

### WORLD HEALTH ORGANIZATION INTERNATIONAL AGENCY FOR RESEARCH ON CANCER LYON, FRANCE

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# Higher levels of vitamin B6 and methionine are associated with a marked decrease in risk of developing lung cancer

### Summary

Smoking is by far the most important risk factor for lung cancer. When people stop smoking their risk decreases but it remains high compared to people who have not smoked; finding ways to reduce this remaining risk is important. A study led by the International Agency for Research on Cancer (IARC) and published today in JAMA<sup>1</sup> shows a reduction in lung cancer risk among people with higher levels of vitamin B6 and methionine. The observed decrease is large, with risk being more than halved in those with high levels of both, and if proven to be causal would suggest ways in which diet could be used to change lung cancer risk. This analysis was funded by the World Cancer Research Fund.

### Background

Lung cancer is the most common cancer in the world with an estimated 1.6 million new cases in 2008, representing 1 in 8 of all new cancers. It is also the most common form of cancer death in the world comprising nearly 1 in 5 of all deaths from cancer. Tobacco smoking is responsible for at least 8 out of 10 cases of lung cancer, although many of these occur among people who have stopped smoking but remain at increased risk. Identifying ways to reduce lung cancer risk could have important public health benefits, especially among people who have stopped smoking.

### Diet plays an important part in cancer risk

Appropriate levels of B-vitamins are vital for the cell to make and maintain DNA and disruption of these processes has been suspected of playing a role in cancer. Foods containing high levels of B-vitamins and related compounds may therefore be important in reducing risk. Compounds that interact closely with B-vitamins include methionine, an essential amino acid, and homocysteine. Vitamin B9 (or folate) can be found in fruits and green leafy vegetables; vitamin B6 is common in fish, meat, potatoes and whole grains; and methionine is present in various seeds, nuts, cereals, fish and meats.

## Measuring intake of B-vitamins as a marker of cancer risk

Estimating vitamin levels taken from blood samples before any disease onset provides a direct measure of vitamin status. This is important for vitamins that come from many food sources and are therefore difficult to measure using questionnaires. It is however only possible to do such studies when blood samples have been collected on many thousands of volunteers who are then followed up to see who develops a cancer and who does not.

### The largest ever study on diet and cancer

The <u>EPIC study</u> is the largest, so-called *prospective*, study of diet and nutrition in the world. Coordinated through IARC and Imperial College London, this study includes questionnaire information on 520,000 European volunteers, 385,000 of whom also gave a blood sample. All participants were free of cancer at the start and were followed up for an average of 5 years.

<sup>&</sup>lt;sup>1</sup> Serum B Vitamin Levels and Risk of Lung Cancer. JAMA, June 16, 2010 – Volume 303, No. 23, pp. 2377–2385

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### Comparing cases to controls

Nearly 900 people within the EPIC study who developed a lung cancer were identified and compared to 1770 comparable people who did not develop a cancer.

Blood samples taken at the start of the study were measured for 4 B-vitamins (B2, B6, folate (B9) and B12), as well as methionine and homocysteine.

### Lower Vitamin B6 and methionine levels associated with lung cancer

As Brennan and colleagues report in JAMA, blood measures of vitamin B6 and methionine were markedly lower in people who went on to develop lung cancer, irrespective of whether they smoked or not. Overall, people with above average levels of B6 and methionine had less than half the risk of developing lung cancer than those with below average levels. A lower risk was also seen with higher levels of folate consumption. The results were the same for people who had never smoked, those who had quit smoking prior to the start of the study, and for continuing smokers. The lower risk was also observed regardless of time interval since blood collection, indicating the results were not explained by the early stages of the disease. The large sample size meant that chance could reasonably be ruled out as an explanation of the results, and the similarity of the results between never smokers and smokers meant that the findings were not explained by the cases smoking more.

"The size of this study, and the strong association observed, provide confidence that the association is real. Whether they are causing the lower risk, or whether they are a marker of the real causal factor, will require further studies", said Paul Brennan. One of the EPIC co-ordinators, Dr Paolo Vineis from Imperial College London, added, 'it has always been thought that diet may be important in lung cancer risk, in addition to smoking. This study gives the strongest evidence to date of a link between diet and lung cancer'.

### Translating basic research into public health action

IARC Director, Dr Christopher Wild said that 'the main priority for lung cancer prevention is to get people who smoke to stop, and to ensure young people do not start. However, in many western countries up to half of lung cancers now occur among people who have quit smoking or who have never smoked, and in certain parts of the world lung cancer is common among never smokers. This highlights the need to find additional ways to reduce lung cancer risk in these groups'.

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### To Media:

For a copy of the study, please contact the JAMA media relations department at mediarelations@jamaarchives.org or +1 312-464-JAMA (5262) Also see JAMA's For the Media website, www.jamamedia.org

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