Casual Friday Series

Chronic Kidney Disease and How to Support

A BIOGENETIX CLINICAL PRESENTATION

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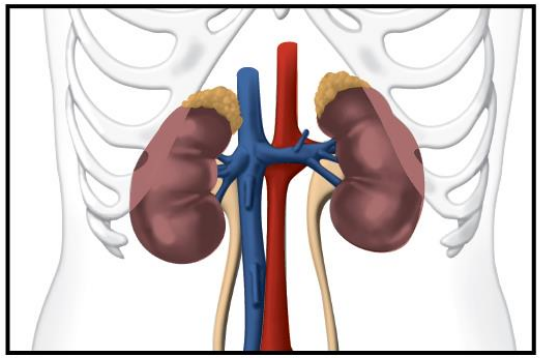
Kidney Anatomy



https://open.oregonstate.education/app/uploads/sites/157/2021/02/2610_The_Kidney_revised.png

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Kidney Diseases

1. Acute Kidney Injury (AKI):

1. A sudden loss of kidney function, often reversible with prompt treatment.
2. Causes include severe dehydration, infections, injury, or blocked blood flow to the kidneys.
3. Symptoms: Decreased urine output, swelling, fatigue, and confusion.

2. Chronic Kidney Disease (CKD):

1. A gradual loss of kidney function over months or years.
2. Common causes include diabetes (diabetic nephropathy), high blood pressure (hypertensive nephropathy), glomerulonephritis (inflammation of kidney filters), and polycystic kidney disease (a genetic disorder causing cysts in the kidneys).
3. Stages range from 1 (mild) to 5 (end-stage renal disease, or ESRD), based on the glomerular filtration rate (GFR), a measure of kidney efficiency.
4. Symptoms (often appear in later stages): Fatigue, swelling (edema), itchy skin, high blood pressure, and dark or foamy urine.

3. Further Complications:

1. **Kidney Stones:** Hard deposits that can block urine flow and cause pain or infection.
2. **Glomerulonephritis:** Inflammation of the glomeruli (tiny filtering units in the kidneys).
3. **Nephrotic Syndrome:** A condition causing excessive protein loss in urine, leading to swelling and low blood protein levels.

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5 Stages of CKD

The 6 CKD categories, known as stages 1 through 5.
Stage 3 is separated into 3a and 3b:

- G1: GFR 90 mL/min/1.73 m^2 and above with evidence of kidney disease, such as hematuria or proteinuria
- G2: GFR 60 to 89 mL/min/1.73 m^2
- G3a: GFR 45 to 59 mL/min/1.73 m^2
- G3b: GFR 30 to 44 mL/min/1.73 m^2
- G4: GFR 15 to 29 mL/min/1.73 m^2
- G5: GFR less than 15 mL/min/1.73 m^2 or treatment by dialysis

https://www.ncbi.nlm.nih.gov/books/NBK535404/

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CMP14+LP+TP+TSH+5AC+CBC/D/P...

	Test	Current Result and Flag		Previous Result and Date	Units	Reference Interval
	Chemistries [01]					
	Glucose [01]	72			mg/dL	70-99
▲	**Hemoglobin A1c** [01]	**6.0**	**High**		%	4.8-5.6
	Please Note: [01]	Prediabetes: 5.7 - 6.4 Diabetes: >6.4 Glycemic control for adults with diabetes: <7.0				
	Uric Acid [01]	5.1			mg/dL	3.0-7.2
				Therapeutic target for gout patients: <6.0		
	BUN [01]	12			mg/dL	6-24
▲	**Creatinine** [01]	**1.17**	**High**		mg/dL	0.57-1.00
▼	**eGFR**	**54**	**Low**		mL/min/1.73	>59
	BUN/Creatinine Ratio	10				9-23
	Sodium [01]	143			mmol/L	134-144
	Potassium [01]	4.2			mmol/L	3.5-5.2
	Chloride [01]	104			mmol/L	96-106
	Carbon Dioxide, Total [01]	24			mmol/L	20-29
	Calcium [01]	9.9			mg/dL	8.7-10.2
	Phosphorus [01]	3.5			mg/dL	3.0-4.3
	Magnesium [01]	2.2			mg/dL	1.6-2.3
	Protein, Total [01]	7.7			g/dL	6.0-8.5

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CMP14+LP+TP+TSH+5AC+CBC/D/P...

	Test	Current Result and Flag		Previous Result and Date		Units	Reference Interval
	Chemistries [01]						
	Glucose [01]	94		85	10/15/2024	mg/dL	70-99
▲	**Hemoglobin A1c** [01]	**5.7**	**High**	5.6	01/17/2024	%	4.8-5.6
	Please Note: [01]	Prediabetes: 5.7 - 6.4 Diabetes: >6.4 Glycemic control for adults with diabetes: <7.0					
	Uric Acid [01]	4.0				mg/dL	3.0-7.2
		Therapeutic target for gout patients: <6.0					
	BUN [01]	19		13	10/15/2024	mg/dL	8-27
	Creatinine [01]	0.97		0.95	10/15/2024	mg/dL	0.57-1.00
	eGFR	63		65	10/15/2024	mL/min/1.73	>59
	BUN/Creatinine Ratio	20		14	10/15/2024		12-28
	Sodium [01]	140		141	10/15/2024	mmol/L	134-144
	Potassium [01]	4.1		4.5	10/15/2024	mmol/L	3.5-5.2
	Chloride [01]	103		104	10/15/2024	mmol/L	96-106
	Carbon Dioxide, Total [01]	24		25	10/15/2024	mmol/L	20-29
	Calcium [01]	9.9		10.3	10/15/2024	mg/dL	8.7-10.3
	Phosphorus [01]	3.7				mg/dL	3.0-4.3
	Magnesium [01]	2.2				mg/dL	1.6-2.3
	Protein, Total [01]	6.7		6.9	10/15/2024	g/dL	6.0-8.5

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Comp. Metabolic Panel (14)

	Test	Current Result and Flag		Previous Result and Date	Units	Reference Interval
▲	**Glucose** [01]	**207**	**High**		mg/dL	70-99
▲	**BUN** [01]	**30**	**High**		mg/dL	6-24
▲	**Creatinine** [01]	**1.12**	**High**		mg/dL	0.57-1.00
▼	**eGFR**	**58**	**Low**		mL/min/1.73	>59
▲	**BUN/Creatinine Ratio**	**27**	**High**			9-23
	Sodium [01]	142			mmol/L	134-144
	Potassium [01]	4.1			mmol/L	3.5-5.2
	Chloride [01]	101			mmol/L	96-106
	Carbon Dioxide, Total [01]	28			mmol/L	20-29
	Calcium [01]	9.6			mg/dL	8.7-10.2
	Protein, Total [01]	7.2			g/dL	6.0-8.5

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Causes

Statistical causes of CKD vary globally, with the most common primary diseases leading to CKD and, ultimately, end-stage renal disease (ESRD) being:

- Type 2 diabetes (30%-50%)
- Type 1 diabetes (3.9%)
- Hypertension (27.2%)
- Primary glomerulonephritis (8.2%)
- Chronic tubulointerstitial nephritis (3.6%)
- Hereditary or cystic diseases (3.1%)
- Secondary glomerulonephritis or vasculitis (2.1%)
- Plasma cell dyscrasias or neoplasm (2.1%)
- Sickle cell nephropathy, which accounts for less than 1% of ESRD patients in the United States.

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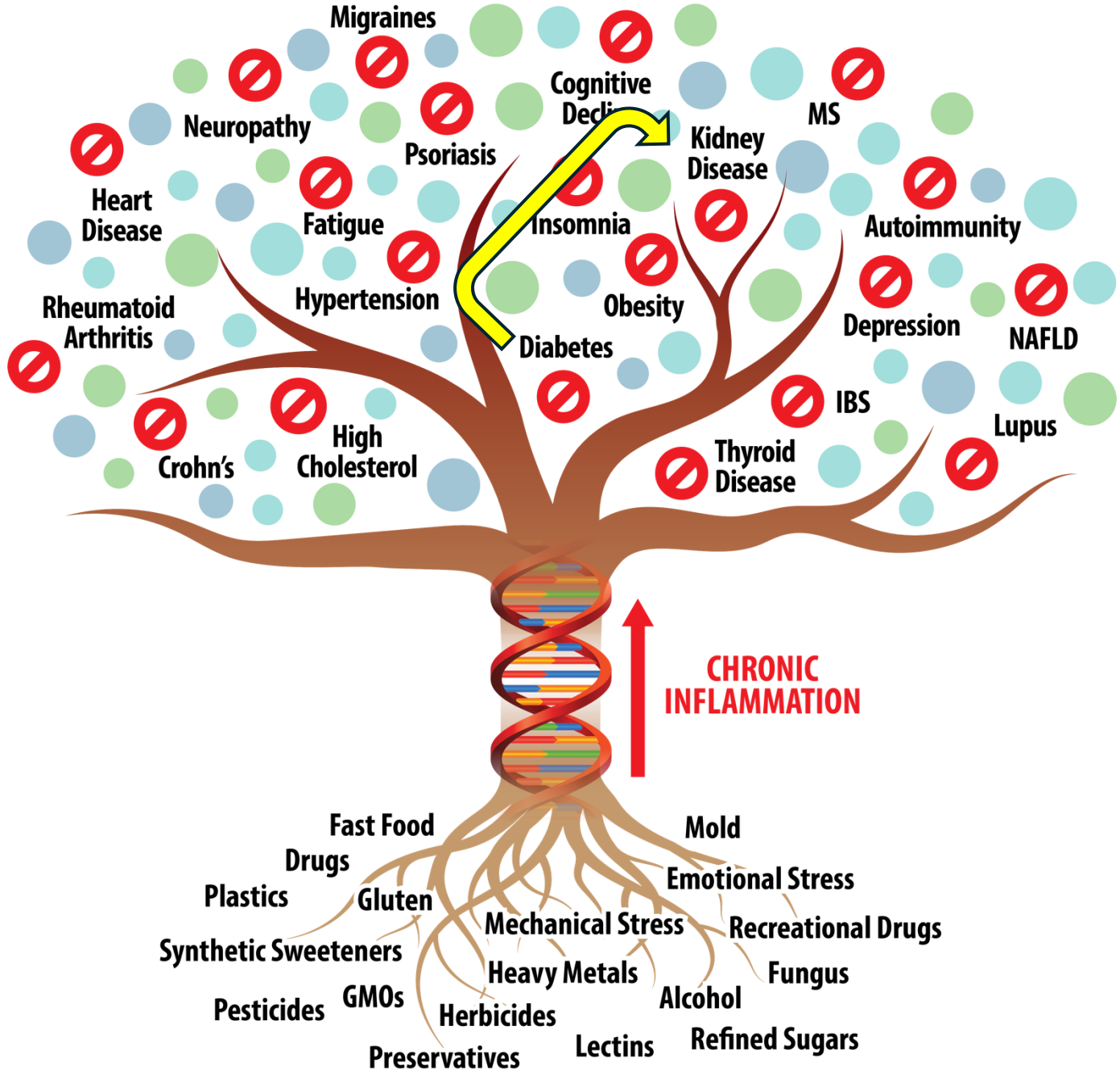
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Psoriasis
Cognitive Decl
MS
Kidney Disease
Heart Disease
Fatigue
Insomnia
Autoimmunity
Rheumatoid Arthritis
Hypertension
Obesity
Depression
NAFLD
Diabetes
IBS
Lupus
Crohn's
High Cholesterol
Thyroid Disease
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Mold
Drugs
Emotional Stress
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Mechanical Stress
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GMOs
Alcohol
Herbicides
Lectins
Refined Sugars
Preservatives

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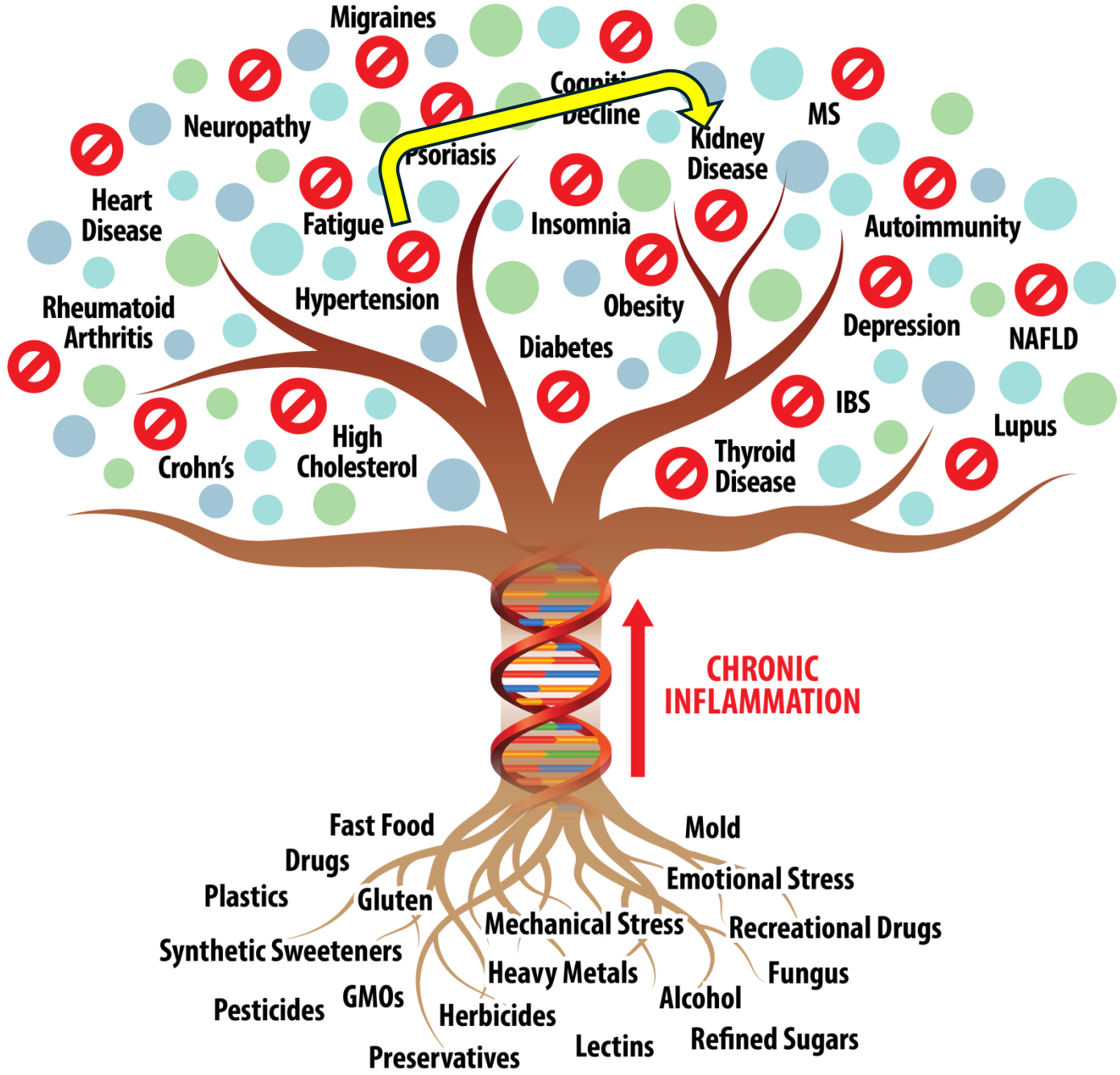
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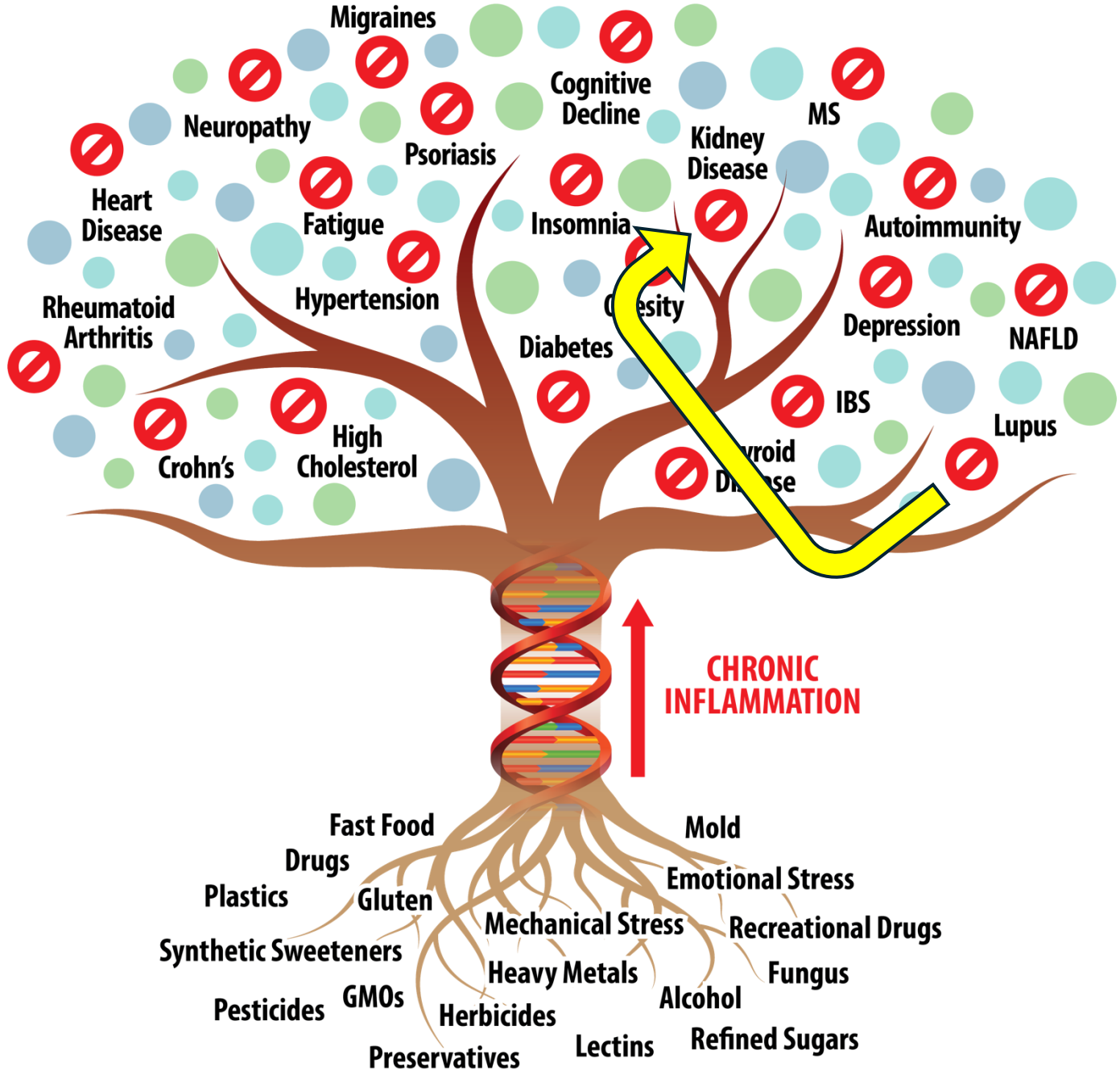
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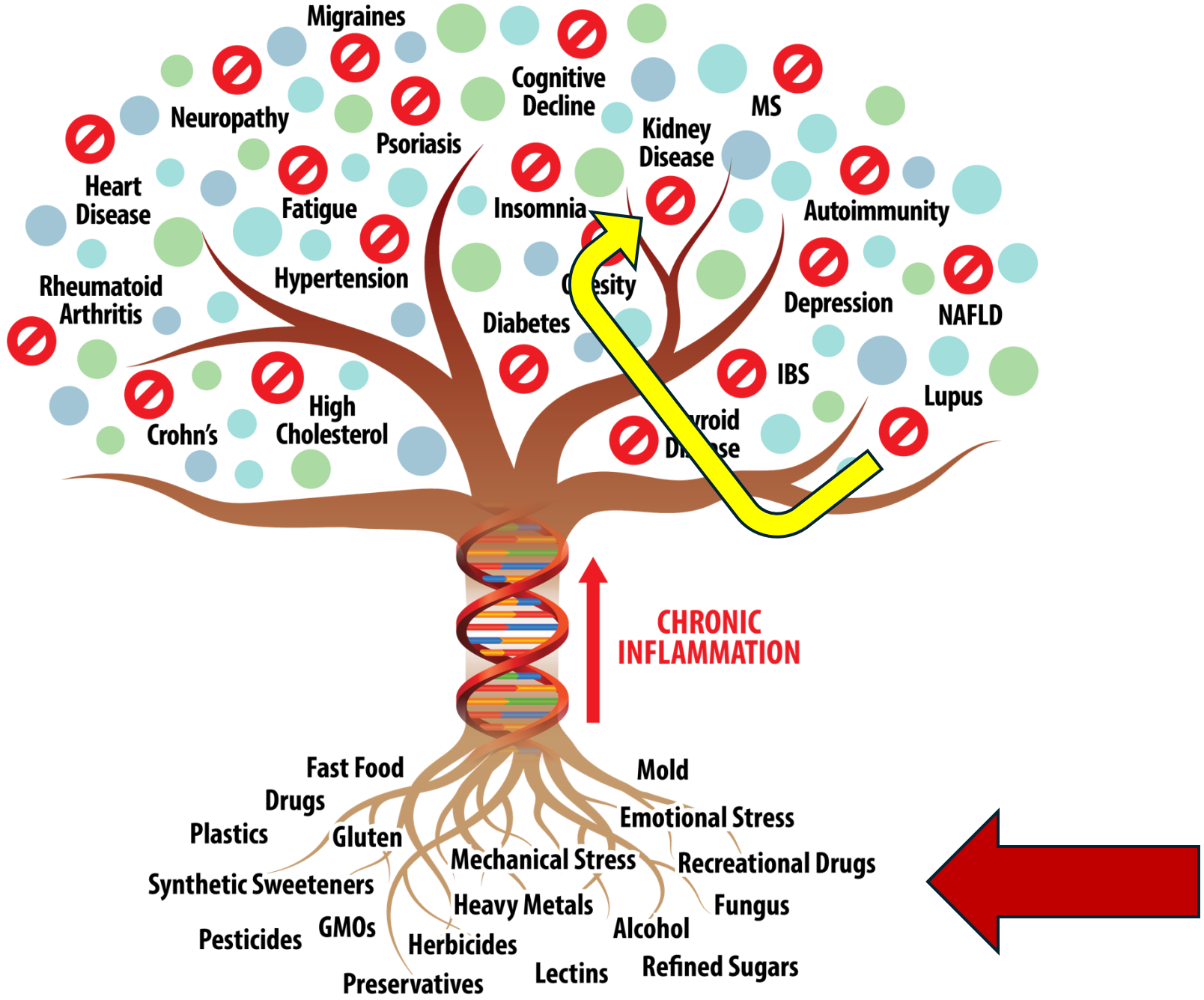
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Toxins (Basel). 2021 Nov 28;13(12):848. doi: 10.3390/toxins13120848

Urinary Biomarkers of Mycotoxin Induced Nephrotoxicity—Current Status and Expected Future Trends

Zsolt Ráduly [1,2,*], Robert G Price [3], Mark E C Dockrell [4], László Csernoch [2], István Pócsi [5]

The intensifying world-wide spread of mycotoxigenic fungal species has increased the possibility of mycotoxin contamination in animal feed and the human food chain. Growing evidence shows the deleterious toxicological effects of mycotoxins from infants to adults, while large population-based screening programs are often missing to identify affected individuals. The kidney functions as the major excretory system, which makes it particularly vulnerable to nephrotoxic injury. However, few studies have attempted to screen for kidney injury biomarkers in large, mycotoxin-exposed populations. As a result, there is an urgent need to screen them with sensitive biomarkers for potential nephrotoxicity. Although a plethora of biomarkers have been tested to estimate the harmful effects of a wide spectrum of toxicants, β_2-microglobulin (β_2-MG) and *N*-acetyl-β-D-glucosaminidase (NAG) are currently the dominant biomarkers employed routinely in environmental toxicology research. Nevertheless, kidney injury molecule 1 (KIM-1) and neutrophil gelatinase-associated lipocalin (NGAL) are also emerging as useful and informative markers to reveal mycotoxin induced nephrotoxicity. In this opinion article we consider the nephrotoxic effects of mycotoxins, the biomarkers available to detect and quantify the kidney injuries caused by them, and to recommend biomarkers to screen mycotoxin-exposed populations for renal damage.

Table 1.

Mycotoxins with established nephrotoxic effects.

Mycotoxin	Model System	Doses	Nephron Segment Involved	References
Ochratoxin A	mice, monkey, human	over 10 ng/kg bw	proximal tubules	[45]
Citrinin	mice, rabbit	35–200 mg/kg bw	proximal tubules	[28]
Zearalenone	mice	40 mg/kg bw	general kidney damage, not characterized	[33]
Fumonisin B1	quail chicks	200 ppm	proximal tubules, proximal convoluted tubules	[46]
Sterigmatocystin	mice, monkey	10–144 mg/kg bw	collecting ducts	[38]
Aflatoxin B1	mice	30–200 µg/kg bw	proximal tubule and general kidney damage	[42,47]

https://pmc.ncbi.nlm.nih.gov/articles/PMC8708607/

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Mycotoxins represent one of the major environmental toxicants threatening human health today. Exposure can be via food consumption, inhalation, dermal contact or through occupational exposure [6,14,15]. The most prevalent toxins in the food chain are: aflatoxins (AFs), ochratoxin A (OTA), patulin (PAT), fumonisins, citrinin (CIT), ergot alkaloids, trichothecenes like deoxynivalenol (DON), T-2 toxin (T-2) and zearalenone (ZEN) [16]. Because of the growing concern about mycotoxin-associated health problems including kidney injury, a search for suitable markers to quantify mycotoxin toxicity is urgently required. The most predominant exposure is to OTA and CIT, current methods for detecting exposure include just the determination of urinary levels of mycotoxins and/or their excreted forms [6,17,18,19]. As mycotoxins are naturally occurring secondary metabolites are often consumed by people, the exact nephrotoxic mechanisms should be clarified as well.

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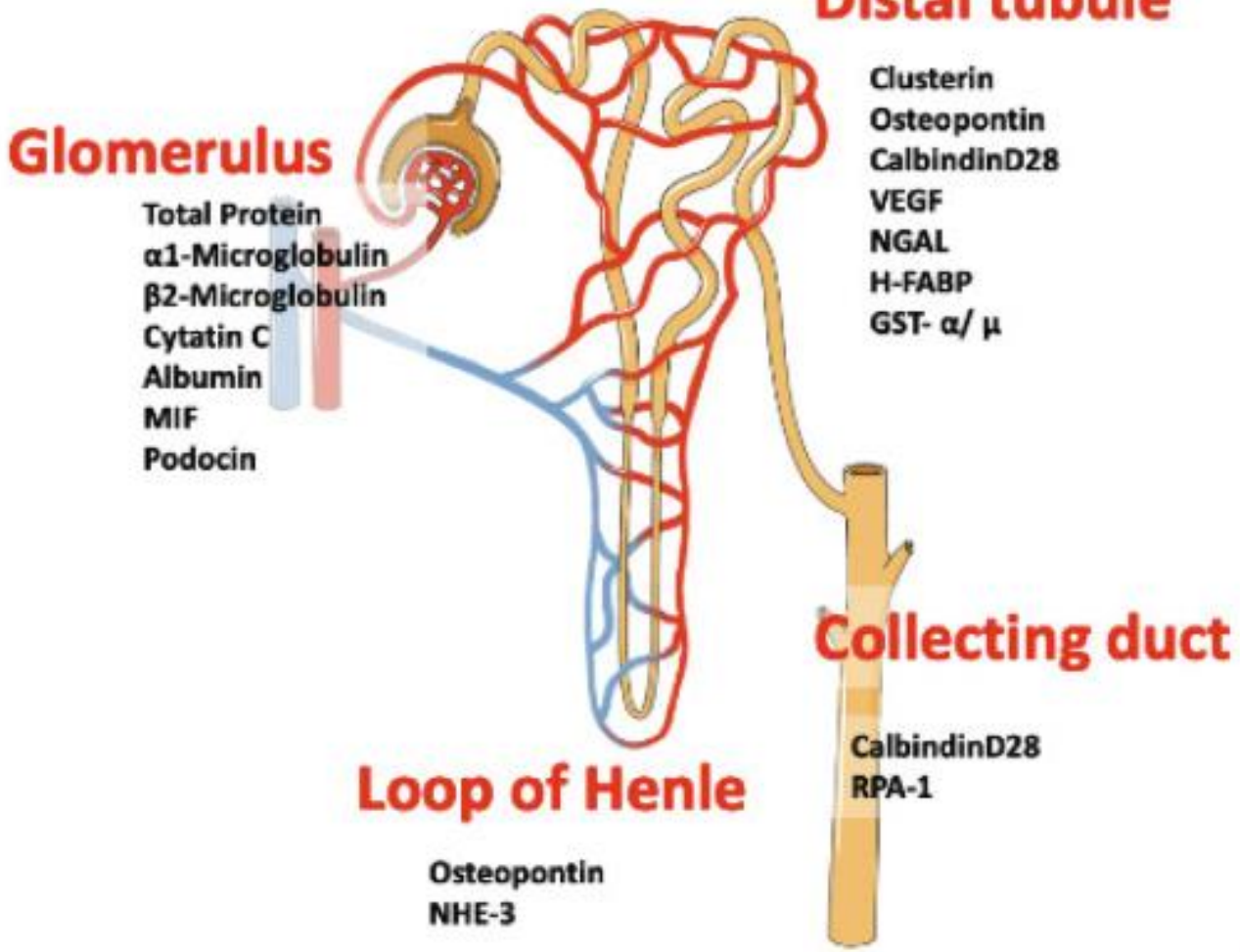
Proximal tubule

α1-Microglobulin
Kim-1
GST- α
Cystatin C
NGAL

β2-Microglobulin
Clusterin
Osteopontin
VEGF
Timp-1

NAG
RBP
HGF
NHE-3
L-FABP
TFF-3

Netrin-1
IL-18
Cyr61
Exosomal fetuin-A
Total Protein



Glomerulus

Total Protein
α1-Microglobulin
β2-Microglobulin
Cytatin C
Albumin
MIF
Podocin

Distal tubule

Clusterin
Osteopontin
CalbindinD28
VEGF
NGAL
H-FABP
GST- α/ μ

Collecting duct

CalbindinD28
RPA-1

Loop of Henle

Osteopontin
NHE-3

https://pmc.ncbi.nlm.nih.gov/articles/PMC8708607/

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Table 2.

Laboratory based assays that could be used to screen for renal tubular damage in affected populations.

Biomarker	Mycotoxins	Technique(s)	References
NGAL	OTA, AFB1, CIT	Immunoassays ELISA	[7,102,127]
KIM-1	OTA, AFB1, CIT	Immunoassays (ELISA, MSD-ECL)	[7,127,128,129]
NAG	OTA, CIT	Enzymatic assays	[7]
Cystatin C	OTA, AFB1, CIT	Immunoassays, ELISA	[7,105,127,129]
L-FABP	OTA, CIT	Immunoassays, ELISA	[7]
β_2-MG	OTA, CIT	Immunoassays, ELISA	[7]
TIMP-1	OTA	Immunoassays, ELISA	[7,129]
clusterin	OTA	Immunoassays, ELISA	[7]
osteopontin	OTA	Immunoassays, ELISA	[7]

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https://pmc.ncbi.nlm.nih.gov/articles/PMC8708607/

High (>95th percentile)

Mycotoxins | Heavy Metals | Environmental Toxins

TEST NAME	CURRENT RESULT	PREVIOUS RESULT	CURRENT RESULT / PREVIOUS RESULT	REFERENCE
Aflatoxin B1 (AFB1)	13.19		0 3.9 6.93	≤6.93 ng/g
Aflatoxin G1	6.58		0 3.68 6.53	≤6.53 ng/g
Deoxynivalenol(DON)	85.48		0 37.9 67.4	≤67.47 ng/g
Fumonisins B2	22.86		0 4.05 7.2	≤7.2 ng/g
Fumonisins B3	33.82		0 6.08 10.8	≤10.8 ng/g
Ochratoxin A (OTA)	21.29		0 3.83 6.8	≤6.8 ng/g
Arsenic*	63.8		0 11.9 52	≤52 ug/g

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High (>95th percentile)

Mycotoxins | Environmental Toxins

TEST NAME	CURRENT RESULT	PREVIOUS RESULT	CURRENT RESULT / PREVIOUS RESULT	REFERENCE
Aflatoxin B1 (AFB1)	8.9		0 — 3.9 — 6.93	≤6.93 ng/g
Deoxynivalenol(DON)	118.76		0 — 37.9 — 67.4	≤67.47 ng/g
Diphenyl Phosphate (DPP)	3.96		0 — 1.1 — 3.7	≤3.7 ug/g

Moderate (75th-95th percentile)

Mycotoxins | Heavy Metals | Environmental Toxins

TEST NAME	CURRENT RESULT	PREVIOUS RESULT	CURRENT RESULT / PREVIOUS RESULT	REFERENCE
Aflatoxin G1	3.86		0 — 3.68 — 6.53	≤6.53 ng/g
Aflatoxin M1	5.51		0 — 3.6 — 6.4	≤6.4 ng/g
Mercury*	1.12		0 — 0.57 — 1.61	≤1.61 ug/g

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High (>95th percentile)

Mycotoxins | Environmental Toxins

TEST NAME	CURRENT RESULT	PREVIOUS RESULT	CURRENT RESULT / PREVIOUS RESULT	REFERENCE
Fumonisins B1	17.81		0 — 3.45 — 6.13	≤6.13 ng/g
Fumonisins B3	35.58		0 — 6.08 — 10.8	≤10.8 ng/g
Zearalenone (ZEN)	2.26		0 — 0.38 — 0.67	≤0.67 ng/g
Phenyl glyoxylic Acid (PGO)*	1085.63		0 — 285 — 518	≤518 ug/g
Triclosan (TCS)*	554.24		0 — 29.9 — 358	≤358 ug/g

* Indicates NHANES population data reference ranges.

Moderate (75th-95th percentile)

Mycotoxins | Heavy Metals | Environmental Toxins

TEST NAME	CURRENT RESULT	PREVIOUS RESULT	CURRENT RESULT / PREVIOUS RESULT	REFERENCE
Dihydrocitrinone	13.2		0 — 9.3 — 16.5	≤16.53 ng/g
Ochratoxin A (OTA)	5.9		0 — 3.83 — 6.8	≤6.8 ng/g
Roridin L2	4.16		0 — 3.83 — 6.8	≤6.8 ng/g
Arsenic*	23.07		0 — 11.9 — 52	≤52 ug/g

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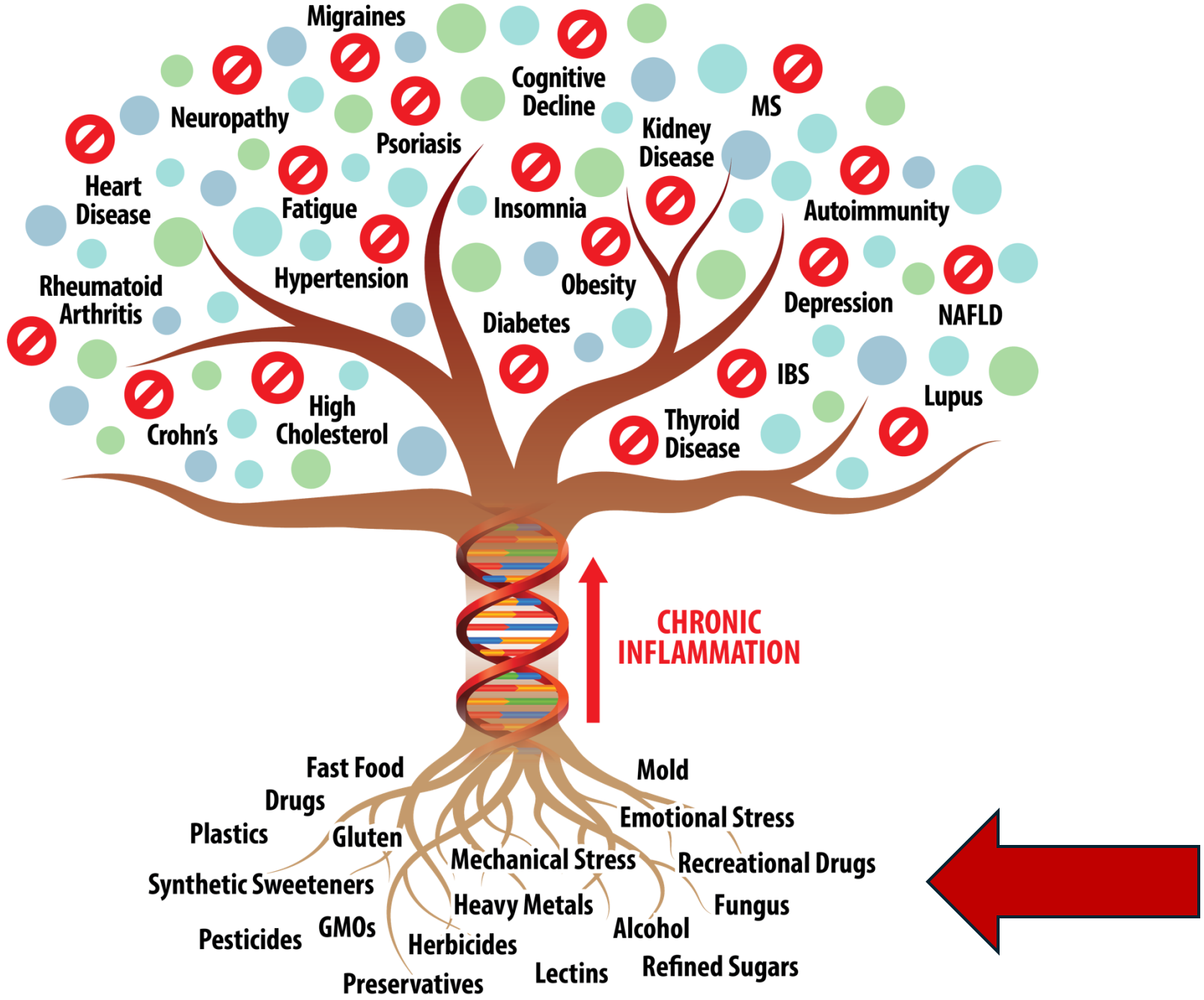
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Alcohol
Preservatives
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Support Plan

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https://pmc.ncbi.nlm.nih.gov/articles/PMC6682908/

https://pmc.ncbi.nlm.nih.gov/articles/PMC10861109/

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Support Plan

https://pmc.ncbi.nlm.nih.gov/articles/PMC6989347/
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Submit your case to the CC team

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