

P.L. Selvais
 J. Henrion
Hôpital de Jolimont
Gastroenterology Unit,
159 rue Ferrer,
B-7100 Haine Saint Paul,
Belgium.

Majed Odeh
Department of Internal Medicine 'B',
Bnai Zion Medical Center
and Technion Faculty of Medicine,
Israel Institute of Technology,
P.O. Box 6477,
Haifa 31063, Israel.

References

- Crosby, W.H. A history of phlebotomy therapy for haemochromatosis. *Am J Med Sci* 1991, **301**: 28–31.
- Niedereau, C., Fischer, R., Sonnenberg, A., Stremmel, W., Trampisch, H.J. & Strohmeyer, G. Survival and causes of death in cirrhotic and non cirrhotic patients with primary hemochromatosis. *N Engl J Med* 1985, **313**: 1256–1262.
- Stocks, A.L. & Powell, L.W. Pituitary function in idiopathic haemochromatosis and cirrhosis of the liver. *Lancet* 1972, **ii**: 298–299.
- Bomford, A. & Williams, R. Long term results of venesection therapy in idiopathic haemochromatosis. *Q J Med* 1976, **45**: 611–623.
- Lufkin, E.G., Baldus, W.P., Bergstrahl, E.J. & Kao, P.C. Influence of phlebotomy treatment on abnormal hypothalamic-pituitary function in genetic haemochromatosis. *Mayo Clin Proc* 1987, **62**: 473–479.
- Kelly, T.M., Corwin, E.Q., Meikle, A.W. & Kushner, J.P. Hypogonadism in hemochromatosis: reversal with iron depletion. *Ann Intern Med* 1984, **101**: 629–632.
- Siemons, L.J. & Mahler, C. Hypogonadotropic hypogonadism in hemochromatosis: recovery of reproductive function after iron depletion. *J Clin Endocrinol Metab* 1987, **65**: 585–587.
- Thiebaut, P., Luton, J.P., Halaby, G., Baglin, A.C. & Bricaire, H. Insuffisance gonadotrope isolée révélatrice d'une hémochromatose primitive. *Ann Endocrinol (Paris)* 1976, **37**: 463–464.
- Cazzola, M., Ascari, E., Barosi, G. et al. Juvenile idiopathic haemochromatosis: a life threatening disorder presenting as hypogonadotropic hypogonadism. *Hum Genet* 1983, **65**: 149–154.

Aspirin and risk of fatal colon cancer

Sir,

Recent studies have demonstrated that regular use of aspirin at low doses may reduce significantly the risk of fatal colon cancer.^{1–3} However, how aspirin might produce this beneficial effect is unknown. I suggest two possible mechanisms.

First, it has been recently demonstrated that aspirin enhances the production of interferon- α and interferon- γ ,^{4–6} and these two compounds have been shown to produce beneficial effects in the treatment of colon cancer.^{7–12} In addition, it was recently found that the level of interferon- γ in extracts of human colorectal adenocarcinomas decreased progressively with the advance of clinical stage, and the levels of interferon- γ of the patients with distant metastases were significantly lower than those of the patients without distant metastases.¹³

Second, production of tumour necrosis factor- α from the macrophages increases with the addition of aspirin,^{14,15} and the tumoricidal activity of this monokine is well established.

Thus, the suggested above two mechanisms for aspirin reducing the risk of fatal colon cancer seem to be reasonable.

References

- Thun, M.J., Namboodiri, M.M., Health, C.W., Jr. Aspirin and reduced risk of fatal colon cancer. *N Engl J Med* 1991, **325**: 1593–1596.
- Rosenberg, L., Palmer, J.R., Zauber, A.G., Warshauer, M.E., Stolley, P.D. & Shapiro, S. A hypothesis: nonsteroidal anti-inflammatory drugs reduce the incidence of large-bowel cancer. *J Natl Cancer Inst* 1991, **83**: 355–358.
- Kune, G.A., Kune, S. & Watson, L.F. Colorectal cancer risk, chronic illnesses, operations, and medications: case control results from the Melbourne Colorectal Cancer Study. *Cancer Res* 1988, **48**: 4399–4404.
- Cesaroi, T.C., Yousefi, S. & Carandang, G. The regulation of interferon production by aspirin, other inhibitors of the cyclooxygenase pathway and agents influencing calcium channel flux. *Bull NY Acad Med* 1989, **65**: 26–35.
- Antonelli, G., Mastino, A., Amicucci, P., Turriziani, O., Favalli, C. & Garaci, E. Mechanism of production of interferon- γ : role of arachidonic acid metabolites. *J Biol Regul Homeost Agents* 1990, **4**: 13–18.
- Hsia, J., Sarin, N., Oliver, J.H. & Goldstein, A.L. Aspirin and thymosin increase interleukin-2 and interferon- γ production by human peripheral blood lymphocytes. *Immunopharmacology* 1989, **17**: 167–173.
- Fiedler, W., Zeller, W., Peimann, C.J., Weh, H.J. & Hossfeld, D.K. A phase II combination trial with recombinant human tumor necrosis factor and gamma interferon in patients with colorectal cancer. *Klin Wochenschr* 1991, **69**: 261–268.
- Toth, C.A. & Thomas, P. The effect of interferon treatment on 14 human colorectal cancer cell lines: growth and carcinoembryonic antigen secretion *in vitro*. *J Interferon Res* 1990, **10**: 579–588.
- Muro, M., Naomoto, Y. & Orita, K. Mechanism of the combined antitumor effect of natural human tumor necrosis factor- α and natural human interferon- α on cell cycle progression. *Jpn J Cancer Res* 1991, **82**: 118–126.
- Blottiere, H.M., Douillard, J.Y., Kaprowski, H. & Steplewski, Z. Humoral and cellular responses of colorectal cancer patients treated with monoclonal antibodies and interferon- γ . *Cancer Immunol Immunother* 1990, **32**: 29–37.
- Schiller, J.H., Storer, B., Bittner, G. & Horisberger, M.A. Characterization of the synergistic antiproliferative effects of interferon gamma and tumor necrosis factor on human colon carcinoma cell line. *J Interferon Res* 1990, **10**: 129–139.
- Wadler, S., Lemmersky, B., Atkins, M., Kikwood, J. & Petrelli, N. Phase II trial of fluorouracil and recombinant interferon alpha-2a in patients with advanced colorectal carcinoma: an Eastern Cooperative Oncology Group Study. *J Clin Oncol* 1991, **9**: 1806–1810.
- Numata, A., Minagawa, T., Asano, M., Nakane, A., Katoh, H. & Tanabe, T. Functional evaluation of tumor-infiltrating mononuclear cells. Detection of endogenous interferon- γ and tumour necrosis factor- α in human colorectal adenocarcinoma. *Cancer* 1991, **68**: 1937–1943.
- Larrick, J.W. & Kunkel, S.L. Is Reye's syndrome caused by augmented release of tumour necrosis factor? *Lancet* 1986, **ii**: 132–133.
- Corkey, B.E., Geschurind, J.F., Deeney, J.T., Hale, D.E., Dauglas, S.D. & Kilpatrick, L. Ca^{2+} responses to interleukin-1 and tumor necrosis factor in cultured human skin fibroblasts: possible implication for Reye's syndrome. *J Clin Invest* 1991, **87**: 778–786.