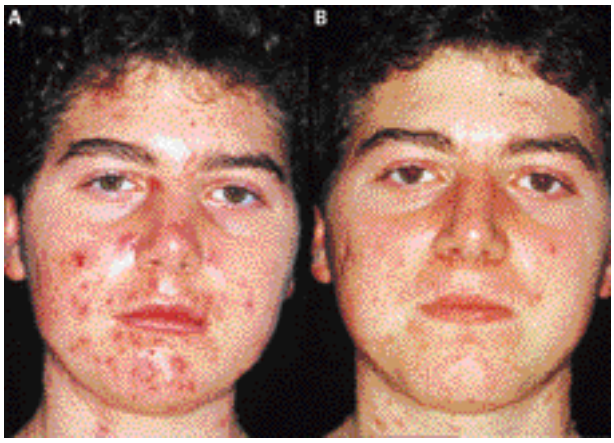

Patient before treatment (A) and after 18 months of low-dose methylprednisolone (B)
The patient gave his permission for publication of these photographs.

and acne fulminans, a severe variant of acne accompanied by systemic inflammatory symptoms. The 15-year-old had a 3-month history of deteriorating acne (figure A). Neither systemic minocycline nor systemic isotretinoin controlled the disease. He suddenly developed fever, leucocytosis, a raised erythrocyte sedimentation rate, and arthralgias. Although serum concentrations of testosterone, leutenising hormone, and follicle stimulating hormone were within normal limits, concentrations of androstenedione, dehydroepiandrosterone, and 17-hydroxyprogesterone (17-OHP) were raised. There was also an abnormal increase of 17-OHP in response to ACTH-stimulation. These results suggested late-onset congenital adrenal hyperplasia (adrenogenital syndrome). He was given, in addition to isotretinoin, a short course of oral methylprednisolone (initial dose 1 mg/kg body weight per day) and improved strikingly. After discontinuation of isotretinoin and on low dose methylprednisolone his condition has remained stable with only mild acne, but no major flare up for 18 months (figure B).

Exogenous androgens have also been documented as a trigger for acne fulminans.[2] In women or prepubertal children with severe acne disorders of androgen metabolism are routinely considered and are extensively dealt with in the literature (reviewed in ref 3). Androgen excess in men with severe acne has been much less studied, and there may be a tendency to underestimate its relevance in clinical practice. Men with persistent acne had significantly higher serum levels of androgens than a group of aged-matched normal men,[4] and excess androgens of adrenal origin were commonly found in men with severe acne.[5] The frequency and importance of androgen excess for the variable phenotype of male acne patients warrants further investigation.

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Sublingual therapy for cobalamin deficiency as an alternative to oral and parenteral cobalamin supplementation

Georges Delpre, Pinhas Stark, Yaron Niv

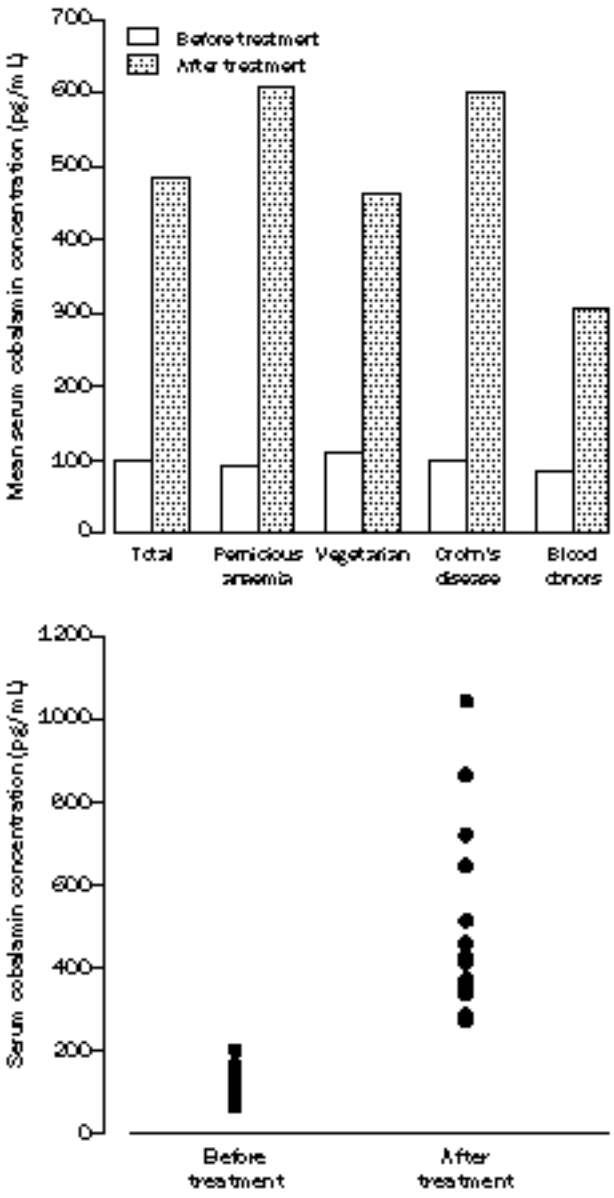
Effectiveness of sublingual cobalamin-replacement therapy was studied in 18 people with cobalamin deficiency. Administration was efficacious and convenient, and compliance was high.

The traditional treatment of cobalamin (vitamin B_{12}) deficiency, including pernicious anaemia, food-cobalamin malabsorption in the elderly, vegetarianism, and other deficiency states, is by intramuscular injections.[1] However, several drawbacks are attributed to this route of administration, commonly resulting in discontinuation of therapy. Injections can be painful, are difficult in patients who have a tendency to bleed or who are very thin, are difficult to provide for patients who are elderly or disabled, and are costly if given by health professionals.[1,2] Oral cobalamin-replacement therapy has, however, proved reliable and effective,[2–5] but is rarely prescribed.[1,4] Additionally, oral therapy is not efficient in patients with diarrhoea, vomiting, or who are otherwise unable to take or tolerate oral medication.[3,5]

In a prospective open-labelled study, we treated 18 consecutive patients with cobalamin deficiency of various causes with sublingual cobalamin preparation, and assessed the efficacy of treatment. Cobalamin deficiency was defined as serum cobalamin concentration less than 200 pg/mL (normal concentration 200–900 pg/mL), shown by two consecutive tests. Ten men and eight women were enrolled. The mean age was 48·1 years (range 23–80). Five patients had pernicious anaemia, seven were vegetarians, and two had Crohn's disease (ileitis). Four patients, all male, were long-term blood donors. No patient was anaemic. We gave patients sublingual nuggets of 1000 μg cobalamin (Solgar Laboratories, Leonia, NJ, USA). Cobalamin is isolated from yeast fermentation medium, which provides a product that is technically yeast free.

On the basis of preliminary results (data unpublished) two sublingual nuggets of cobalamin (total daily dose of 2000 μg), were given for 7–12 days, after informed consent was obtained. To ensure full compliance and complete absorption of the drug, we asked patients to drink a glass of water to avoid mouth dryness, and then to hold nuggets under their tongue, until completely dissolved, 30 min before breakfast. We measured serum cobalamin concentrations before therapy and 2 days after completion of the loading phase. Although all patients followed the instructions, three patients took the drug for 12–14 days, and one patient continued to take the drug for 28 days by his own decision.

The mean serum cobalamin concentration before treatment was 127·9 pg/mL (SD 42·6). Normalisation of serum cobalamin concentration was seen in all patients (figure). The mean serum cobalamin concentration after completion of the short-term loading phase was 515·7 pg/mL (235·0). An increase in cobalamin concentration as much as four-fold compared with pretreatment concentration was seen in most patients. In a few patients, higher increase in cobalamin concentrations was achieved. The mean change in serum cobalamin concentration of 387·7 pg/mL (215) was significant ($p=0·0001$ in Student's *t* test). No patient had side-effects. All participants found the method of administration convenient and preferred it to intramuscular injections.



Distribution of cases by cobalamin deficiency state (top) and serum cobalamin concentrations before and after sublingual cobalamin treatment (bottom)

We conclude that sublingual cobalamin is an effective, safe, and convenient treatment, which provides rapid restoration of serum cobalamin concentrations and should be considered as an alternative method of administration.

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Decrease of vancomycin-resistant enterococci in poultry meat after avoparcin ban

Annalisa Pantosti, Maria Del Grosso, Silvia Tagliabue, Agostino Macrì, Alfredo Caprioli

In Italy, 18 months after the ban of avoparcin, the percentage of poultry meat samples containing *vanA* gene-positive vancomycin-resistant enterococci fell from 14·6% to 8%.

Avoparcin was used as a growth promoter in food animals in most European countries, including Italy, until April, 1997, when the EU banned its use because there was increasing resistance in enterococci, isolated from both animals and human beings, to vancomycin. Avoparcin has cross-resistance with vancomycin, and therefore in the gut of animals this antibiotic can select for high-level vancomycin-resistant enterococci (VRE) carrying the transposon borne *vanA* gene, which can be transferred to other bacteria.[1] VRE are detected in the faeces of animals in farms using avoparcin, but not in farms not using avoparcin,[2] nor in farms in the USA where avoparcin has never been authorised for use in animals.[3] Moreover, VRE can be found in uncooked food of animal origin, especially chickens, in Europe, but not in the USA.[2,3]

Although the risk of transmission of animal VRE to human beings via the food chain has not been precisely measured, the effect of the vaoparcin ban on the prevalence of VRE in animal-derived uncooked food can be evaluated.With this aim a study was carried out in Italy with the support of the Italian Ministry of Health. We examined raw poultry samples (whole carcasses and poultry cuts) obtained from food processing plants in two separate surveys: before the avoparcin ban (March, 1997) and 18 months afterwards (October, 1998). The samples were collected throughout 1 month in each survey by staff of three Regional Veterinary Laboratories (Istituti Zooprofilattici Spermentali) in north and central Italy. VRE were isolated after enrichment in vancomycin-containing media (6 mg/L). PCR was used to detect the *vanA* resistance gene and to confirm the identification of the species *Enterococcus faecium*.[4]

There was a lower prevalence of VRE harbouring the *vanA* gene in the samples collected 18 months after the ban of avoparcin: the percentage of samples containing VRE fell from 14·6% (49/334) to 8% (22/271, p=0·012). In both surveys, several *vanA*-positive enterococcal species were found, including *E faecium*, *E faecalis*, *E durans*, and *E hirae*. *E faecium* was the most common species: its prevalence decreased from 9·3% of the samples in the first survey, to 7% in the second survey, but the difference was not statistically significant.

Although further study is necessary to confirm a trend, our findings suggest that several months after the avoparcin ban, there is a moderate reduction in VRE contamination of poultry products and the consumer is less likely to come across vancomycin-resistant enterococci bearing the potentially transferable *vanA* gene. After the ban of tetracyclines as growth promoters in 1971, Smith did not find a reduction in the frequency of tetracycline-resistant *Escherichia coli* in pigs.[5] However, tetracyclines were and still are largely used as therapeutic medicines in the animal industry, whereas there is no similar use for avoparcin or other glycopeptide antibiotics.

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