Role of Mycotoxins in Disease Development in Poultry

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Feed Safety across the Value Chain

Raw Material Trader/ Oilseed crusher

- Crusher hygiene - RM
- Harbour Decontamination

Commercial Feedmill

- Feed mill hygiene – RM/Feed
- Mycotoxin risk management
- Milling efficiency

Integrator/ Home mixer

- Feed hygiene – RM/Feed
- Mycotoxin Risk Management

Food Processor

- By-product preservation
- Mycotoxin risk management (AFm1)

Feed Safety GAP analysis → Llab Services → Technical Solutions → Dosing Equipment

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Mycotoxins' Human and Economic Toll

Naturally occurring **molds** leave **poisons** called **mycotoxins** on **corn** and **other crops**.

Mycotoxins can **cause disease** and **death** in **humans** and **animals**

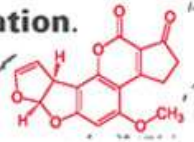
and have been linked to **public-health crises** around the **world**.

Regulations aim to **limit mycotoxin** concentrations in **food**.

Consuming doses of **aflatoxin** above **1 part per million** is **life-threatening**.

Mycotoxin-related damage costs US farmers and **livestock producers** up to **$1 billion** a **year**.

Drought conditions **stress plants**, leaving them **susceptible** to **aflatoxin contamination**.



Gro data, such as

NDVI anomalies and **soil properties**,

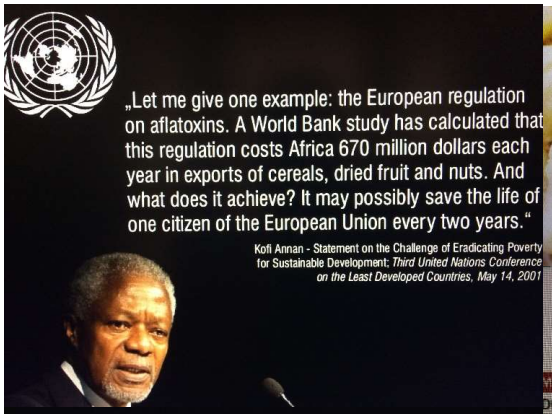
can help **monitor** risk of **mycotoxin damage** to **crops**.

Sources: World Health Organization, Council for Agricultural Science and Technology, Gro Intelligence.

Economic impact of mycotoxins

„Let me give one example: the European regulation on aflatoxins. A World Bank study has calculated that this regulation costs Africa 670 million dollars each year in exports of cereals, dried fruit and nuts. And what does it achieve? It may possibly save the life of one citizen of the European Union every two years."

Kofi Annan - Statement on the Challenge of Eradicating Poverty for Sustainable Development: *Third United Nations Conference on the Least Developed Countries, May 14, 2001*



THE WORLD BANK

Otsuki T., Wilson J.S. and Sewadeh M.
"Saving two in a billion: quantifying the trade effect of European food safety standards on African expo
Food Policy 26, 495-514, 2001

The value of African food exports and human health risk under the new EU harmonized standard relative to those under the alternative regulatory scenarios

	Relative to Codex*	Relative to the pre-EU harmonization (1998 trade)**
Loss in the value of African Food exports	US$ 670 000 000	US$ 340 000 000
Number of cancer death saved	2.3 persons	0.9 persons

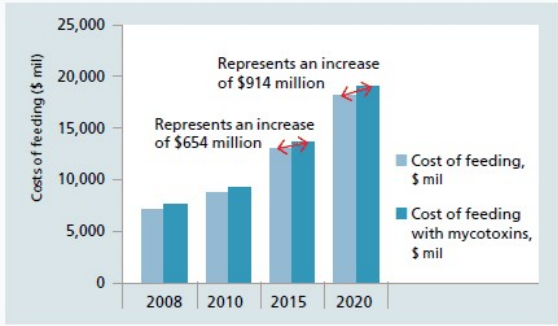
* 9ppb aflatoxin B_1, calculated from Codex 15ppb aflatoxin total standard
** 4.8ppb aflatoxin B_1 (average of 1998 individual EU countries aflatoxin regulations)

Mycotoxins' impact on swine performance

Mycotoxin	[ppb]	Impact	[€/pig]	[€/herd]*
DON	715	7.7 % Increased mortality	5.74	1.722 [2]
OTA & ZON	500 (OTA) 250 (ZON)	54 g decreased Daily Weight Gain	1.70	510 [3]
ZON & DON	250 (ZON) 1000 (DON)	decrease 0.09 FCR	1.88	564 [4]

* average herd size in Sweden: 300
[2] 1% change in mortality is worth 1.49 € a pig (not including labor or medication costs)
[3] 50g/day change in growth rate is worth 1.57 € per pig if pigs are sold at the same weight
[4] 0.1 change in FCR represents 2.09 € per pig (when average feed cost is 223.62 €/ton)

Figure 2. Economic impact of a theoretical 5% increase in FCR for freshwater fishes.



Source: Tacon et al., 2011; Feed company's reports and magazines; Peer-review literature on mycotoxins consequences in fish growth performance

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Mycotoxins

Fusarium toxins

Trichothecenes

- DAS
- Deoxynivalenol
- Nivalenol
- T-2 Toxin

Non-Trichothecenes

- Zearalenone
- Fumonisins
- Moniliformin
- Fusaric acid

Aspergillus toxins

- Aflatoxins
- Ochratoxins
- Cyclopiazonic acid
- Sterigmatocystin
- Fumitremorgens
- Fumitoxins
- Gliotoxin

Penicillium toxins

- Ochratoxins
- Citrinin
- PR Toxin
- Patulin
- Penicillic acid
- Roquefortine C
- Mycophenolic acid

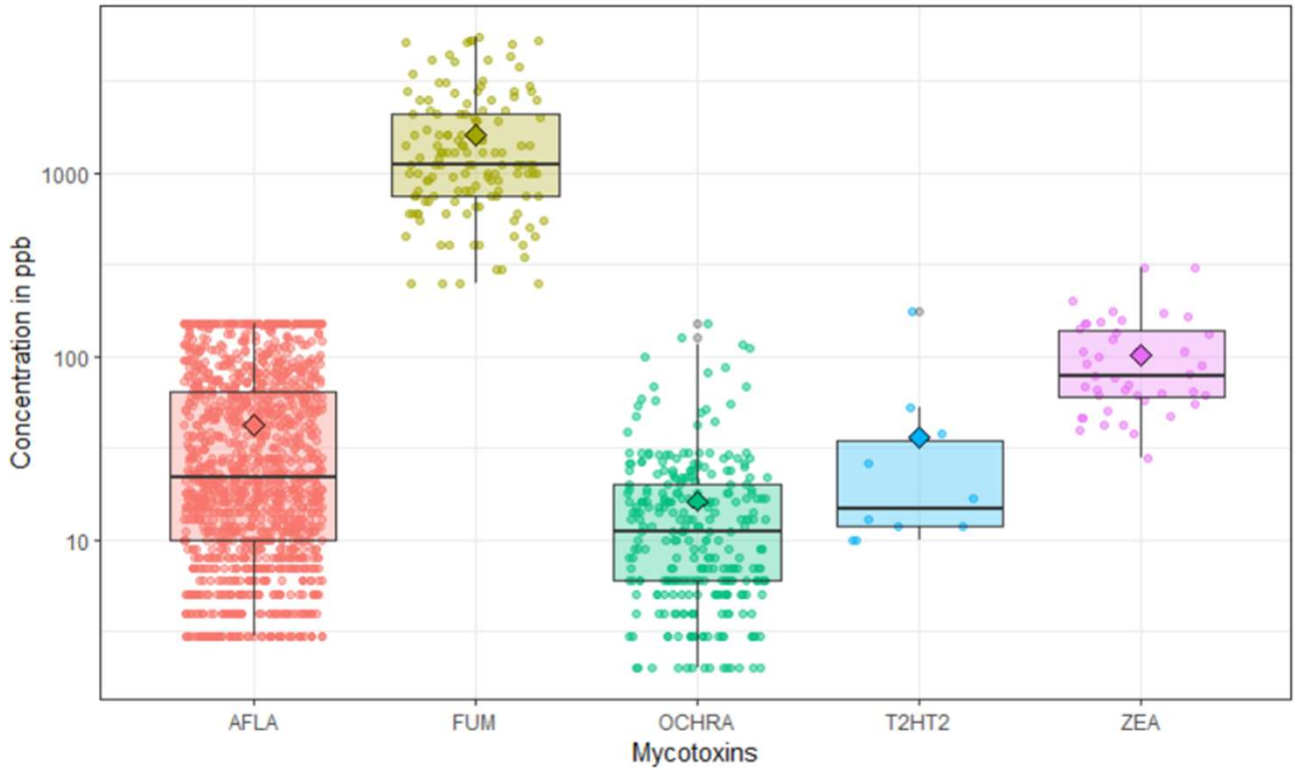
Ergot toxins

- Ergovaline
- Ergocryptine
- Ergotamine

2022 Mycotoxin Contamination in India

Mycotoxin	Total	Total Contaminated	% conta-mination	Average	Median	Minimum	Maximum
AFLA	1433	1301	91	43	44	22	3
ZEA	47	43	91	102	64	79	28
OCHRA	322	279	87	16	19	11	2
FUM	198	137	69	1611	1264	1100	250
T2HT2	135	10	7.4	37	51	15	10

Mycotoxin distribution in Indian raw materials and feeds



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Types of mycotoxin toxicity

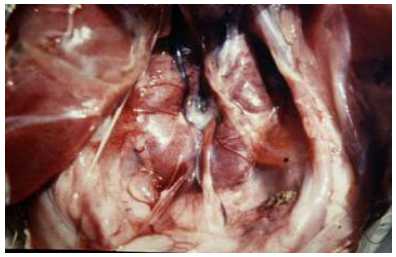
- **Acute toxicity** describes the adverse effects of a mycotoxin that result either from a single exposure or from multiple exposures in a short period of time. To be described as acute toxicity, the adverse effects should occur within 14 days of the administration of the substance.

- **Subacute toxicity** (repeat dose toxicity) focuses on adverse effects occurring after administration of a single dose or multiple doses of a mycotoxin per day for a period of 14–28days.

- **Chronic toxicity** describes the development of adverse effects as a result of long-term exposure of poultry to a mycotoxin or groups of mycotoxins.

Adverse effects of mycotoxins in Poultry

AF: Enlarged and pale liver

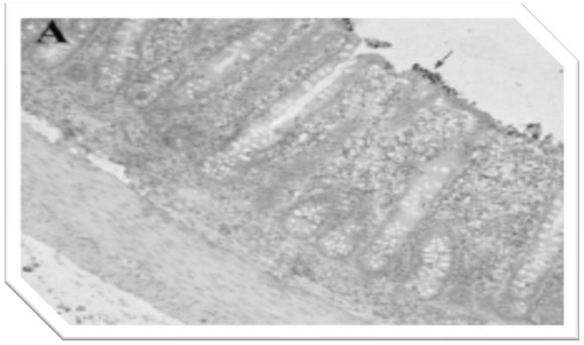


OTA: Enlarged kidneys

T-2 toxin: Oral lesions

AF/OTA/*Fusarium*: diarrhea/wet litter

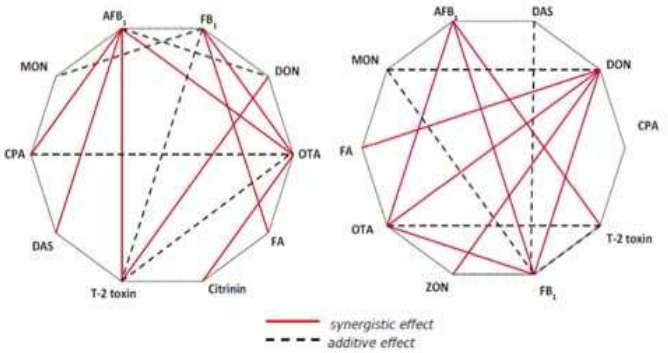
DON/T-2: Intestinal lesions



T-2/FBs: Increased intestinal bacteria colonisation

Why chronic toxicity is hard to diagnose?

- No clear animal symptoms
- Low levels of Multiple mycotoxins in the feed
- Limited number of mycotoxins analysed in the feed
- Masked mycotoxins in the feed
- Mycotoxin Interactions (additive/synergy)



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The concerns of modern poultry farms: Mycotoxins and Gut Health

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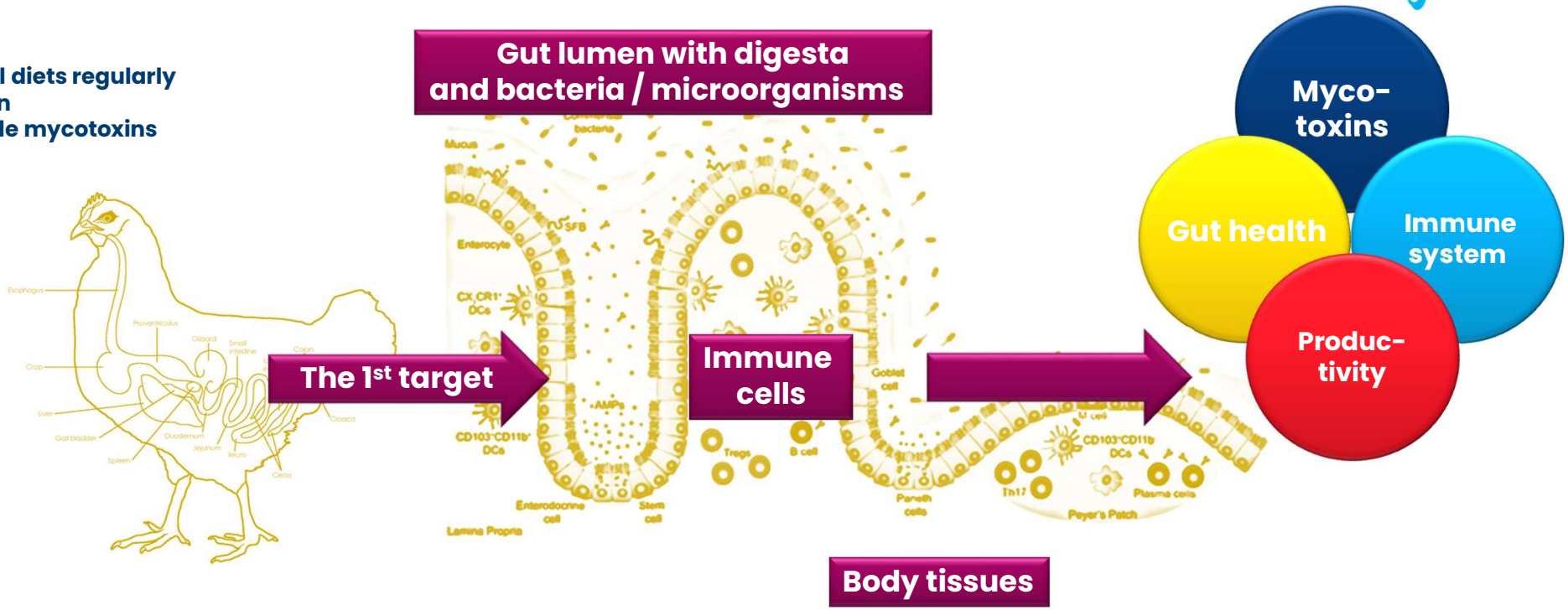
Animal diets regularly contain multiple mycotoxins



The intestinal tract is the 1st site of contact (even at low mycotoxin concentrations)
Intestinal epithelial cells are the 1st target cells affected by all mycotoxins
Intestinal epithelial cells create the essential barrier between gut lumen and body tissue

Source: Prof. Fink-Gremmels

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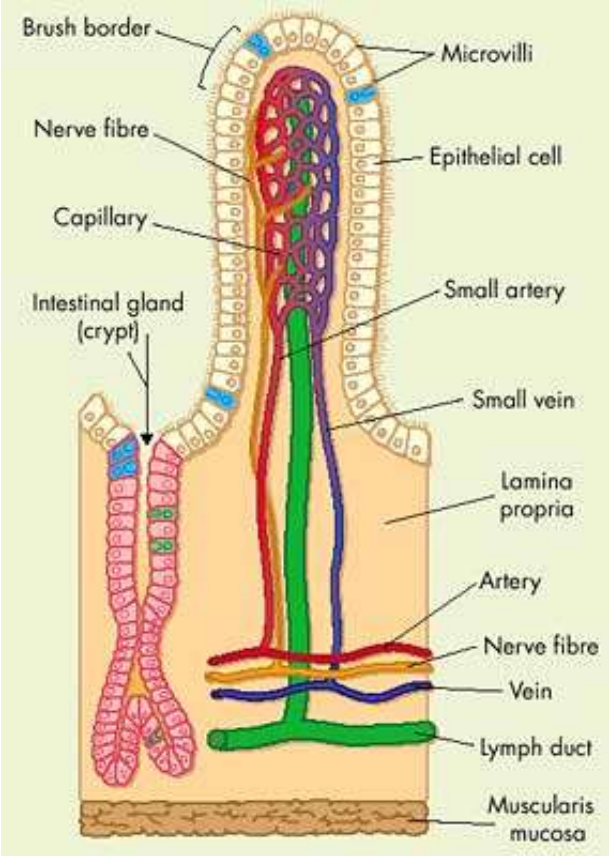
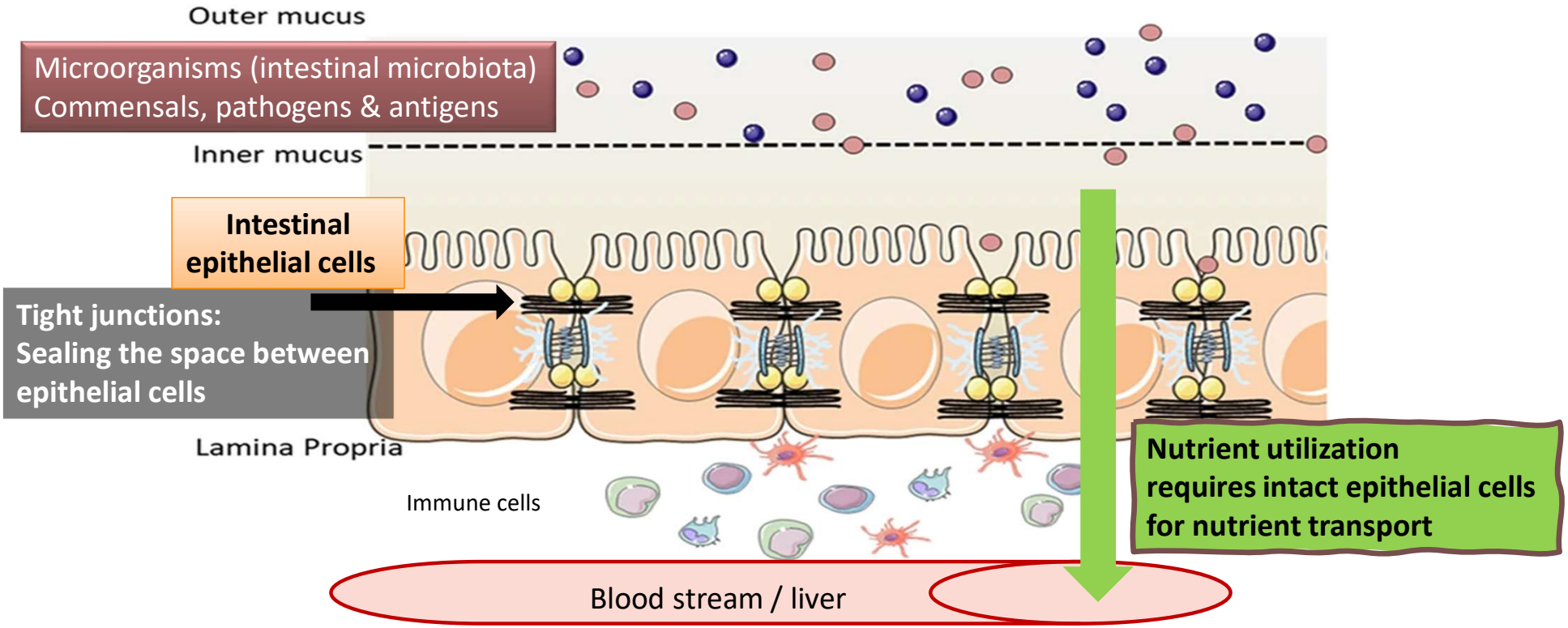
Structure of intestinal villi



Mycotoxin impact on gut health

Mycotoxins	Adverse effects
Aflatoxins	• the disruption of intestinal barrier function; poor intestinal cell proliferation and cell death; compromised intestinal immunity
Ochratoxins	• altered intestinal nutrient absorption; increased intestinal permeability; intestinal cell death; decreased villi height
T-2 toxin / DON	• poor intestinal water and glucose absorption (diarrhea); necrotic lesions in GIT; shortening of intestinal villi (poor nutrient absorption); increased intestinal permeability (lowered tight junction proteins); decreased IL-8* cytokine (responsible for pathogen removal); decreased mucin production
Fumonisins	• decreased cell viability and proliferation; altered intestinal barrier integrity by suppressing tight junction protein; increased intestinal permeability; increased mucin secretion/depletion of goblet cells; altered gut immunity

Epithelial cells and tight junction (TJ): the life-saving intestinal barrier



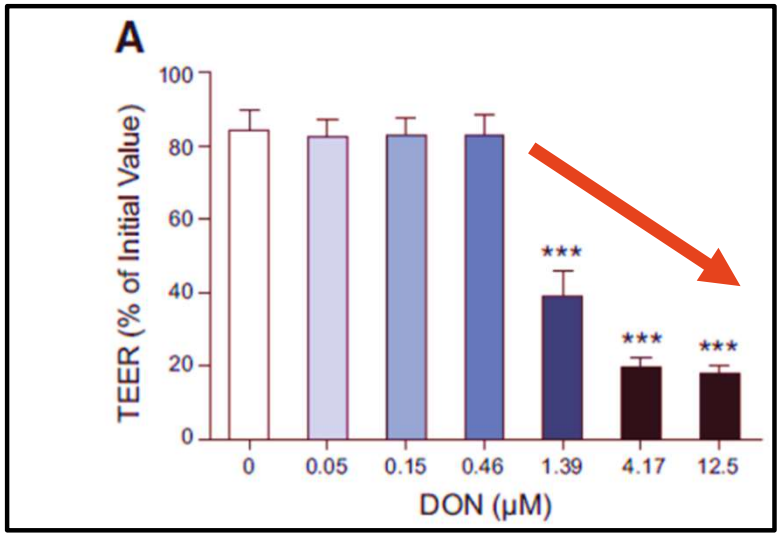
Drawing taken from Chelakkot et al., 2018

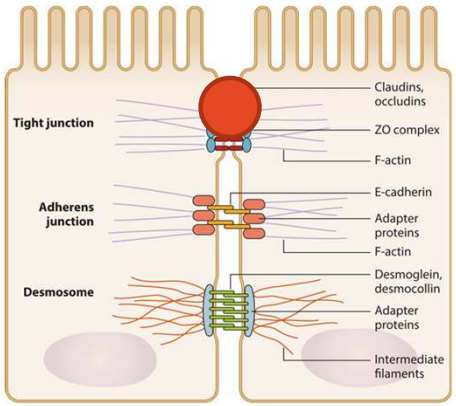
Intestinal barrier: the detrimental effects of DON (deoxynivalenol)

In vitro

Epithelial integrity

Transepithelial electrical resistance (TEER)

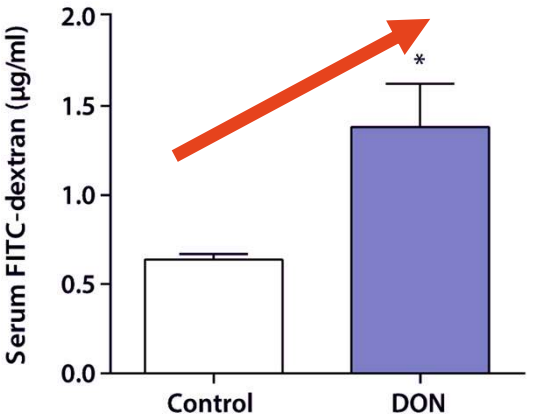




In vivo

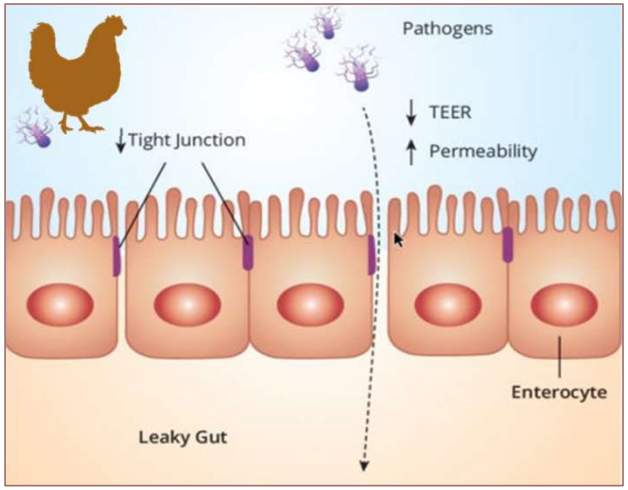
Passage of intestinal content

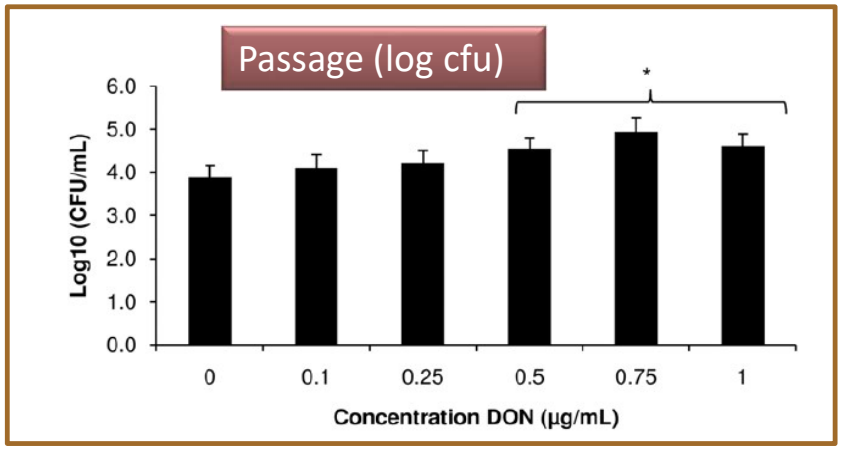
(FITS dextran as model)

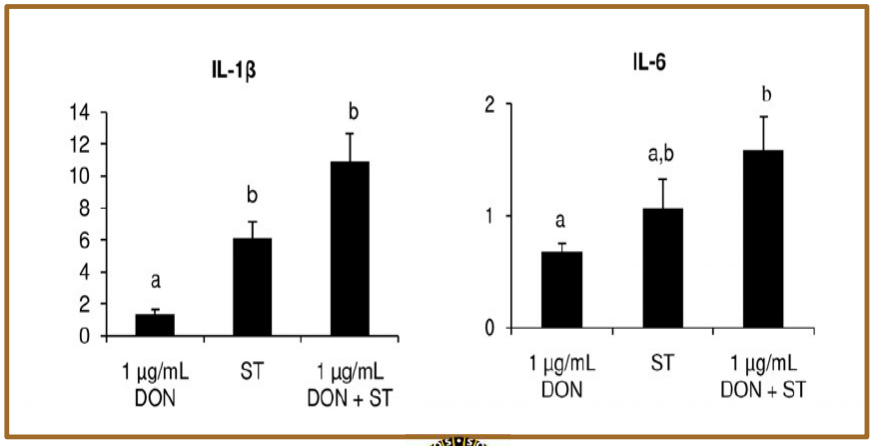


DON affects the TJ complex resulting in increased permeability (loss of epithelial integrity)

Clinical effect: Trans-epithelial Transfer of *Salmonella typhimurium*







Inflammatory response

(*in vitro*: IPEC cells)

Vandenbroucke et al., 2011

Impact of mycotoxins on immune responses

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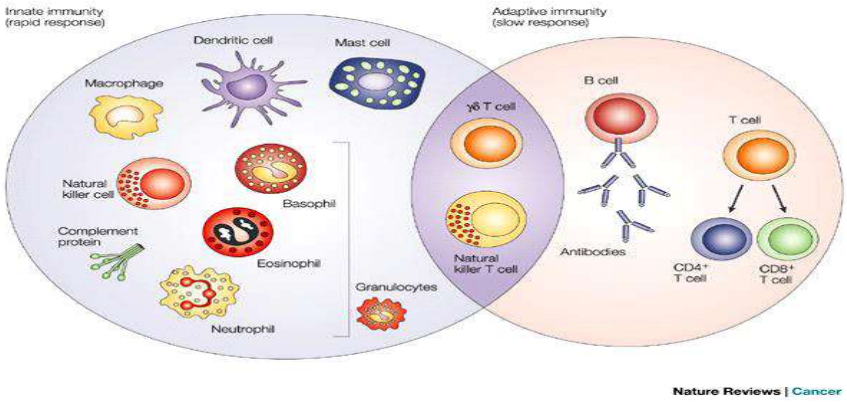
Immune system

Innate immunity	Adaptive immunity
First line defense Ready to be mobilized upon infection	**Second line defense** Requires time (up to days) to react to infection
Non-specific Reacts to broad range of infections / organisms	**Antigen specific**
No immunological memory	**Immunological memory**

Physical barriers
- Skin
- Mucosal membranes

Chemical barriers
- pH
- Enzymes
- …

Cellular barriers
- Phagocytes incl. macrophages
- Natural killer cells
- Granulocytes
- …



Humoral immunity
- B cells

Cellular immunity
- T cells

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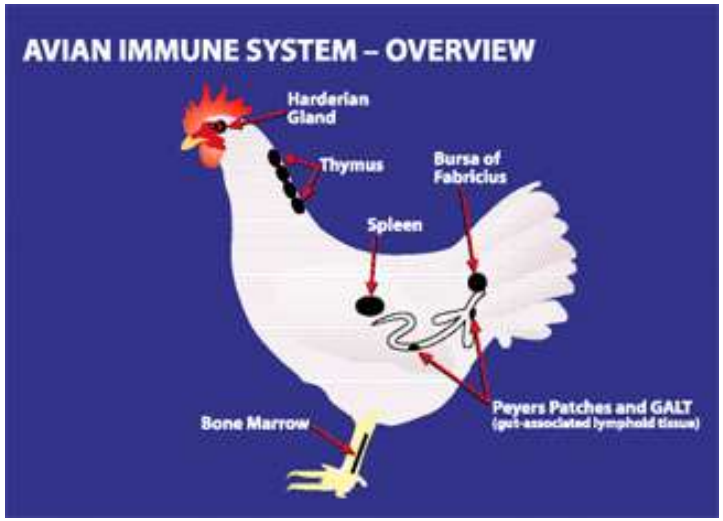
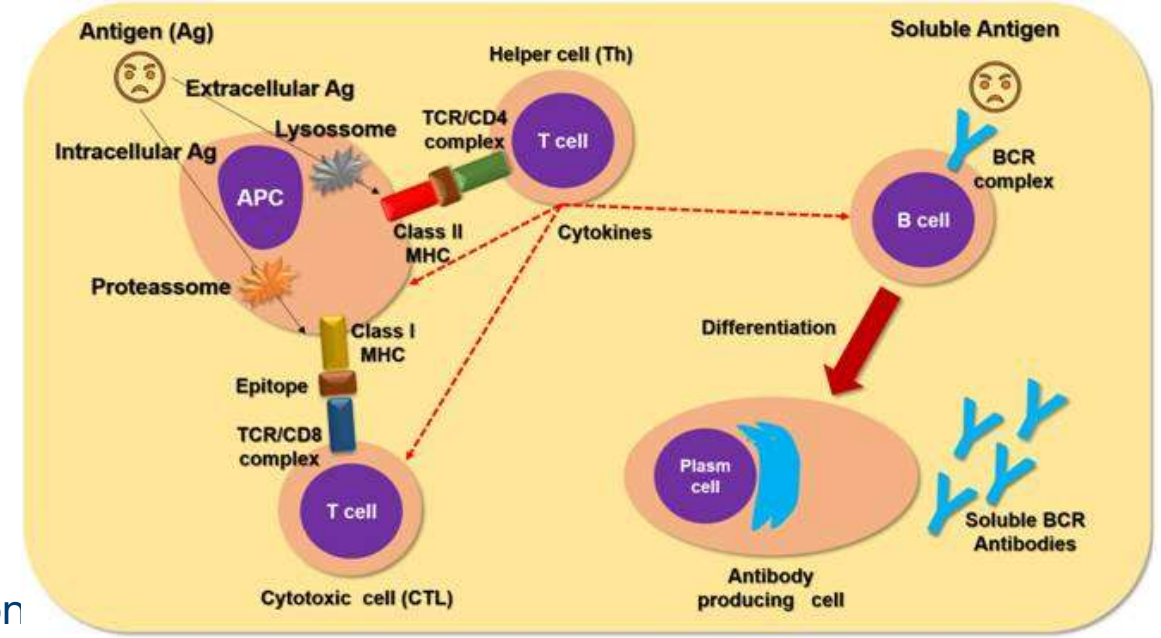
Immune system of poultry



Source: canadianpoultrymag.con



Junior et al., 2018

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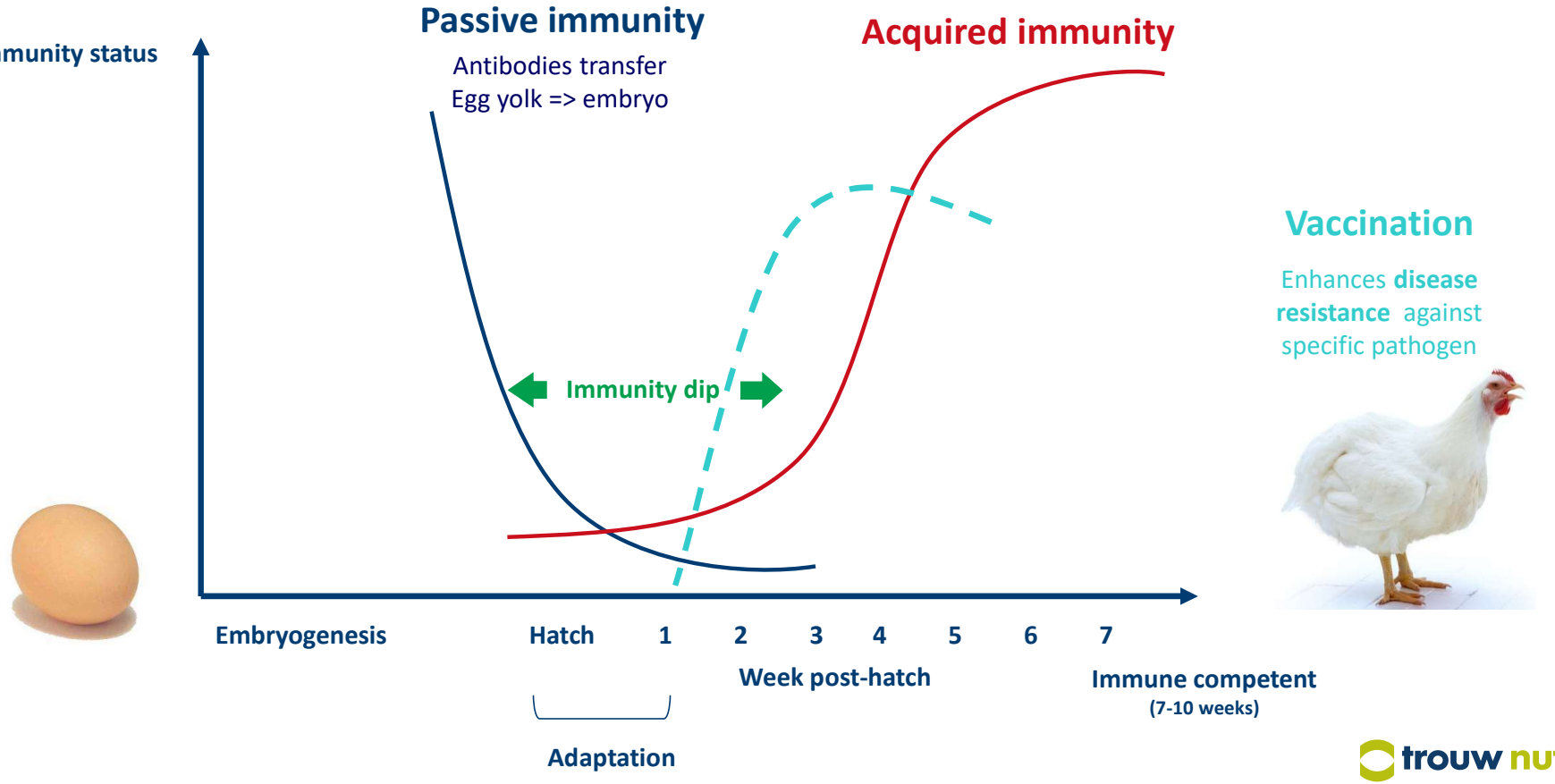
Immune system development in poultry



Vaccination

Enhances **disease resistance** against specific pathogen

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Impact of mycotoxins on immune responses

Mycotoxins	Adverse effects
Aflatoxins	increased gene expression of IL-6, reduced complement and interferon, suppressed macrophagic phagocytosis, suppressed DTH, reduced weight of thymus and bursa, poor antibody titers, vaccination failures
Ochratoxins	regression of lymphoid organs, lymphocyte depletion, poor DTH, antibody response is affected to a lesser extent
T-2 toxin	regression of bursa of Farbricius, leucopenia, proteinemia, immunosuppression, increased disease incidences
DON	interferes with DNA, RNA and protein synthesis, immunosuppression, poor antibody titers, increased disease incidences
Fumonisins	Thymus atrophy, decreased spleen weight, increased susceptibility to E. coli and other bacteria

Multiple mycotoxins lowered antibody titre against NCD & IBD

Treatment	NCD titres, log_{10}		IBDV titres, log_{10}	
	day 21	day 42	day 21	day 42
Control	1.36 [a]	1.07 [a]	1103 [a]	1625 [a]
Multiple mycotoxins*	0.96 [b]	0.51 [b]	700 [b]	981 [b]
***p*-value**	0.006	<0.0001	<0.0001	0.0001

*250ppb each of AF, OTA and T-2 toxin

Malathi et al., 2019

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T-2 toxin Reduces the Efficacy of Anticoccidial Drug in Chickens

Protocol

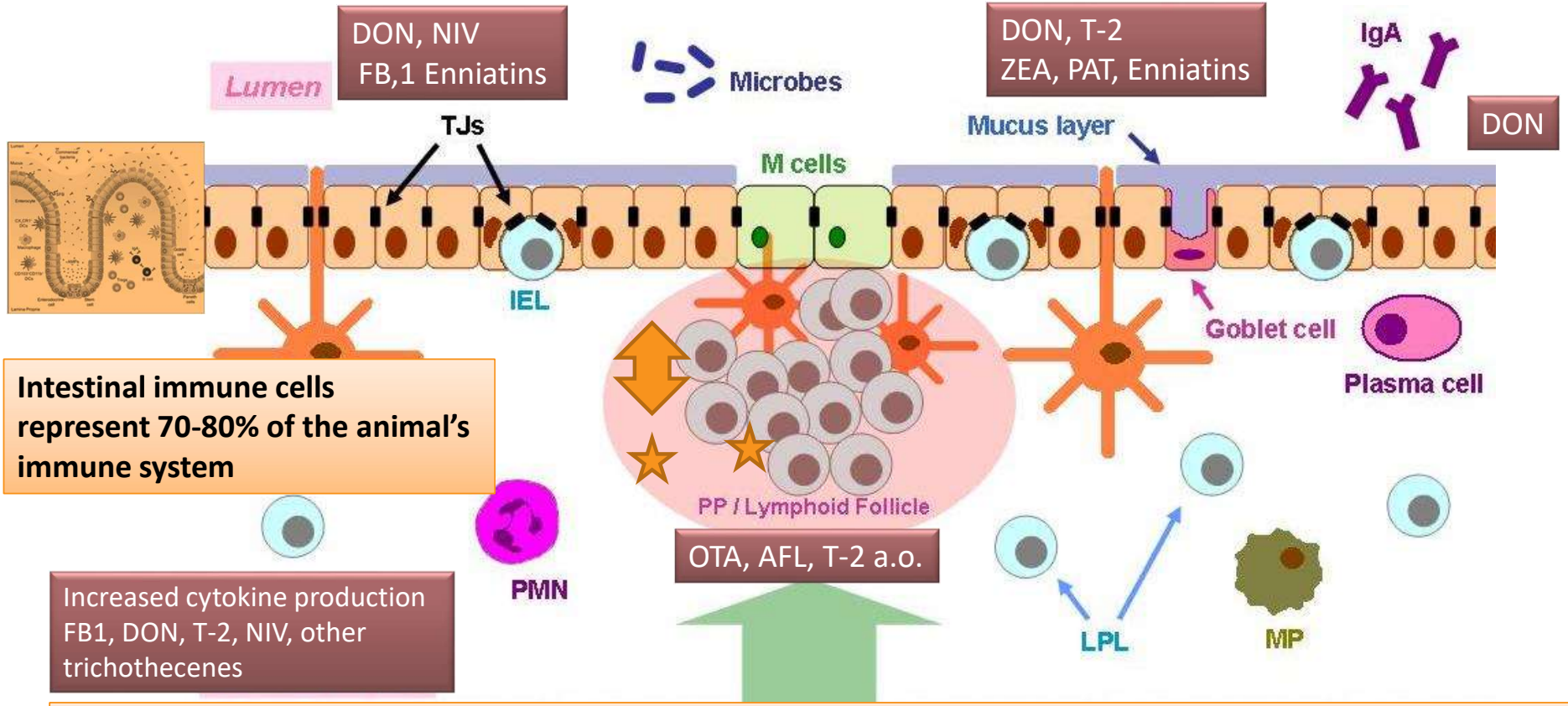
Day 7 of age:
Oral inoculation with *Eimeria tenella*
Day 15 of age:
Necropsy
Day 6 to 15 of age:
Ingestion of food with Lasalocid (75 ppm) ± T-2 toxin

Results

Treatment	Mortality	Lesion
None	90 %	100 %
Lasalocid	0 %	0 %
+ T-2 (6 ppm)	35 %	100 %
+ T-2 (1 ppm)	5 %	45 %
+ T-2 (0.5 ppm)	0 %	10 %

Source: Varga and Vanyi, 1992

Mycotoxins affect the animal's resilience to infectious agents



Interaction with infectious diseases,
& vaccination programs in all animal species

Source: Prof. Fink-Gremmels

Trouw Nutrition's 10-point system for **Mycotoxin Risk Management**

1. Ploughing

2. Crop rotation

3. Crop management

4. Harvest management

5. Grain treatment
Fylax

6. Optimal grain transportation

7. Feed mill hygiene
Fylax

8. TOXO application in feed

9. Optimal feed transportation

10. Gut health/immunity Management **AMR**

Swamy, 2021

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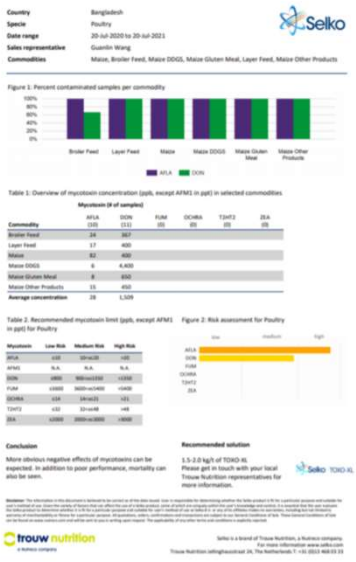
What is the best way to diagnose mycotoxin issues?

Take into account all the following factors;

- History of raw material sourcing
- Mycotoxin analysis report
- Poultry symptoms
- Post-mortem findings



Swamy, 2020

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Conclusions

- It is hard to differentiate the negative effects of mycotoxins on gut health and immune responses in poultry.
- Leaky gut caused by mycotoxins can initiate cascade of events leading to increased susceptibility of birds against pathogens.
- Some mycotoxins can affect immune cells directly leading to lowered Cell- and antibody-mediated immune responses.
- Mycotoxin Risk Management strategy combining mycotoxin binding concept along with means of improving gut health and immunity are of paramount importance in not only enhancing animal health and performance but also improving the bottom line of business operations.

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Thank You

Happy to Answer Any Questions

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