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Lung cancer associated with beta-carotene supplementation in smokers

● **A meta-analysis of four randomised trials in a total of 109 394 subjects showed a statistically significant increase in the risk of lung cancer among smokers who used dietary supplements containing beta-carotene, at a mean dose of 20 to 30 mg/day. This contradicts the results of observational studies conducted in the 1990s.**

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In the 1990s, observational studies suggested that a diet rich in fruit and vegetables could reduce the risk of lung cancer. Because of its antioxidant properties, it was thought that beta-carotene, a vitamin A precursor that is abundant in fruit and vegetables, might help prevent primary lung cancer. However, intervention studies of beta-carotene supplementation in smokers provided unexpected results: two of three randomised trials comparing beta-carotene supplementation with placebo or vitamin E supplementation showed a statistically significant increase in the incidence of lung cancer, while the third trial showed no difference (1).

A meta-analysis of clinical trials was published in 2008, and its conclusions remain valid.

A meta-analysis including more than 100 000 subjects. A meta-analysis of 4 randomised controlled trials examined the relationship between beta-carotene supplementation and the risk of lung cancer (**a**)(2). A total of 109 394 persons were enrolled: 54 955 in the beta-carotene groups and 54 439 controls. Beta-carotene supplements of 20 to 30 mg/day were taken for 2 to 12 years (2).

Lung cancer was more frequent in the beta-carotene groups (odds ratio 1.21, 95% confidence interval (CI) 1.09 to 1.34) (**b**).

Similar results were obtained in a more recent cohort study. The VITAL study (VITamins And Lifestyle) retrospectively analysed the effect of supplementation with beta-carotene, vitamin A, lutein or lycopene over a 10-year period in 77 126 subjects aged 50 to 76 years. Those who took beta-carotene for at least 4 years had a three-fold increase in the risk of small cell lung cancer (95%CI: 1.29 to 8.07) (3).

Disturbing results in smokers. In smokers, beta-carotene supplementation was associated with a statistically significant increase in the risk of lung cancer (odds ratio 1.24; 95%CI 1.1 to 1.39) (2).

In contrast, there was no statistically significant difference in the risk of lung cancer in the subgroups of former smokers (odds ratio 1.10; 95%CI 0.84 to 1.45) or never-smokers (odds ratio 0.73; 95% CI 0.33 to 1.59).

In practice: beta-carotene supplementation is not advisable for smokers. There is strong evidence that beta-carotene supplementation increases the risk of lung cancer, at least in smokers. Smokers who want to reduce their risk of developing lung cancer would be better advised to quit smoking rather than rely on beta-carotene supplements (4).

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a- The 4 randomised trials analysed in this meta-analysis included the Women's Health Study and 3 trials (in a total of almost 70 000 subjects) examined in issue 171 of Prescrire in 1997 (refs 1,2,5).
Details of the four trials:
• the double-blind ATBC trial (Alpha Tocopherol Beta-Carotene Cancer Prevention Trial): 29 133 Finnish male smokers aged 50 to 69 years who took beta-carotene 20 mg/day or vitamin E 50 mg/day for a median of 6.1 years;
• the American CARET trial (Beta-Carotene and Retinol Efficacy Trial): 18 314 smokers, former smokers or individuals exposed to asbestos, who took beta-carotene 30 mg/day plus vitamin A 25 000 IU/day for a median of 4 years;
• the Physicians' Health Study: a double-blind randomised placebo-controlled trial involving 22 071 US male physicians aged 40 to 84 years who took beta-carotene 50 mg every other day for a median of 12 years;
• Women's Health Study: this double-blind randomised placebo-controlled trial involved 39 876 US female healthcare professionals aged over age 45, 49% of whom were current or former smokers. They took beta-carotene at a dose of 50 mg/day every other day for a median of 2.1 years.
b- The odds ratio is the ratio of the odds that an event will occur in one group to the odds that it will occur in another group. It provides a fair estimate of the relative risk of an event occurring provided some conditions are met (refs 6,7).

Selected references from Prescrire's literature search.
1- Prescrire Editorial Staff "Free radicals and antioxidants: beware of fashionable trends" *Prescrire Int* 1997; **6** (30): 113-115.
2- Tanvetyanon T and Bepler G "Beta-carotene in multivitamins and the possible risk of lung cancer among smokers versus former smokers: a meta-analysis and evaluation of national brands" *Cancer* 2008; **113** (1): 150-157.
3- Satia JA et al. "Long-term use of ß-carotene, retinol, lycopene, and lutein supplements and lung cancer risk: results from the vitamins and lifestyle (VITAL) study" *Am J Epidemiol* 2009; **169** (7) 815-828.
4- Prescrire Rédaction "Idées-Forces Prescrire: sevrage tabagique" *Rev Prescrire* 2009; **29** (313). Full version: www.prescrire.org: 5 pages.
5- Lee IM et al. "Beta-carotene supplementation and incidence of cancer and cardiovascular disease: the Women's health study" *J Natl Cancer Inst* 1999; **91** (24): 2102-2106.
6- Prescrire Rédaction "Rapport de cotes: une estimation du risque relatif, sous certaines conditions" *Rev Prescrire* 2008; **28** (298): 626-629.
7- Prescrire Rédaction "L'intervalle de confiance: une fourchette qui rend compte de l'incertitude statistique" *Rev Prescrire* 2008; **28** (298): 630-633.

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Benfluorex: yet more valve disorders

● **Analysis of health insurance databases.**

In November 2009, the French Health Products Safety Agency finally suspended marketing authorisation for *benfluorex*, due to the risk of cardiac valve disorders (1,2). Reports were increasing, and a French study based on hospital data confirmed the risks associated with this drug.

In 2009 the French national health insurance system conducted a study of one million diabetic patients, about 43 000 of whom had been exposed to *benfluorex* (3). Compared to unexposed patients, those exposed to *benfluorex* in 2006 had approximately a 3-fold increased risk of being hospitalised for valve failure in 2007, while in 2008 the risk of valve replacement surgery with extracorporeal circulation was about 4 times higher. Both increases were statistically significant.

This is an excellent example of how analysis of health insurance databases can contribute to improving patient safety.

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Selected references from Prescrire's literature search.
1- Prescrire Editorial Staff "Benfluorex: increasing reports of valve disorders" *Prescrire Int* 2010; **19** (105): 17.
2- Prescrire Rédaction "Benfluorex: enfin retiré du marché !" *Rev Prescrire* 2010; **30** (315): 13.
3- Cnamts "Benfluorex et valvulopathies cardiaques: une étude de cohorte sur 1 048 173 personnes traitées pour diabète" 9 November 2009: 13 pages.

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