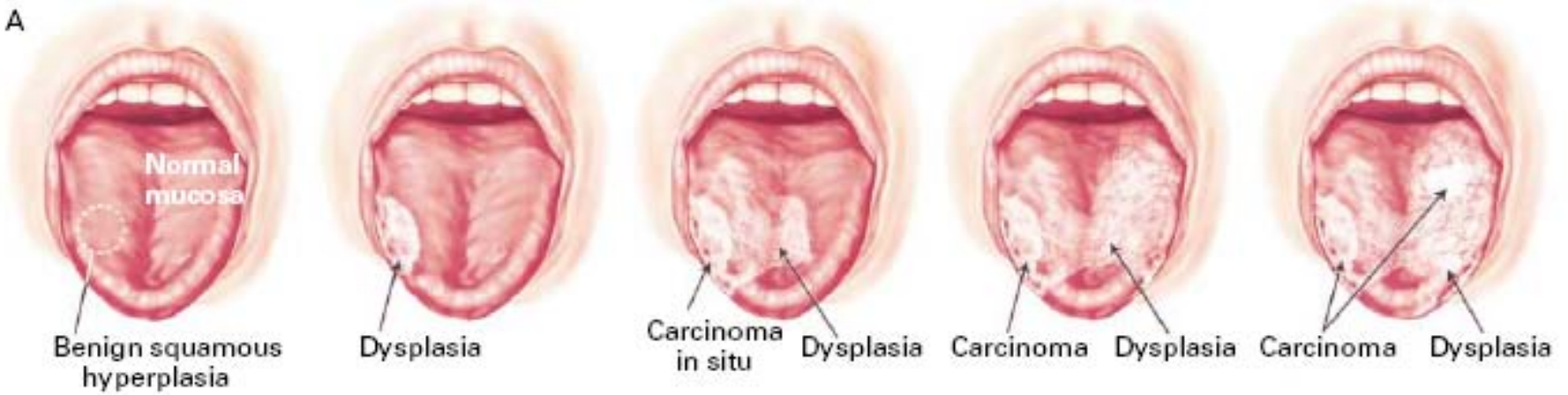


Berries and Cancer

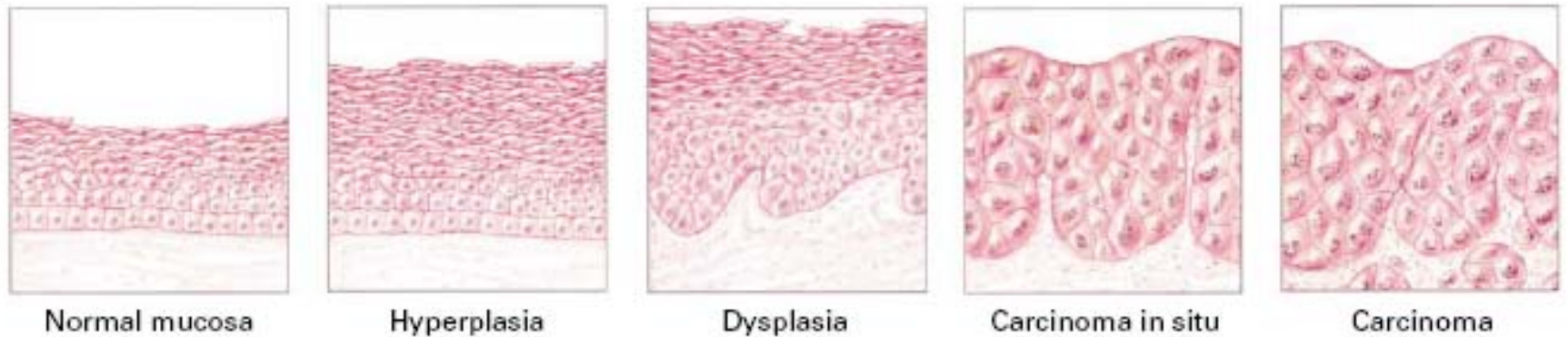


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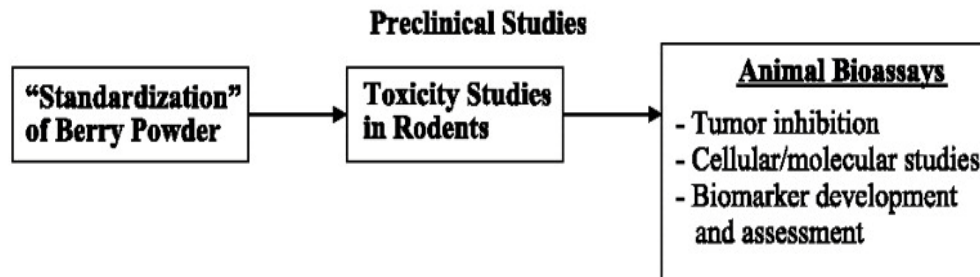


B



Forastiere, A, et al, N Engl J Med. 2001
Dec 27;345(26):1890-900.

Scheme for assessing berries (or other foodstuffs) for chemopreventive efficacy



Clinical Trials

Phase I

- Safety / tolerability
- Pharmacokinetics of bioactive compounds (e.g. anthocyanins, ellagic acid)

"Pilot" Studies in At-Risk Populations

- ~10–30-plus patients
- Internally controlled
- Biomarkers
 - a. lesion size, histopathology
 - b. cellular
 - c. molecular

Phase II

- ~100-plus patients
- Randomized, placebo-controlled
- Biomarkers
 - a. lesion size & histopathology
 - b. cellular
 - c. molecular

Phase III

- ~1000-plus patients
- Randomized, placebo-controlled
- Reduction in cancer occurrence

Berry types with cancer inhibitory potential (so far)

Acai

Blackberries

Black raspberries

Blueberries

Cranberries

Goji

Noni

Red raspberries

Strawberries

Animal studies - Organs where berries prevent cancer

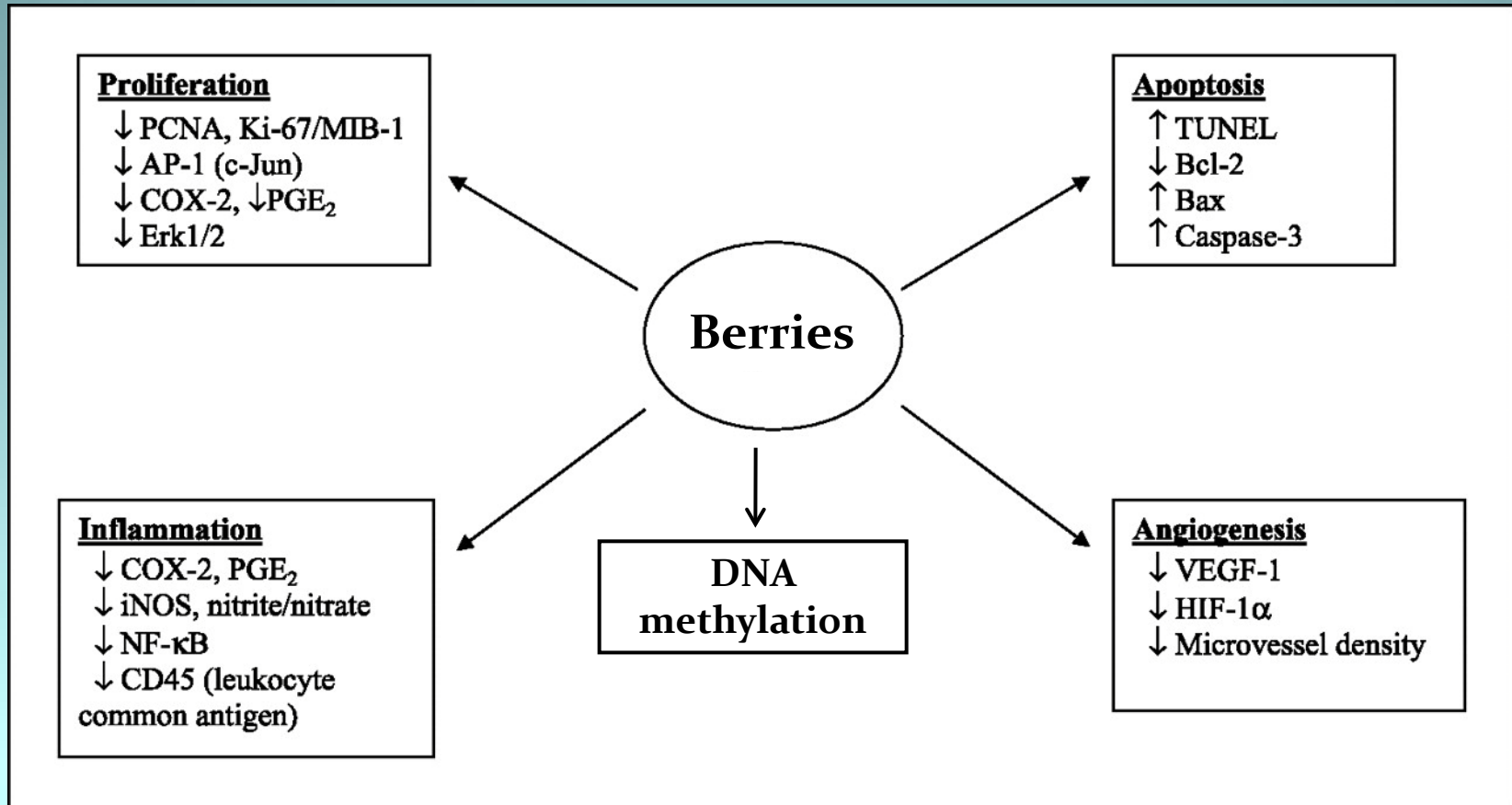
- Conclusive
 - Bladder
 - Breast
 - Colon
 - Esophagus
 - Oral cavity
 - Skin
- Inconclusive
 - Lung
 - Prostate

Mechanisms of berry action

Cellular level

- Antioxidant activity
- Influence carcinogen metabolism
- Stimulate apoptosis
- Reduce inflammation
- Inhibit angiogenesis
- Promote cell adhesion
- Promote cell-cell communication
- Inhibit enzymes involved in tissue invasion and metastasis

Effects of Berries on Molecular Events in Carcinogenesis



Some bioactive constituents in berries

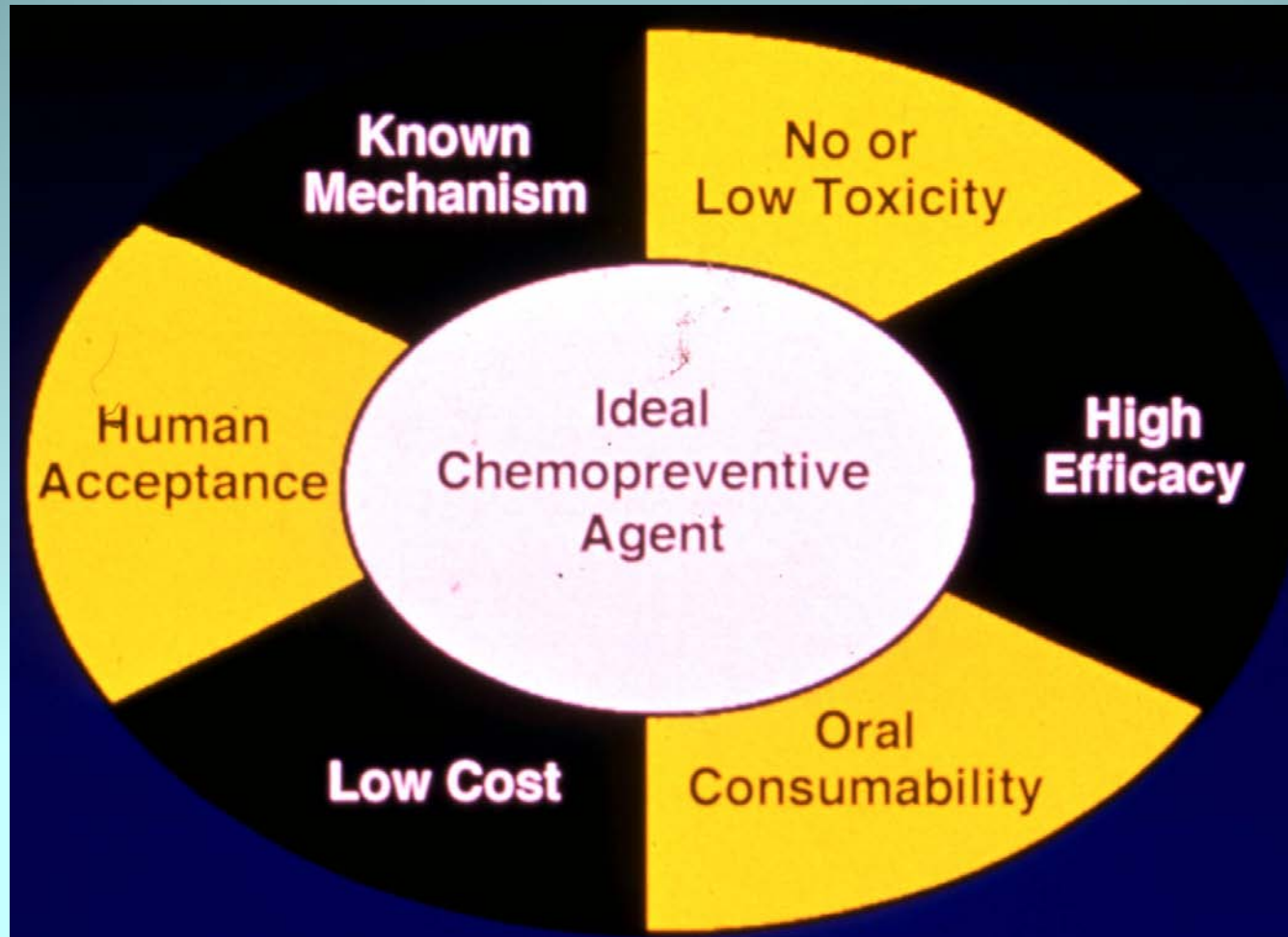
- Phenolic acids (hydroxycinnamic and hydroxybenzoic acids)
- Flavonoids (anthocyanins, flavanols, flavonols)
- Condensed tannins (proanthocyanins)
- Hydrolyzable tannins (ellagitannins and gallotannins)
- Stilbenoids, lignans, triterpenes and sterols
- Vitamins (A, C, E, folic acid)
- Minerals (calcium, selenium)

Seeram, N.P. (2006) Berries. In Heber, D., Blackburn, G., Go, V. and Milner, J. (eds.) Nutritional Oncology. Elsevier, Inc., Amsterdam, the Netherlands, pp. 615–628 Chapter 37.

High Risk Human Populations

- Individuals with hereditary predisposition to cancer
- Persons with high exposure to carcinogens (e.g., tobacco smokers)
- Persons with premalignant lesions (e.g., Barrett's esophagus, oral leukoplakia, colonic polyps, actinic keratosis, etc.)
- Individuals who have been treated for cancer and remain at high risk for recurrent disease

Qualities of an Ideal Chemopreventive Agent



Some results from human trials

Black raspberries

- Oral leukoplakia (dysplasia) - histologic regression by berry gel
- Barrett's esophagus - ↓ oxidative stress
- Colorectal cancer - ↓ proliferation, ↑ apoptosis, demethylation of suppressor genes
- FAP (rectal polys) - ~35% regression
- Prostate cancer - no reduction in serum PSA

Strawberries

- Esophageal dysplasia - histologic regression

Future studies-humans

- Additional clinical trials in patients with pre-cancerous lesions
- Initiate trials to determine if berries prevent recurrent cancer
- Initiate therapeutic trials in which berries or their constituents are used in conjunction with chemo/radiotherapy
- Berries alone for cancer treatment?