

ALIMENTATION ET CANCER DU SEIN

INTRODUCTION

- 30 tonnes d'aliments ingérés au cours d'une vie

- 50 000 litres de boissons



- Nutriments : protides, lipides, glucides
- Vitamines, sels minéraux
- Ethanol, additifs, pesticides



*Gregg Segal, Daily Bread
what kids eat around the world 2019*

EPIDEMIOLOGIE

- COMMENT ON ETABLIT UN RAPPORT ENTRE LA NOURRITURE ET LA SURVENUE DE PATHOLOGIES ET NOTAMMENT DES CANCERS ?
- COMPLÉMENTARITÉ DES TYPES D'ÉTUDES POUR BÂTIR UN FAISCEAU DE PREUVES

LES ETUDES ÉPIDÉMIOLOGIQUES

- LES ÉTUDES ÉCOLOGIQUES
- LES ÉTUDES CAS-TÉMOINS
- LES ÉTUDES DE COHORTE
 - NURSES'HEALTH STUDY
 - EPIC
 - NUTRINET SANTÉ
- LES ESSAIS CONTROLÉS RANDOMISÉS
 - SUVIMAX
 - SULFOLOM3

APPROCHES EXPÉRIMENTALES

- IN VITRO
- SUR ANIMAUX
 - INSULINORÉSISTANCE/ HYPERINSULINISME
 - INFLAMMATION CHRONIQUE
 - STRESS OXYDATIF
 - PERTURBATIONS MÉTABOLIQUES
 - DYSBIOSES

Mécanismes sous-tendant les relations
nutrition-santé
dans les pathologies chroniques

Tableau de classification des facteurs alimentaires cancérigènes selon les principales sources scientifiques (monographies OMS/CIRC – centre international de recherche contre le cancer)

| Catégorie CIRC | Niveau de preuve de cancérogénicité | Exemples alimentaires | Types de cancer associés | Commentaires / Mécanismes |
|------------------|---|---|---|--|
| Groupe 1 | Cancérogène pour l'homme | - Viandes transformées (charcuteries, bacon, saucisses, jambon) - Boissons alcoolisées - Aflatoxines (toxines de moisissures sur les céréales, noix, arachides) - Arsenic inorganique dans l'eau potable | - Cancer colorectal - Cancer du foie - Cancers de la bouche, pharynx, larynx, œsophage (alcool) | Preuves solides chez l'humain ; effets directs sur l'ADN, inflammation, formation de composés N-nitrosés, etc. |
| Groupe 2A | Probablement cancérogène pour l'homme | - Viande rouge (bœuf, porc, agneau) - Aliments frits ou grillés à haute température (formation d'amines hétérocycliques et HAP) - Boissons très chaudes (>65°C, ex. maté, café brûlant) - Acrylamide (formé lors de la cuisson à haute température) | - Cancer colorectal - Pancréas - Prostate - Œsophage | Données limitées chez l'humain mais suffisantes chez l'animal. |
| Groupe 2B | Peut-être cancérogène pour l'homme | - Pickles asiatiques (certains types fermentés) - Café (selon température et préparation) - Certains additifs ou contaminants (ex. fumée de bois mal filtrée) | - Estomac - Œsophage | Données limitées chez l'humain et l'animal. |
| Groupe 3 | Inclassable quant à sa cancérogénicité | - Thé, sucre, amidon, lait - Additifs alimentaires courants (ex. aspartame — selon dernières évaluations non cancérogène) | — | Pas assez de preuves pour conclure. |
| Groupe 4 | Probablement non cancérogène pour l'homme | - Caprolactame (rarement alimentaire) | — | Aucune preuve de cancérogénicité. |

SUMMARY OF STRONG EVIDENCE ON DIET, NUTRITION, PHYSICAL ACTIVITY AND THE PREVENTION OF CANCER



| | MOUTH, PHARYNX, LARYNX (2007) | NASOPHARYNX (2007) | OESOPHAGUS SQUAMOUS CELL CARCINOMA (2016) | OESOPHAGUS ADENOCARCINOMA (2016) | LUNG (2007) | STOMACH (2016) | PANCREAS (2012) | GALLBLADDER (2015) | LIVER (2015) | COLORECTUM (2011) | BREAST PREMENOPAUSE (2017) | BREAST POSTMENOPAUSE (2017) | OVARY (2014) | ENDOMETRIUM (2013) | PROSTATE (2014) | KIDNEY (2015) | BLADDER (2015) | SKIN (2007) |
|---|-------------------------------|---------------------------|---|----------------------------------|---------------------------|---------------------------|-------------------------------------|---------------------------|---------------------------|---------------------------|----------------------------|-----------------------------|---------------------------|---------------------------|-------------------------------------|---------------------------|---------------------------|-------------------------------------|
| Foods containing dietary fibre | | | | | | | | | | Convincing decreased risk | | | | | | | | |
| Aflatoxins | | | | | | | | | Convincing increased risk | | | | | | | | | |
| Non-starchy vegetables | Probable decreased risk | | | | | | | | | | | | | | | | | |
| Garlic | | | | | | | | | | Probable decreased risk | | | | | | | | |
| Fruits | Probable decreased risk | | | Probable decreased risk | | | | | | | | | | | | | | |
| Red meat | | | | | | | | | | | Convincing increased risk | | | | | | | |
| Processed meat | | | | | | Probable increased risk | | | | | Convincing increased risk | | | | | | | |
| Cantonese-style salted fish | | Probable increased risk | | | | | | | | | | | | | | | | |
| Diets high in calcium | | | | | | | | | | Probable decreased risk | | | | | | | | |
| Foods preserved by salting | | | | | | Probable increased risk | | | | | | | | | | | | |
| Glycaemic load | | | | | | | | | | | | | Probable increased risk | | | | | |
| Arsenic in drinking water | | | | | Convincing increased risk | | | | | | | | | | | | Convincing increased risk | Convincing increased risk |
| Mate | | | Probable increased risk | | | | | | | | | | | | | | | |
| Alcoholic drinks | Convincing increased risk | Convincing increased risk | | | | | | | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | | | | Probable decreased risk | | |
| Coffee | | | | | | | Substantial effect on risk unlikely | | Probable decreased risk | | | | Probable decreased risk | | | | | |
| Beta-carotene | | | | Convincing increased risk | | | | | | | | | | | Substantial effect on risk unlikely | | | Substantial effect on risk unlikely |
| Physical activity (moderate and vigorous) | | | | | | | | | Convincing decreased risk | | Probable decreased risk | | Probable decreased risk | | | | | |
| Physical activity (vigorous) | | | | | | | | | | | Probable decreased risk | | Probable decreased risk | | | | | |
| Body fatness ¹⁰ | | | Convincing increased risk | | Probable increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk |
| Body fatness in young adulthood | | | | | | | | | | Probable decreased risk | Probable decreased risk | | | | | | | |
| Adult weight gain | | | | | | | | | | | Convincing increased risk | | | | | | | |
| Adult attained height ¹⁴ | | | | | | | | | | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk |
| Greater birth weight | | | | | | | | | | | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk |
| Lactation | | | | | | | | | | Probable decreased risk | Probable decreased risk | | | | | | | |

NIVEAUX DE PREUVE DES RELATIONS ENTRE LES FACTEURS NUTRITIONNELS PRÉSENTÉS DANS CE RAPPORT ET DIFFÉRENTES LOCALISATIONS DE CANCERS

| | Tumeurs solides | | | | | | | | | | | | | | | | | Hémopathies malignes | | | | | | | | | | | | |
|---|-------------------------------------|-------------------------------------|--|---------------------------|------------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|--|
| | Nasopharynx | Tête et cou | Bouche (cavité orale), pharynx, larynx | Oesophage | Adénocarcinome oesogastrique | Estomac | Intestin grêle | Colon-rectum | Pancréas | Ampoule de Vater | Foie | Vésicule biliaire | Rein | Vessie | Sein (avant la ménopause) | Sein (après la ménopause) | Endomètre | Col de l'utérus | Ovaire | Prostate | Testicule | Poumon | Thyroïde | Peau | Lymphome hodgkinien | Lymphome non hodgkinien | Leucémie | Myélome multiple | | |
| Boissons alcoolisées | | | Convincing increased risk | | | | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | |
| Surcharge pondérale | | | Convincing increased risk | | Probable increased risk | | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | |
| Viandes rouges | | | Convincing increased risk | | | | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | |
| Charcuteries | | | Convincing increased risk | | | | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | Convincing increased risk | |
| Sel et aliments salés | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Compléments alimentaire à base de bêta-carotène | Substantial effect on risk unlikely | Substantial effect on risk unlikely | Substantial effect on risk unlikely | | | Convincing increased risk | | | | Convincing increased risk | | | | | | | | | | | | | Convincing increased risk | | | | | | | |
| Produits laitiers | | | | | | | | Convincing decreased risk | | | | | | | Convincing decreased risk | Convincing decreased risk | | | | | Convincing decreased risk | | | | | | | | | |
| Activité physique | | | Convincing decreased risk | | | | | Convincing decreased risk | | Convincing decreased risk | | | | | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | |
| Sédentarité | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Fruits | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | |
| Légumes (non féculents) | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | |
| Fibres alimentaires | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | |
| Allaitement | | | | | | | | | | Convincing decreased risk | | | | | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | Convincing decreased risk | |



¹ signifie que le niveau de preuve est nouvellement établi depuis le rapport WCRF/AICR 2007 ou le CUP WCRF/AICR 2010, 2011, 2012, 2013, 2014
¹⁰ signifie que le niveau de preuve a été modifié depuis le rapport WCRF/AICR 2007 ou le CUP WCRF/AICR 2010, 2011, 2012, 2013, 2014
¹⁴ consommation de compléments alimentaires à base de bêta-carotène à fortes doses, en particulier chez les fumeurs et les personnes exposées à l'amiante

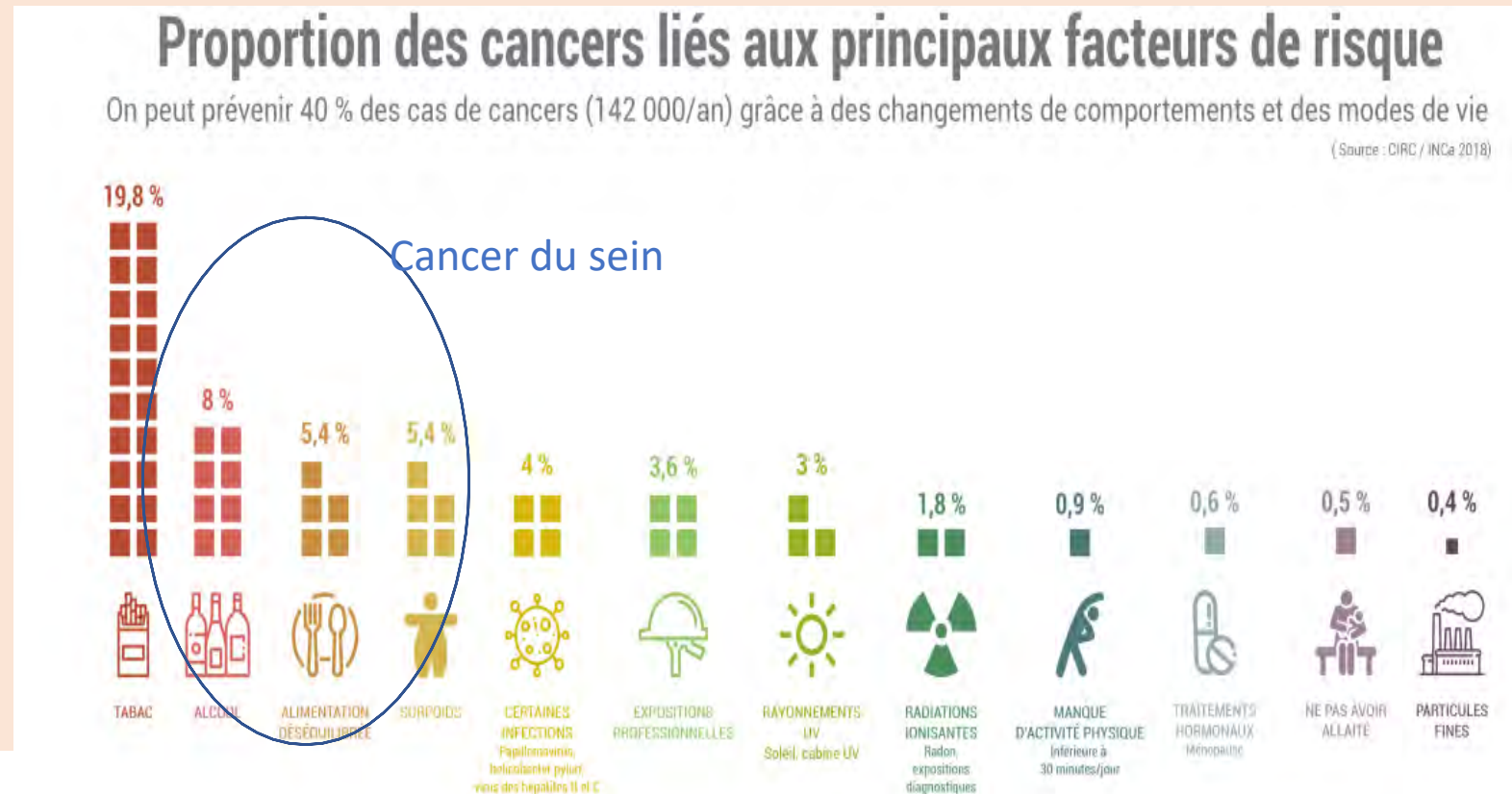
NUTRITION ET PRÉVENTION PRIMAIRE DES CANCERS : ACTUALISATION DES DONNÉES

EPIDEMIOLOGIE

- RESULTATS : LES CANCERS EVITABLES (40%)

- PREVENTION

- PRIMAIRE
- TERTIAIRE



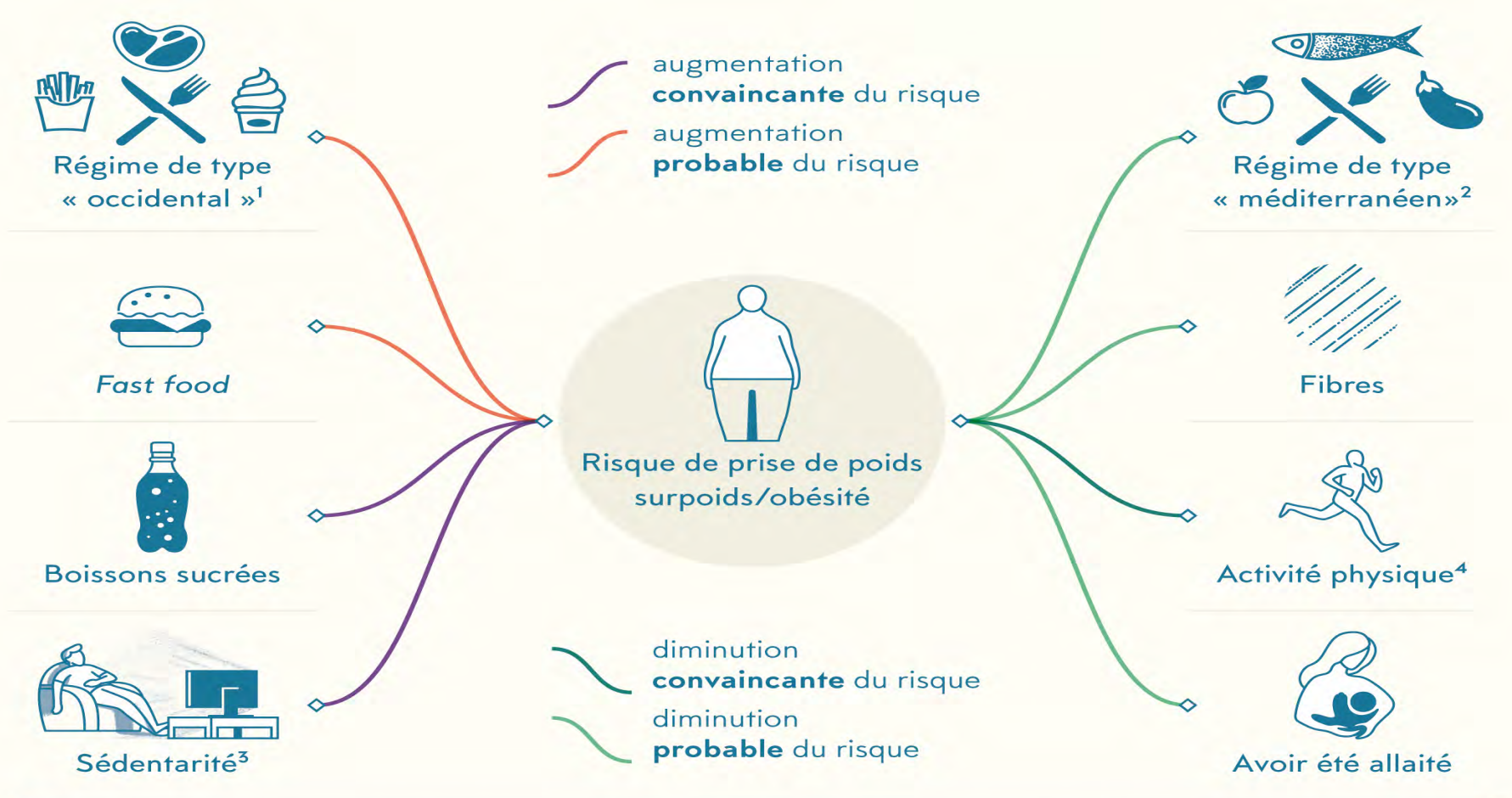
FACTEURS FAVORISANTS ETABLIS DANS LE CANCER DU SEIN

- ALCOOL
- SURPOIDS ET OBESITE / ALIMENTATION DÉSÉQUILIBRÉE
- ALIMENTATION TRANSFORMÉE ET ULTRATransFORMÉE
- LES XENOBIOTIQUES ?
- VITAMINES ?

Alcool et risque de cancer du sein

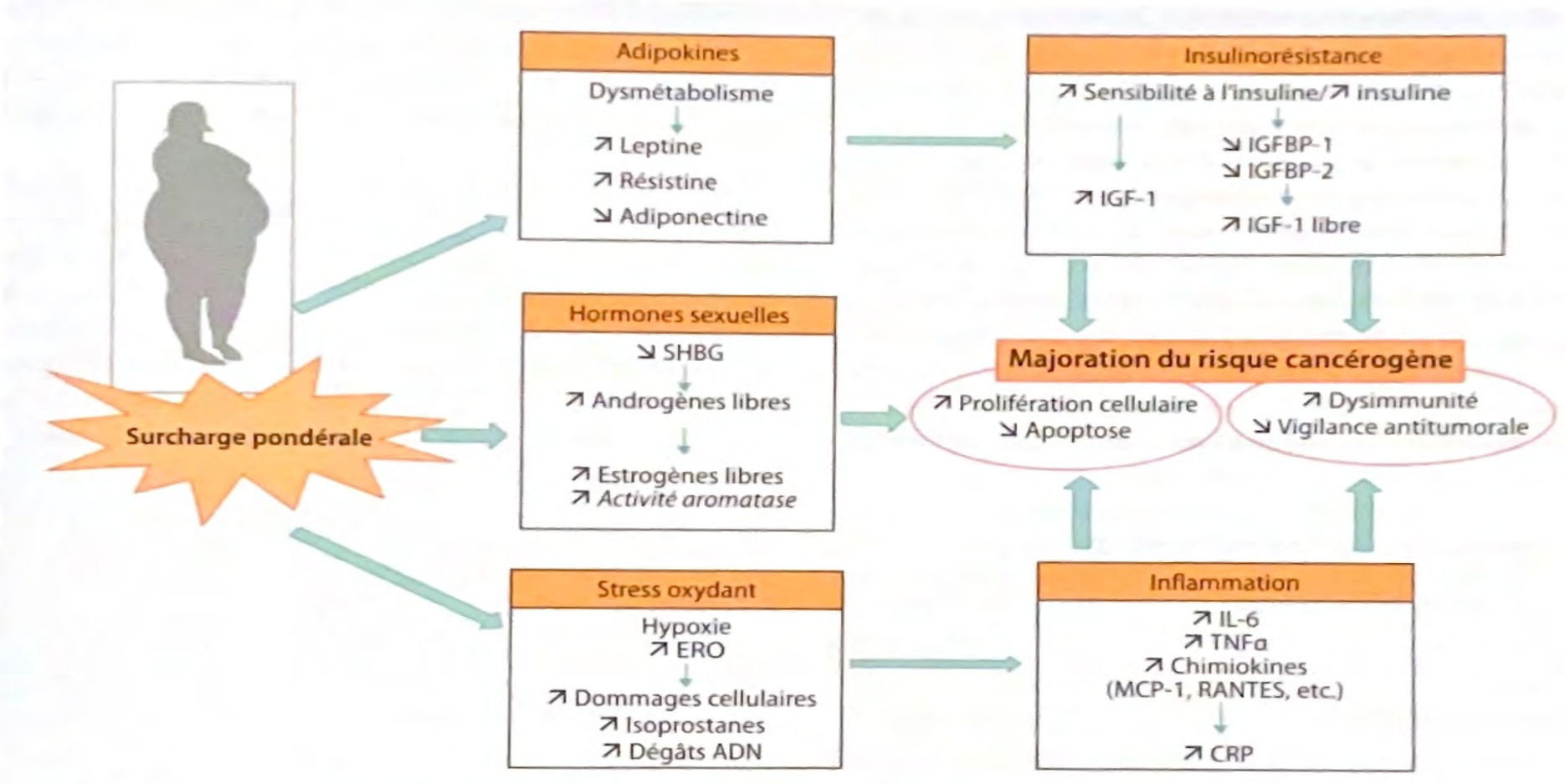
- Facteur avéré convaincant (WCRF 2018)
- Femmes ménopausées ++
- Meta-Analyse (53 études, 2002) RR de 1,32 pour 35 à 44 g d'alcool /j et RR 1,46 pour > 45 g/J
- Effet bénéfique sur la survie d'une consommation modérée d'alcool (vin)
- Pas d'impact démontré sur le risque de rechute
- Corrélation entre conso d'alcool et THS : ↑ oestradiolémie

Surpoids et obésité et risque de cancer du sein



- 1 Régime se caractérisant par une consommation élevée de produits gras, sucrés et de viandes
- 2 Régime se caractérisant par une consommation élevée en aliments d'origine végétale et en poisson
- 3 Sédentarité mesurée par le temps d'exposition aux écrans
- 4 Activité physique du type marche

SURPOIDS ET CANCER DU SEIN



IGF : *Insulin-like Growth Factor* ; IGFBP : *Insulin-like Growth Factor Binding Protein* ; SHBG : *Sex Hormone-Binding Globulin* ; ERO : espèces réactives de l'oxygène ; IL-6 : interleukine 6 ; TNF : *Tumor Necrosis Factor* ; CRP : protéine C réactive.

Figure 1. Facteurs pouvant contribuer au risque majoré de cancérogenèse mammaire associé à la surcharge pondérale chez la femme ménopausée.

Implication directe des aliments

- Viandes et charcuteries

- Augmentation de 20% du risque de KS chez les non ménopausées

Linós E et al. Red meat consumption during adolescence among premenopausal women and risk of breast cancer. *Cancer Epidemiol Biomarkers Prev* 2008;17(8):2146-51.

- Non retrouvé dans l'étude EPIC

- 319 826 femmes suivies pdt 8,8 ans pour la viande, œufs
- Discrète augmentation pour la charcuterie

- Produits laitiers

- Résultats contradictoires plutôt en faveur (prévention tertiaire)
- Bio ++

- Soja :

- Alimentation ok
- Pas de compléments alimentaires à base de soja

- Boissons sucrées

Les xénobiotiques

- Bisphénols
 - Dans les emballages et contenants plastiques notamment
 - Effets oestrogéniques → stimulation sur la prolifération cellulaire mammaire; effet carcinogène mammaire probable non prouvé jusqu'à présent
 - En cours d'étude
- Dioxines (polluants organiques perpétuels)
 - Association entre le risque de métastases par cancer du sein et concentration adipocytaire de dioxine
- Pesticides
 - NutriNet Santé (68 946 femmes sur 5 ans) diminution du risque de cancer du sein chez les consommatrices bio (biais du mode de vie?)

L'alimentation ultra transformée

- Etude prospective NutriNet Santé
 - classification NOVA
- Augmentation du risque de surpoids et d'obésité
- Augmentation linéaire du risque de cancer du sein chez les femmes ménopausées

toute augmentation de 10 % de la proportion d'ultra transformés dans l'alimentation est associée à une augmentation de 11 % du risque de cancer du sein, mais uniquement chez les femmes ménopausées (+13 %), y compris après ajustement ($p = 0,05$).

Types de régimes

- Régime DASH → RH-
 - Fruits et légumes + produits laitiers (Dietary Approaches to Stop Hypertension)
 - Exclusion de l'alcool
 - Petimar J et al. Am J Clin Nutr 2019 ; 109(5) : 1393-401.
- Régime pro inflammatoire
 - Riche en sucres et en graisses, alcool, aliments raffinés et ultratransformés, pauvres en fibres
 - Augmentation du risque de KS RH+ (Asie +)
 - Meta Analyse Wang L et al. Eur J Clin Nutr 2019
- Jeûne
 - Pas de lien dans la prévention ou la PEC des KS
 - Perte de poids et baisse des défenses immunitaires
 - Rapport INSERM 2014 et NACRe 2017
- Jeûne restrictif
- Régime cétogène

vitamines

- Vitamine C et E ,caroténoïdes pour leurs effet anti oxydants
 - → pas d'effet bénéfique démontré dans les différents essais de supplémentation
- Vitamine D
 - → plusieurs études cas-témoins et prospectives suggèrent un effet protecteur de la vitamine D et de l'exposition solaire vis-à-vis du cancer du sein

ALIMENTATION ET HORMONOTHERAPIE

- **GESTION DU POIDS ET/ OU DE LA PRISE DE POIDS**

- 50% des patientes recevant un TTT adjuvant (chimio et/ ou hormonothérapie)
- 3 à 5 kg en moyenne (1^e année +++)
- Objectif :
 - Tendre vers un poids santé
 - Diminuer la masse grasse
- Régime
 - équilibré
 - riche en fruits et légumes, céréales complètes et légumes secs
 - Non ou peu transformé
- + activité physique régulière :
 - 30 min d'endurance / j
 - Deux fois par semaine au moins de renforcement musculaire

ALIMENTATION ET HORMONOTHERAPIE

- HYPERCHOLESTÉROLEMIE (et maladies cardiovasculaires)
 - Limiter
 - Viandes rouges < 500 gr par semaine
 - Charcuteries < 150 gr par semaine (ou 25 gr par jour)
 - L'alcool
 - Privilégier en AG insaturés type oméga 3
 - 1 Poisson gras / sem
 - Huiles olive/colza/noix
 - 1 poignée d'oléagineux max par jour
 - Fibres ++
 - AP : endurance

ALIMENTATION ET OSTEOPOROSE

- Apport en calcium
 - Produits laitiers : 2 par jour
 - Légumes verts, légumineuses etc
- Apport en vitamine D : poissons gras, œufs, produits laitiers sauf 0%
- +/- supplémentation si nécessaire
- Marche régulière (oscillations induites par les pas)

ALIMENTATION ET HORMONOTHÉRAPIE

- **Asthénie**

- 1^e symptôme décrit par les patientes
- Tellement polyfactorielle

- Conseils
 - Écouter leur plainte
 - « astuces » nutritionnelles :
 - Les fruits
 - Apport de sucre
 - Apport de vitamine C
 - L'eau : veiller à une bonne hydratation
 - Les stimulants naturels tels que le gingembre par exemple

- AP régulière ++++
- Réguler les troubles du sommeil

DOULEURS ET RAIDEURS ARTICULAIRES

1 ALIMENTATION ANTI INFLAMMATOIRE

- **Fruits et légumes** Riches en antioxydants, en fibres et en eau — ils favorisent un bon équilibre hormonal et réduisent l'inflammation.
→ Variez les couleurs : brocoli, épinards, carottes, fruits rouges, agrumes, etc.
- **Oméga-3** Aident à stabiliser les hormones et à réduire l'inflammation.
 - Poissons gras : saumon, maquereau, sardines.
 - Graines de chia, noix, huile de colza ou de lin.
- **Vitamine E et magnésium**
- Le **curcuma**, le **gingembre**, l'**ail**, le **romarin** ou la **cannelle** ont des effets anti-inflammatoires naturels.

2 Bonne hydratation

3 AP : ETIREMENTS (10 MIN PAR JOUR)

BOUFFÉES DE CHALEUR

Aliments à privilégier

- **Fruits et légumes** Riches en antioxydants, en fibres et en eau — ils favorisent un bon équilibre hormonal et réduisent l'inflammation.
→ Variez les couleurs : brocoli, épinards, carottes, fruits rouges, agrumes, etc.
- **Oméga-3** Aident à stabiliser les hormones et à réduire l'inflammation.
- Poissons gras : saumon, maquereau, sardines.
- Graines de chia, noix, huile de colza ou de lin.
- **Vitamine E et magnésium** Ces nutriments peuvent **atténuer les bouffées de chaleur** et l'irritabilité.
- Vitamine E : avocat, amandes, graines de tournesol.
- Magnésium : cacao pur, banane, amandes, lentilles, flocons d'avoine.
- **Aliments riches en phytoestrogènes AUTORISÉS**

FAIRE DES PETITS REPAS PAUVRES EN GRAISSES SATURÉS

EVITER L'ALCOOL ET LE CAFÉ

AP +++ : ENDURANCE =
MARCHE ACTIVE 30 MIN PAR JOUR

MANGER MIEUX BOUGER PLUS

