Peran Monitoring Biologis dalam Pengelolaan Dampak Kesehatan Akibat Pajanan Pestisida

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Disclosure statement

I have no conflict of interest to disclose regarding the material presented in this presentation

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Pendahuluan (1)

- Di Indonesia terdapat +27,6 juta rumah tangga usaha pertanian (SUTAS 2018)
- Untuk membasmi hama pertanian, petani menggunakan pestisida termasuk diantaranya insektisida, fungisida, dan herbisida
- Pola penggunaan pestisida:
  - Pestisida multipel
  - Dosis tidak tepat
  - Tidak disertai penggunaan APD yang adekuat
  - Kesadaran akan dampak kesehatan dan pengetahuan tentang cara kerja yang benar masih rendah

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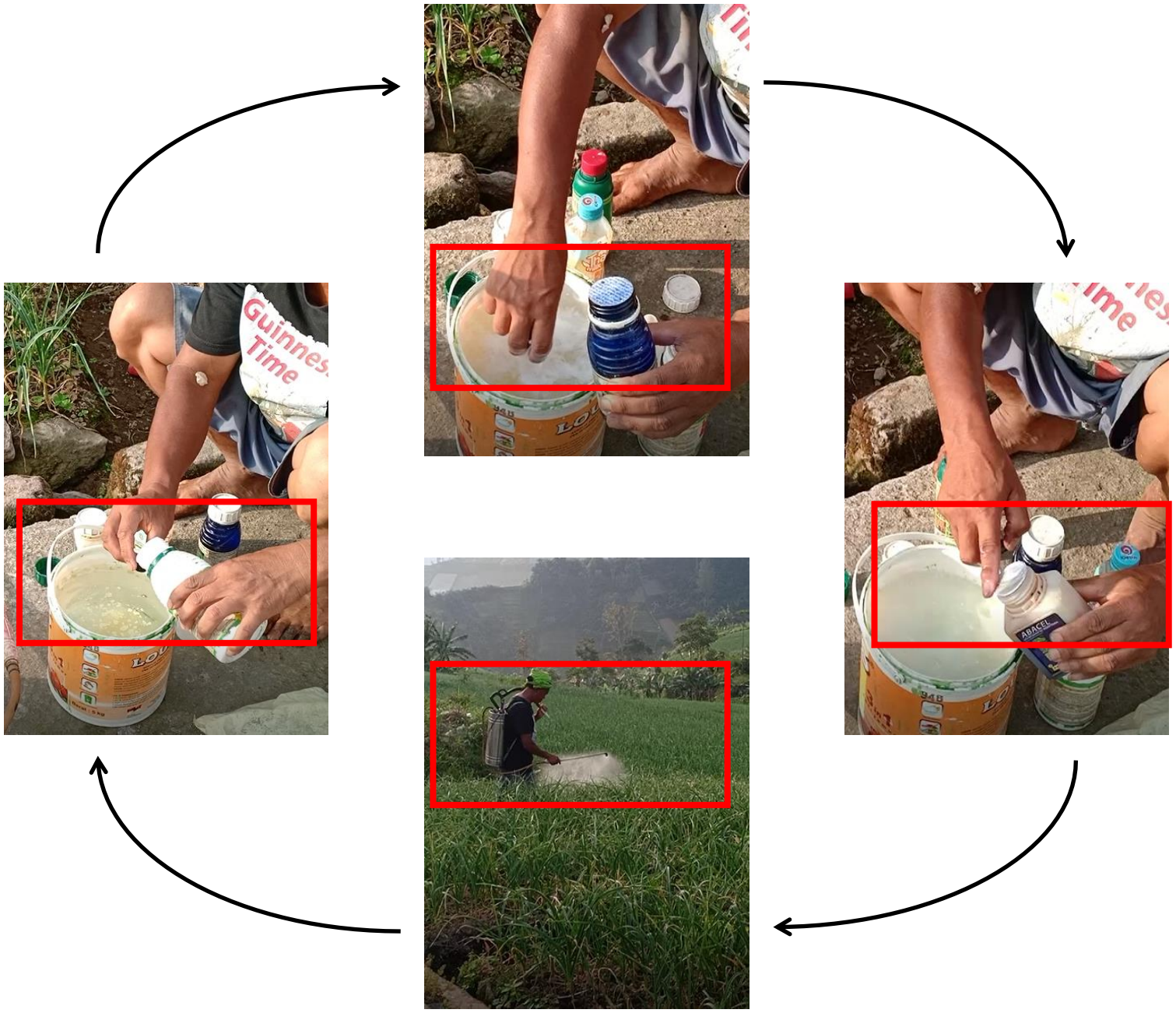

Kegiatan terpajan pestisida

1. Kontak langsung dengan konsentrat
2. Kontak langsung dengan cairan campuran pestisida
3. Tidak mengenakan APD dengan baik
4. Multipel pestisida

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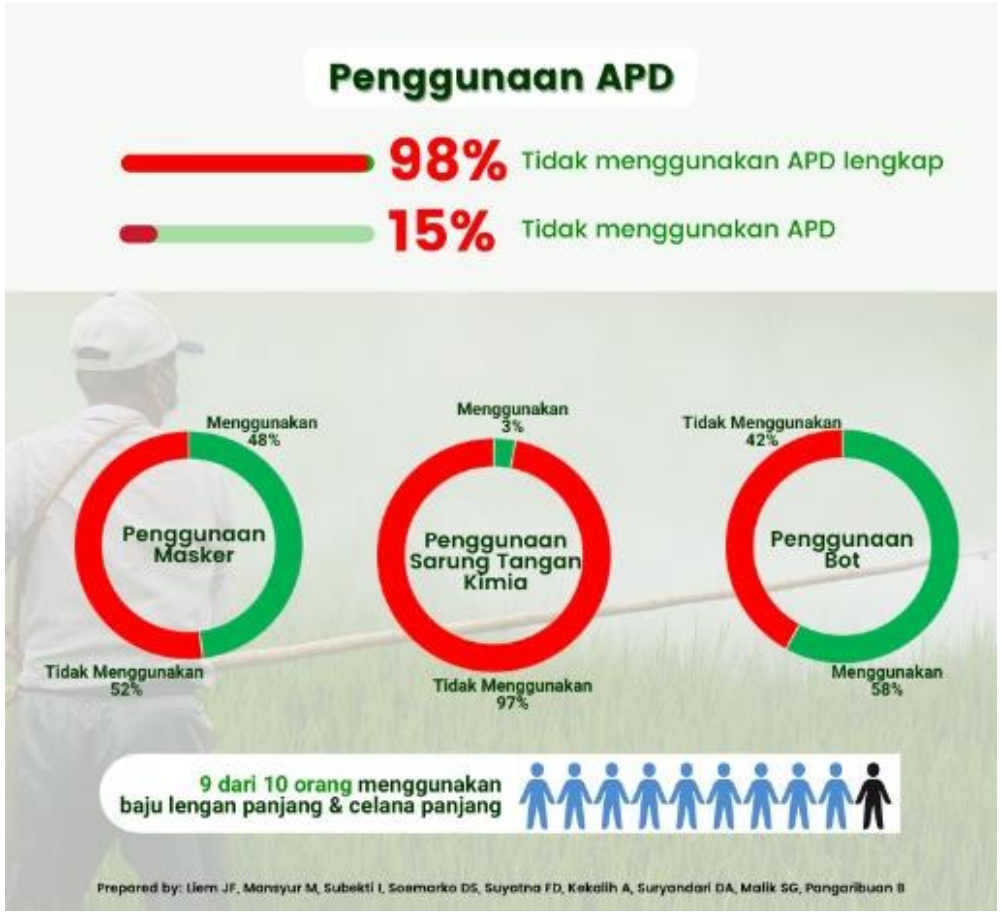
Karakteristik Kegiatan Terpajan Pestisida



Liem JF, Mansyur M, Soemarko DS, Kekalih A, Subekti I, Suyatna FD, et al. BMC Public Health. 2021;21:1066.

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(2)

- Semua pestisida bersifat racun agar efektif melawan hama yang ingin dikendalikan, sehingga pestisida berpotensi berbahaya bagi manusia, hewan, organisme lain, dan lingkungan.
- Sejumlah studi telah memberikan bukti gangguan kesehatan yang berhubungan dengan penggunaan pestisida, namun belum banyak informasi/data mengenai biomarker pajanan, efek, ataupun kerentanan pada petani terkait dengan pajanan pestisida khususnya di Indonesia.

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Pestisida

- Pestisida adalah setiap bahan atau campuran bahan yang ditujukan untuk mengusir, mematikan, atau mengendalikan hama.
- Pestisida dapat digolongkan berdasarkan target spesies atau tujuan penggunaannya, di antaranya insektisida untuk membasmi hama serangga, herbisida membasmi tanaman pengganggu atau gulma, dan fungisida untuk membasmi jamur.

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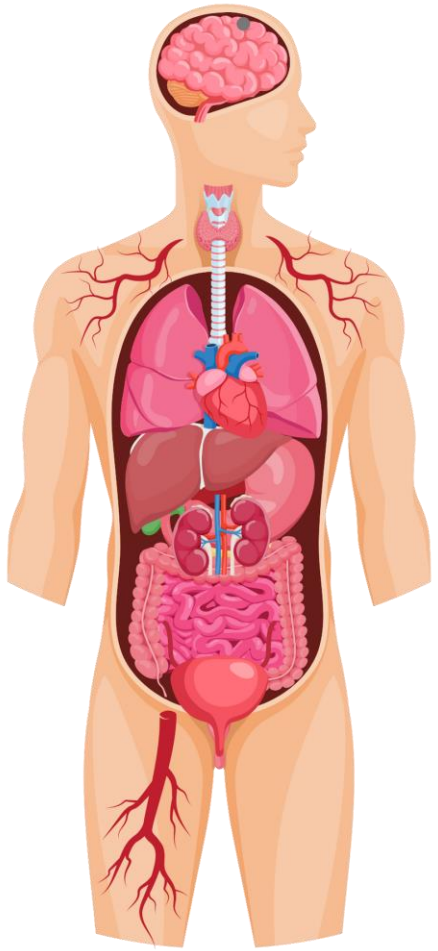
Potensi dampak kesehatan akibat pajanan pestisida

- Gangguan neurologis
- Gangguan endokrin
- Gangguan metabolisme
- Gangguan sistem reproduksi
- Gangguan sistem respirasi
- Gangguan kulit
- Gangguan tumbuh kembang
- Gangguan ginjal
- Gangguan liver
- Gangguan kesehatan mental



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FUNGSI GINJAL PADA PETANI YANG TERPAJAN PESTISIDA ORGANOFOSFAT

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TUJUAN

mengetahui dampak pajanan organofosfat terhadap fungsi ginjal dan karakteristik pekerja petani saat menggunakan pestisida organofosfat.

HASIL

Pajanan pestisida organofosfat mempengaruhi kadar kreatinin, BUN, ataupun asam urat pada petani. Karakteristik petaniseperti tingkat pendidikan, penggunaan APD, durasi penyemprotan, masa kerja petani dan dosis penggunaan pestisida berpengaruh signifikan dengan keracunan organofosfat.

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Literature Review: Hubungan Pajanan Pestisida Organofosfat dengan Gangguan Fungsi Hati pada Pekerja Pertanian

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KESIMPULAN

Dapat disimpulkan pajanan pestisida organofosfat memengaruhi kadar penanda biokimia fungsi hati sesuai dengan tujuan khusus penulisan tinjauan literatur. Penanda biokimia yang dapat digunakan untuk mengetahui kejadian gangguan fungsi hati terhadap pajanan pestisida organofosfat pada petani adalah AST atau SGOT dan ALT atau SGPT yang selalu diujikan pada setiap jurnal yang di-review serta paling banyak menyatakan perbedaan bermakna antara pajanan pestisida dengan gangguan fungsi hati.

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Gangguan Psikiatri pada Sektor Pertanian yang Terpajan Pestisida Organofosfat: *A literature review*

Meisya Claudia Susanto[1)], Johannes Hudyono[2)], Liem Jen Fuk[2)], Susanty Dewi Winata[2)]
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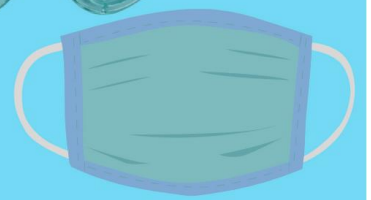
HASIL

Terdapat hubungan bermakna antara pajanan pestisida OP dengan gangguan psikiatri, diantaranya berupa insomnia, kemarahan, kecemasan dan depresi. Usia, dosis pajanan, pemakaian alat pelindung diri (APD) serta perilaku penggunaan pestisida yang tidak aman menjadi faktor risiko keracunan OP.



KESIMPULAN

Pajanan pestisida organofosfat bersama dengan sejumlah faktor risiko individu dan okupasi berhubungan dengan gangguan psikiatri.

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Risk concept

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What chemicals are hazardous?

- Setiap zat, dalam bentuk gas, cair atau padat, termasuk uap dan aerosol yang berpotensi menimbulkan bahaya
- Absorbsi bahan kimia ke dalam tubuh di tempat kerja tersering melalui inhalasi, kontak kulit dan kadang-kadang melalui saluran pencernaan
- Sumber pajanan:
  - Kecelakaan, kebocoran, kerusakan pada alat ventilasi dan proses kerja yang tidak sesuai standar
- *Substances can be **considered hazardous** not solely because of their content (i.e. **chemical ingredients**) but because of **the form** or **way in which they are used** at the workplace.*

Toxic

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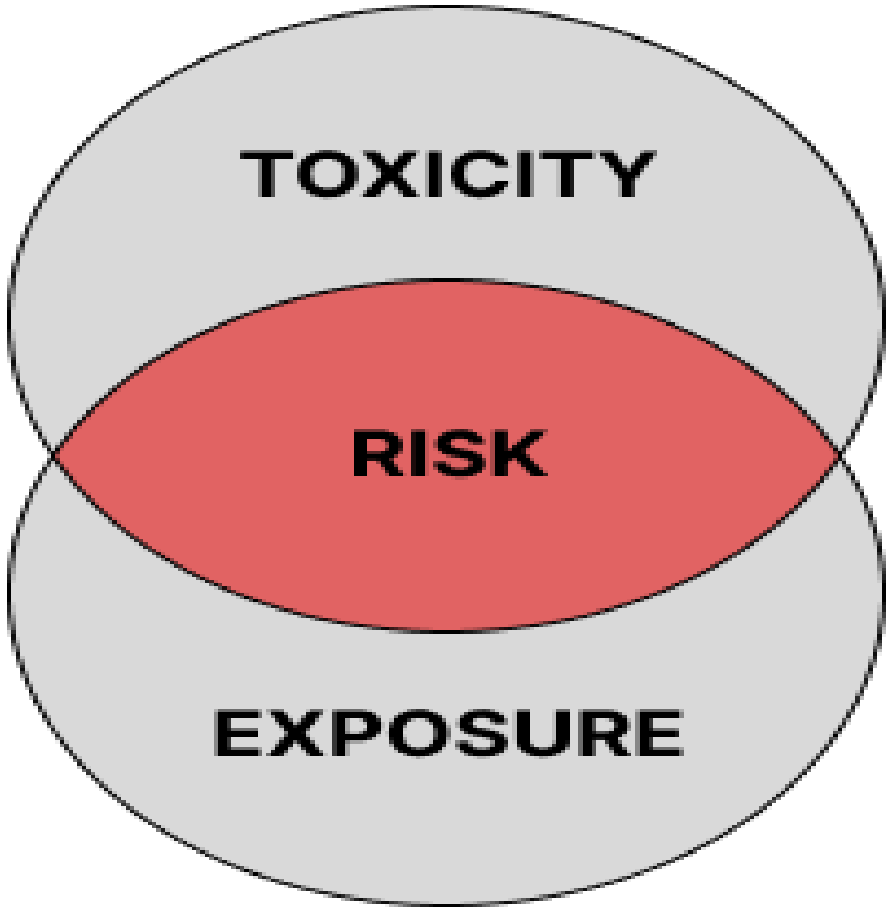
Risk as a function of toxicity and exposure (1)



- Pesticide toxicity is its capacity or ability to cause harmful effects or illness.
- How much of the substance is required to cause harm? i.e., LD_{50}, LC_{50}
- Chemical properties

Class		LD_{50} for the rat (mg/kg body weight)	
		Oral	Dermal
Ia	Extremely hazardous	< 5	< 50
Ib	Highly hazardous	5–50	50–200
II	Moderately hazardous	50–2000	200–2000
III	Slightly hazardous	Over 2000	Over 2000
U	Unlikely to present acute hazard	5000 or higher	

1. Damalas CA, Koutroubas SD. Farmers' exposure to pesticides. Toxics. 2016;4(1):1.
2. Liem JF, et al. Cumulative exposure characteristics. BMC Public Health. 2021;21:1066.
3. Dosemeci M, et al. A quantitative approach for estimating exposure. Ann Occup Hyg. 2002;46(2):245–60.

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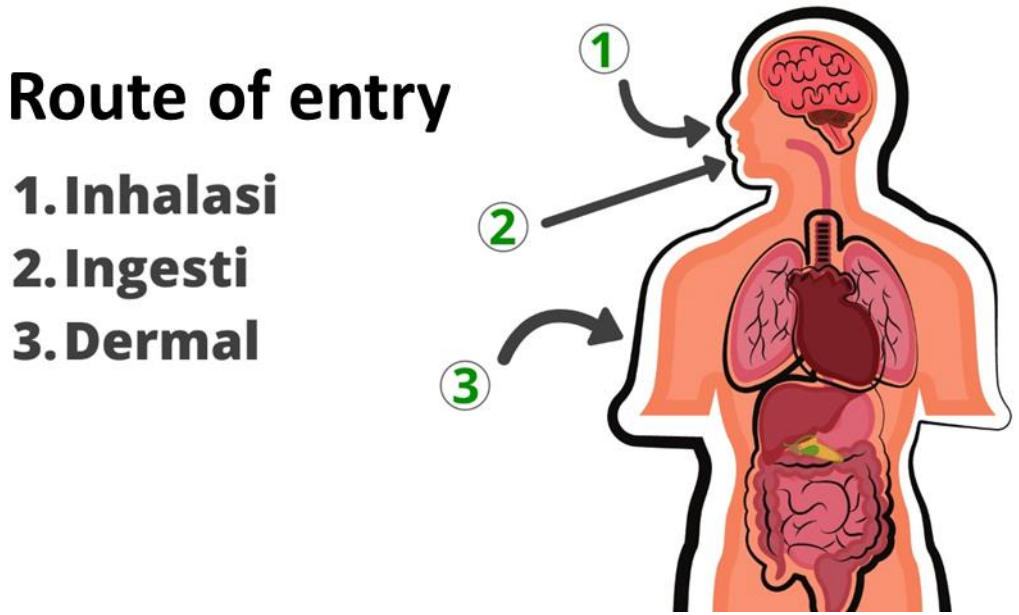
(2)

- Potential source of exposure:
  - Pesticide handling: preparing, mixing, loading, spraying, cleaning used equipment
  - Re-entering sprayed area
  - Manipulating crops
  - Harvesting
- Dose, Concentration, length of exposure, route of entry
- Work practices i.e., application methods, PPE, personal hygiene, spill treatment



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Pengelolaan kesehatan pekerja terpajan pestisida

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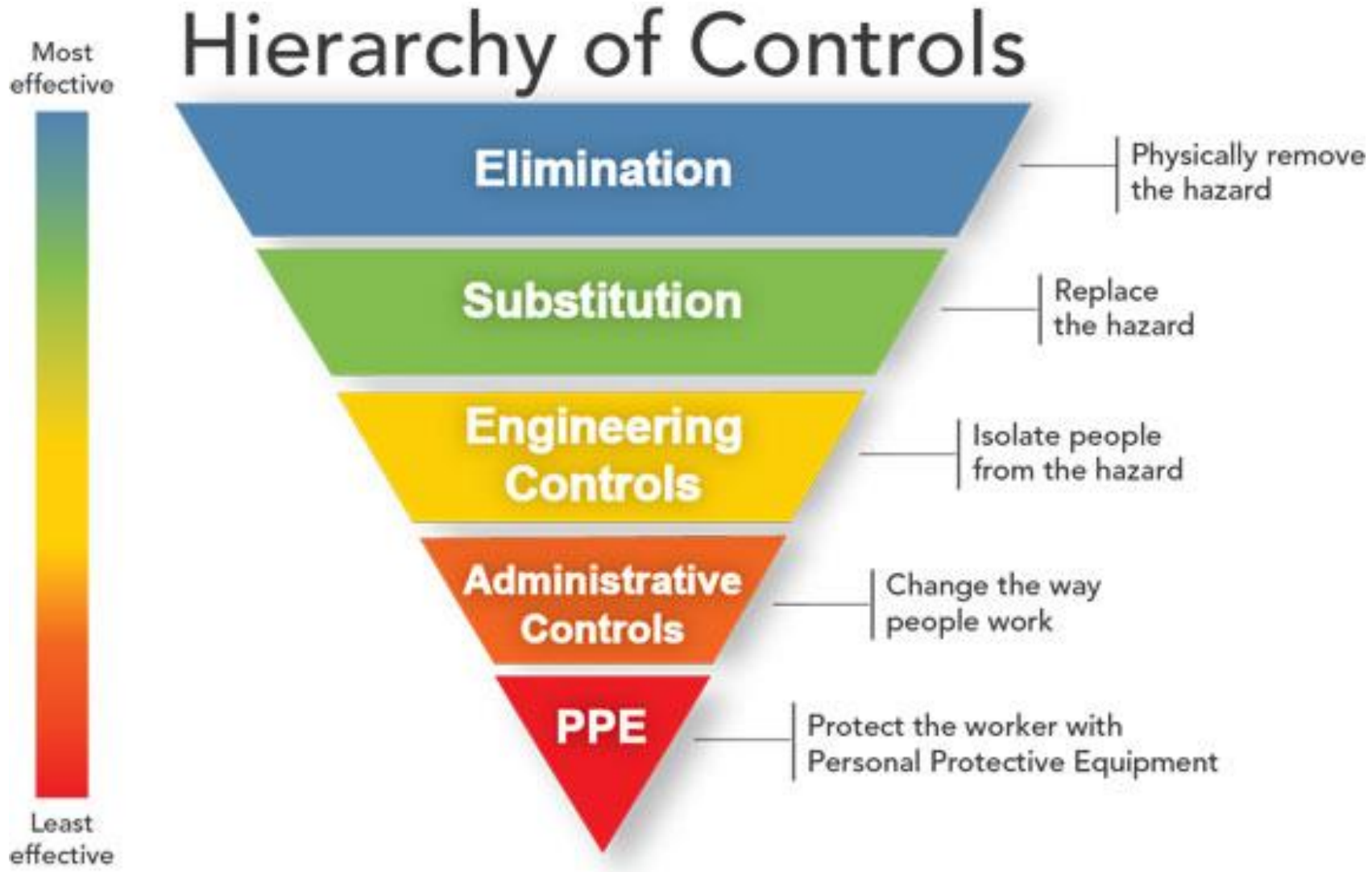

https://www.cdc.gov/niosh/topics/hierarchy/default.html

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Table 2. Minimum PPE and Work Clothing for Pesticide-Handling Activities

Route of Exposure	Toxicity Category of End-Use Product			
	I	II	III	IV
Dermal toxicity or skin irritation potential	Coveralls worn over long-sleeved shirt and long pants	Coveralls worn over short-sleeved shirt and short pants	Long-sleeved shirt and long pants	Long-sleeved shirt and long pants
	Socks	Socks	Socks	Socks
	Chemical-resistant footwear	Chemical-resistant footwear	Shoes	Shoes
	Chemical-resistant gloves	Chemical-resistant gloves	No minimum	No minimum
Inhalation toxicity	Respiratory protection device	Respiratory protection device	No minimum	No minimum
Eye irritation potential	Protective eyewear	Protective eyewear	No minimum	No minimum

Source: Toxicity of Pesticides. Penn State University

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5 Levels of Prevention

Health Promotion

Specific Protection

Early Diagnosis & Prompt Treatment

Disability Limitation

Rehabilitation

SEHAT

ASIMPTOMATIK

SAKIT

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Occupational Surveillance

- Is a program of **medical examinations** and **tests** designed to detect **early warning signs** of harmful exposure. It is expected to discover **early/small changes** in health before advanced or severe damage occurs, although to date medical monitoring tests that accurately measure early health effects have only been **available for a small number of chemicals**.
- In occupational surveillance program, the type of testing needed depends upon the particular chemical involved.
- A complete occupational surveillance program should consist of **industrial hygiene** monitoring, **medical monitoring**, and **biological monitoring** when appropriate.

Biological Monitoring

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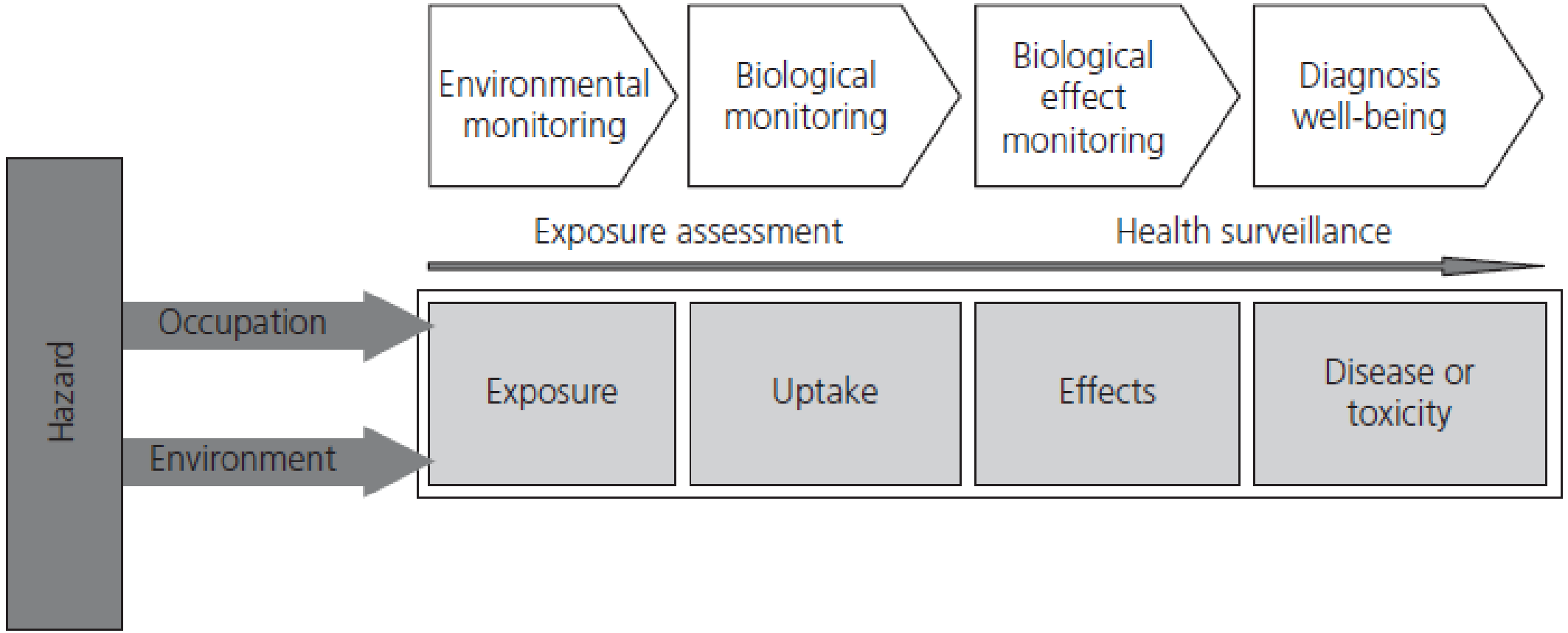
Exposure – disease paradigm



Source: Hunter's Diseases of Occupations

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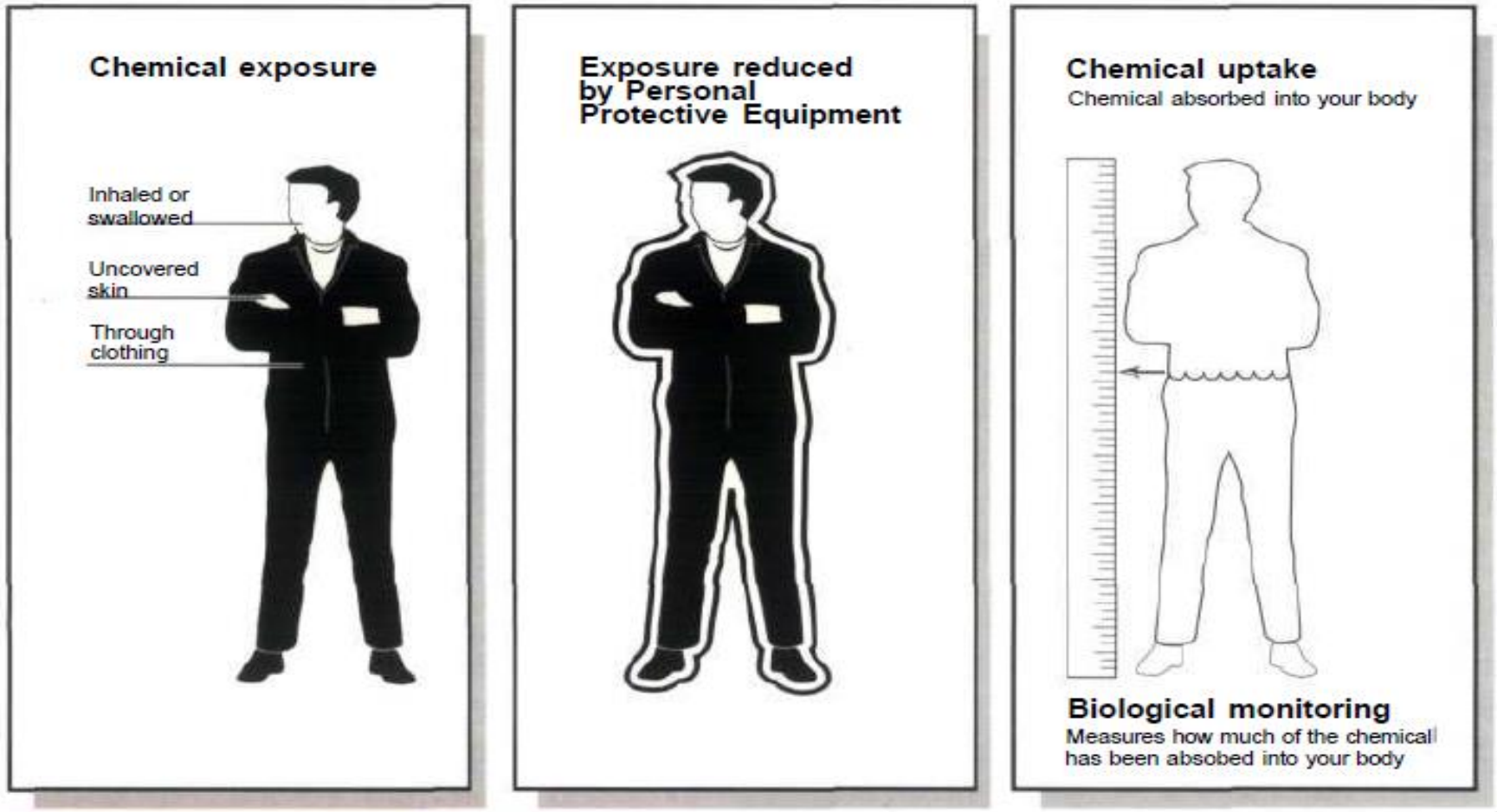
Chemical uptake



Source: HSE – Biological Monitoring at the workplace

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What is Biological monitoring ?

- *Biological monitoring is a method for assessing human **exposure** to chemicals (or their **effects** or their **susceptibility**) by measuring the chemicals, their metabolites or reaction products in human tissues or specimens, such as blood, urine, or hair*

Biomarker of exposure

Biomarker of effect

Biomarker of susceptibility

WHO. Human biomonitoring: facts and figures. Copenhagen: WHO Regional Office for Europe; 2015.

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Biomarker

- *Biomarker typically is the agent or its metabolite(s) or organism intrinsic characteristics in a biological specimen*
- *Objective, quantifiable characteristics of biological processes.*
- *Presence of environmental chemicals in human tissue*
- *Early (pre-clinical) biological effects from environmental exposures*

Biological Matrices

- *The most common matrices used for biological monitoring are urine, blood, and saliva and exhaled air*
- *Blood specimen*
  - *Requires invasive procedure*
- *Urine specimen*
  - *Accuracy of the exposure estimate depends upon the sampling strategy → collection time & urine output*
  - *24-hrs specimens are more representative and usually correlate better with intensity of exposure → seldom feasible.*

Table 1. Biological matrices used in HBM studies

Matrix	Population	Advantages	Limitations	Compounds measured in the matrix
Blood, serum, plasma	General	In equilibrium with all organs and tissues. Well established standard operating procedures (SOPs) for sampling.	Invasive; trained staff and special materials required. Volume limitation. Special conditions for transport and shipment.	POPs, metals/trace elements, organic compounds, tobacco smoke. e.g.: alkylphenols, mercury, lead, BFRs, dioxins, water disinfection byproducts, fluorinated compounds, organochlorine pesticides, organophosphate pesticides, phthalates, PCBs, dioxins.
Urine	General	Non-invasive, easy collection, no volume limitation. Allows analysis of metabolite	Composition of urine varies over time.	Metals/trace elements, organic compounds, tobacco smoke. Metabolites of environmental pollutants. e.g.: mercury, cadmium, arsenic, organochlorine compounds, BPA, organophosphate pesticides, parabens, phthalates, PAHs, benzene.
Hair	General, with few exceptions (i.e. neonates)	Non-invasive; minimum training required for sampling. No special requirements for transport and storage. Information about cumulative exposure during previous months. Segmental analysis is possible.	Hair is exposed to the environment and can be contaminated. Potential variations with subject's hair colour, hair care or race.	Metals/trace elements, POPs e.g.: total mercury, methylmercury, arsenic, cadmium, parabens, organochlorine compounds
Saliva	General	Non-invasive, easy collection	Lower concentrations of analytes than in blood; requires sensitive analytical techniques. Variation in flow rate and composition. The use of stimulant or absorbent pads can interfere with analysis. Less documented for HBM applications.	Metals/trace elements, organic compounds, POPs, tobacco, e.g.: cadmium, phthalates, BPA, PCBs, dioxins

WHO. Human biomonitoring: facts and figures. Copenhagen: WHO Regional Office for Europe; 2015.

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Spot urine in representing the true exposure

- Spot urine specimens have been used in the **biomonitoring of exposure** to xenobiotics in several epidemiological studies. However, the **reliability** of single-spot urine to represent an exposure profile in individuals over time may be affected by differences of the nature of exposure which may vary with exposure intensity, toxicokinetic (i.e., short half-lives) and across individuals.
- Thus, **creatinine correction** is used to **compensate for urine dilution** and has been suggested to **improve the predictability** of chemical exposure over time, as creatinine correction in biomarker concentrations **reduces intra- and inter-individual variability**.

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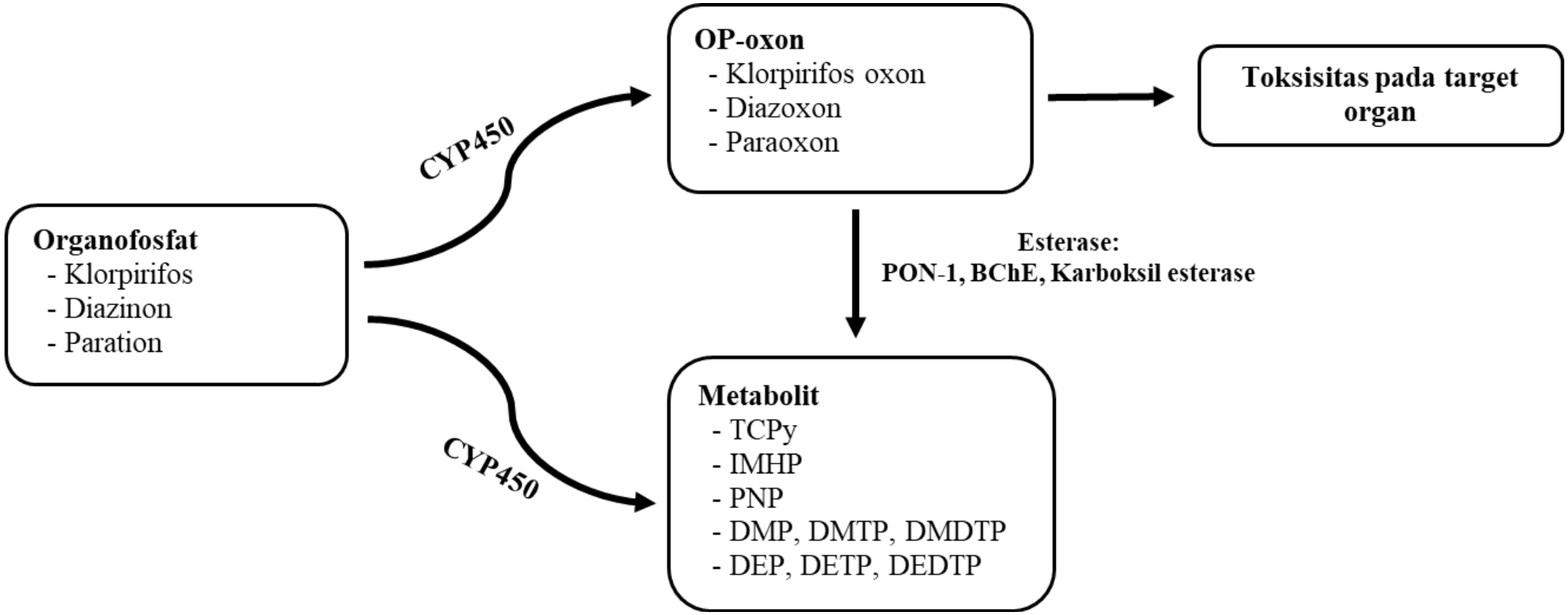
Skema biometabolisme OP



Liem JF. J Kdokt Meditek. 2021;27(1):88–94

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Toksisitas CPF

- Efek toksik pajanan CPF tidak ditimbulkan dari senyawa induknya, melainkan berasal dari metabolit CPF.
- Klorpirifos akan mengalami detoksifikasi menjadi 3,5,6-trichloro-2-pyridinol (TCPy) dan sebaliknya mengalami bioaktivasi menjadi CPF okson (CPF-O), yang merupakan inhibitor poten terhadap asetilkolinesterase (AChE) dan butirilkolinesterase (BChE).
- Penurunan aktivitas hidrolisis AChE merupakan indikator terjadinya toksisitas dan sejauh ini selalu digunakan sebagai penanda pajanan dan efek.

Biomarker of exposure

Pesticide	Class	Function	Metabolites
Mancozeb	EBDC	Fungicide	Ethylene-bis-thiourea (ETU)
Penconazole (PEN)	Triazole	Fungicide	Monohydroxy-penconazole (PEN-OH); Carboxy-penconazole (PEN-COOH)
Imidacloprid	Neonicotinoid	Insecticide	5-hydroxy-imidacloprid (5-OH-IMI)
Cypermethrin	Pyrethroid	Insecticide	Dichlorovynil dimethylcyclopropane carboxylic acid (cis/trans DCCA); 3-phenoxybenzoic acid (3-PBA)
Chlorpyrifos	Organophosphate	Insecticide	3,5,6-trichloropyridinol (TCPy)
Non specific	Organophosphate	Insecticide	Dimethyl alkylphosphate: DMP, DMTP, DMDTP; Diethyl alkylphosphate: DEP, DETP, DEDTP

Biomarker of effect

Toxicity	Biomarker of Effect
Nervous system	AChE, BChE
Thyroid	TSH, FT4, T4, FT3, T3, Thyroglobulin
Reproductive hormone	LH, FSH, progesteron, estradiol, testosteron
Metabolic	Blood glucose, cholesterol
Liver	ALT, AST, GGT, albumin
Kidney	Ureum, creatinine, cystatin C, B2-microglubulin

Biomarker of susceptibility

- Beberapa gen dapat dipertimbangkan untuk menjadi biomarker kerentanan pajanan OP sehubungan dengan aktifitas fungsionalnya pada proses biotransformasi OP seperti gen PON-1, CYP2B6, CYP2C19, CYP3A4.

The role of biomonitoring

- *Biomonitoring provides information about what chemicals get into people*
- *It might be used to estimate exposure.*
- *It provides information on the effectiveness of exposure mitigation efforts.*
- *Used to evaluate health effects of harmful chemicals and prevent occupational disease or impairment*

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Penutup (1)

- Bila penggunaan pestisida kimia belum dapat dihilangkan, maka upaya berikutnya yang perlu dilakukan adalah dengan menurunkan besarnya pajanan.
- Hal ini dapat dilakukan dengan pengendalian administratif melalui pelatihan dan pendampingan tentang pemilihan, penggunaan dan pengelolaan pestisida secara komprehensif yang disertai dengan pengasuhan berkelanjutan perlu diberikan kepada petani pada umumnya dan khususnya pada penyemprot pestisida, serta mendorong penggunaan APD dan pakaian kerja yang memadai.

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(2)

- Sebagai upaya memelihara kesehatan petani dan deteksi dini gangguan kesehatan akibat pajanan pestisida, penilaian dosis pajanan dan pemeriksaan kesehatan perlu diimplementasikan.
- Monitoring biologis berupa markah pajanan dan efek dapat dilakukan sesuai dengan jenis pestisida yang memajani petani.
- Pemeriksaan markah kerentanan berupa variasi genetik dapat bermanfaat dalam memetakan potensi risiko kerentanan genetik dalam kaitannya dengan strategi pengendalian pajanan dan penegakan etiognosis pada individu terpajan pestisida.

Further reading

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Terima Kasih

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