaccine emulsification process

9 产品罐装入库待检 Products canned and stored for inspection

10 成品与半成品检验 Inspection of finished and semi-finished products

抗原液超滤浓缩 疫苗水相制备 疫苗乳化工艺 产品罐装入库待检 成品与半成品检验

猪消化道疾病国际研讨会

4. 大肠杆菌疫苗技术储备：持续监测流行菌株，开发亚单位疫苗

Technical stockpile of Escherichia coli vaccines: continuously monitoring epidemic strains and developing subunit vaccines

- ■ 多联多价疫苗：以菌毒株储备和疫苗生产技术为基础

  Multiplex polyvalent vaccines: based on strain stockpiles and vaccine production technology

- □ 大肠杆菌储备：

  Escherichia coli reserve:

- ● 流行菌株分离鉴定、菌种筛选

  Isolation and identification of epidemic strains, screening of bacterial strains

- ● 产品研发与申报

  Product development and declaration

- ● 生产工艺技术革新（如去除内毒素等工艺）

  Innovation in production process (such as the process of removing endotoxins)

- ■ 基因工程疫苗：

  Genetic engineering vaccine:

- ● 毒素分析，毒素表达与纯化、疫苗制备技术

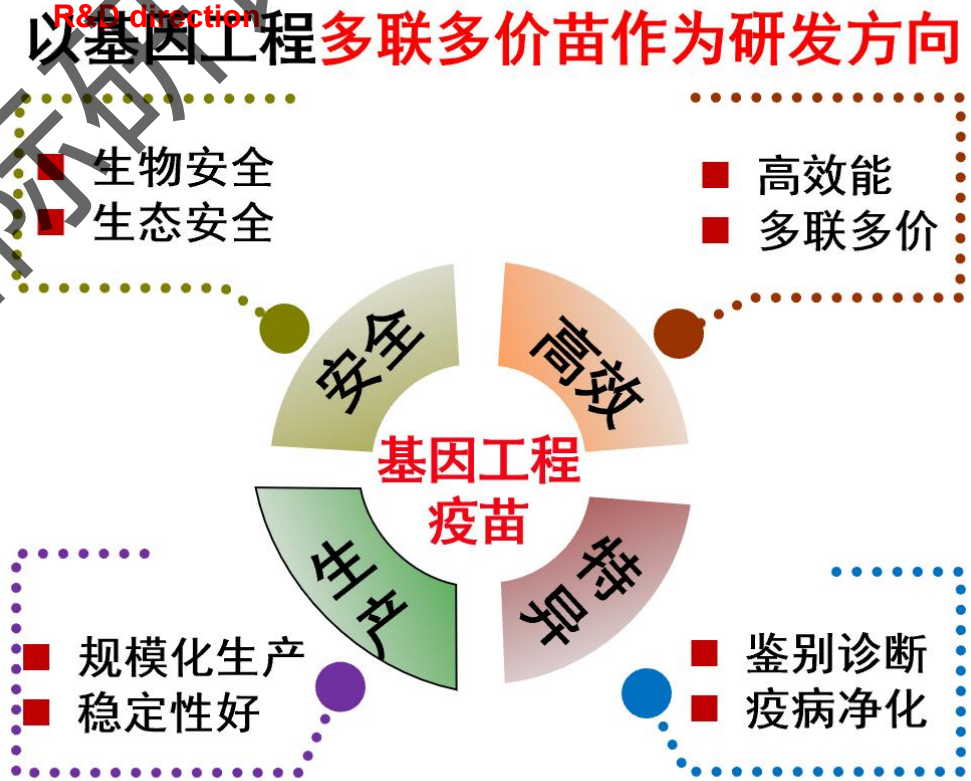
  Toxin analysis, toxin expression and purification, and vaccine preparation technology

SINDER 信得 HILE 海利

猪消化道疾病国际研讨会
International Pig Digestive Diseases Symposium

以基因工程多联多价苗作为研发方向

Genetically engineered multiplex polyvalent vaccine as R&D direction



猪消化道疾病国际研讨会

THANKS
谢谢大家

SINDER 信得
AgriX Technology
农宜科科技
猪消化道疾病国际研讨会
International Pig Digestive Diseases Symposium
猪消化道疾病国际研讨会