THE COMBINED ORAL CONTRACEPTIVE (COC) AT ALTITUDE - IS IT SAFE?

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Brownie Schoene, Seattle, USA

No real data yet available. The Combined oral contraceptive (COC) increases the risk of DVT and PE. Now of course there is felt to be a higher risk for DVT at high altitude in everyone based on the intravascular volume depletion and erythropoiesis potential sedentary time in storms in a tent, etc but it is our general advice to women not to stop the COC: freedom to have more fun (for the heathens who entertain such fantasies) and decreased menstrual flow.

Stephen Bezruschka, Seattle, USA

Women and COC's. I would individualize, if the woman had no problems taking them, and realized we didn't know if there was an increased risk at altitude associated with their use, and she was comfortable with that, and wanted to take them, I'd give my OK. If she was concerned, really a worrier, etc, I'd say, why not stop them.
Tends to be my attitude in everything, if there are no data, focus on what the patient/client seems to want.

Bengt Kayser, Geneva, Switzerland

There is no epidemiological data that shows increased risk of thrombosis or embolism from oral contraceptives at altitude. Especially with the new generation pills these risks are low anyway at low altitude. Therefore: If the woman is NOT taking them at low altitude and has low Hb because of high menstrual blood loss one may consider advising them for reasons of oxygen transport (as well as iron supplementation). For contraception during travel some advice on HIV risk should perhaps not be bad. If the woman is taking oral contraceptives anyway at low altitude there is at present no good reason to stop.

Peter Bartsch, Heidelberg, Germany

Our studies performed at HA in healthy people and those with AMS show that acute exposure does not lead to an increase in in vivo fibrin formation indicating that altitude/hypoxia per se cannot be considered a risk factor for thrombosis. Furthermore fibrinolysis is increased at altitude and during exercise. (Bartsch, *J. Appl Physiol* 66: 2136-2144, 1989). However many circumstances in climbing are thrombogenic: Strenuous prolonged exercise, fluid loss or inadequate intake, trauma or immobility in tents. Combined oral contraceptives (COC) lead to a slightly increased risk of venous and arterial thrombosis. For third generation COC (containing desogestrel or gestodene) the risk for venous thrombosis may be even higher than with older formulations (see 4 papers and editorial in *Lancet* Vol 346 December 16th 1995). This risk of venous thrombosis increases further by a factor 30 when resistance to activated protein C is present when compared with non-COC takers who do not have this genotype. APC resistance is due to a genetic mutation that has a prevalence of 5% in Western Europe. Furthermore we have recently

demonstrated that, in normoxia, activation of coagulation is enhanced after one hour of exhaustive running in women taking third generation OC (Abstract: *Med. Sci Sports Exerc* 28: S84, 1996). As fibrinolysis is also enhanced by exercise, the hemostatic system appears to be balanced during exercise in normoxia. Considering these facts I think that the takinging of oral contraceptives by trekkers is as safe as it can be. I would, however, be extremely cautious in advising women to take the COC when participating in expeditions to extreme altitudes. It is debatable if one should determine APC resistance because of its relatively high prevalence and if present advise against the use of the COC for participating in expeditions.

Peter Nawroth, Heidelberg, Germany
Since there are no studies investigating the safety of COC in high altitude trekkers, I would suggest the following:
a) Women taking COC for longer than 1 year and without a personal and/or family history of thrombosis might continue taking COC while at high altitude. The time period of one year has been selected since thrombotic events are more likely to occur in the first months of COC-use (WHO-study, *Lancet* 346:1575-1582, 1995).
b) COC are not recommended for women not used to taking COC, or COC users of less than 1 year, or women with a personal or family history of venous thrombosis (or other risk factors such as hypertension, hypertension in pregnancy, BMI>25 kg/m2, varicose, veins or a history of rheumatic heart disease). If in these cases the woman wants to take the COC while trekking at high altitude they should be advised about the special risks and lack of hard data, furthermore they should be informed about the early symptoms of venous thrombosis and pulmonary embolism. If a physician is present in the expedition, he might start early treatment with LMW-heparin if a thrombotic event is suspected.

David Murdoch, Christchurch, New Zealand and Andrew Pollard, UK
Although many women have used combined oral contraceptives at high altitude with no reported problems, the many examples of stroke and other thrombotic complications at high altitude should urge caution for all. Women with other risk factors for thrombosis (history of thrombosis, smoking, family history, etc), should not use the combined oral contraceptive at altitude (or at sea level). Healthy women with no known risk factors should probably also avoid taking the combined oral contraceptive if they intend to spend more than a week above 4500 m and should be advised about alternative methods of contraception. Women who are trekking to high altitude for shorter periods (or not going over 4500m on their trek) should be fully informed about the probable but unquantifiable increased risk of thrombosis and advised about alternative methods of contraception, so that they can make their own descision. They should also be advised that dehydration is likely to be a cofactor in thrombogenesis. It would seem unwise to switch to a combined oral contraceptive immediately before an expedition. There are no specific data on which to base such recommendations, which therefore are based on an assessment of the risk. An epidemiological study of sufficient scale to detect an increase in incidence amongst female trekkers is inconceivable and we are unlikely to be able to improve on our current lack of data.
Contraceptives can be useful for reducing menstrual loss which would be convenient on a trek or expedition although breakthrough bleeding is a problem for some women (Sinclair et al 1996). Poor absorption of oral contraceptives as a result of

gastroenteritis could cause additional problems with breakthrough bleeding. Long periods of physical activity and psychological stress at high altitude can also cause menstrual disturbances and may actually reduce menstrual loss (reviewed in Sinclair, et al 1996). The increased risk of thrombosis at high altitude should always be considered before choosing an oestrogen-containing contraceptive with the intention of reducing menstrual loss. Any change (perhaps to a progesterone only preparation or depot injection) should be made more than 3 months before the trip to high altitude in order to reduce the likelihood of menstrual irregularities and other unwanted side effects. Some sanitary protection should be carried because of the possibility of unexpected menstrual disturbance or breakthrough bleeding as a result of diarrhoea or loss of pills.

Lorna Moore, USA
I agree with the general tenor of these remarks. On the basis of an absence of a clear difference in ventilatory acclimatization or incidence of acute mountain sickness in women during the follicular and luteal phases of the menstrual cycle (from our ongoing studies, presented in preliminary form in the 1998 Hypoxia Lake Louise conference), I would concur that effects of the kinds of low-dose COC in common use are unlikely to be significant at moderately high (<14,000 ft) altitudes. At higher altitudes, I would be cautious since there is a chance that the rare but nonetheless potentially real effects of hypoxia and COC might interact unfavorably to cause thrombotic episodes.

Susan Niermeyer, USA
It would seem unwise to begin oral contraceptives specifically for a high-altitude expedition, unless the woman was willing to initiate their use well in advance of her climb (12 months). Previously unexpressed tendency to thromboses and breakthrough bleeding are potential serious complications which negate the usefulness of COC's. Duration and volume of menstrual flow at sea level are not necessarily predictive of conditions at high altitude. Thus, the perceived threat of menstrual blood loss may be greater (or less) than actual. More information should be collected in this area. Use of oral contraceptives for their pregnancy-preventing function strikes me as potentially dangerous in settings of travel. In circumstances other than intercourse with a single, consistent partner, barrier protection is of utmost importance. While Chlamydia and Trichomonas may be a nuisance, pelvic inflammatory disease can destroy fertility permanently, and HIV can destroy a climbing career and a life.

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First some general prnciples should apply.
1. World Health Organisation (WHO) catergories: Let us agree to use the new (1994) WHO categories for contraindications. They call them 1 2 3 4, but I have proposed A B C D instead because in short form they amount to:

A	ALWAYS	)	
B	BROADLY	)	meaning usability of

C	CAUTIOUSLY, with extra CARE	)	the pill in the
		)	condition concerned.
D	DON'T	)	

WHO VERSION:

1. The COC may ALWAYS be used, absolutely no contraindication.
2. The COC is usable in most cases, because the advantages BROADLY or in general outweigh the disadvantages.
3. The COC is rarely to be used, because the disadvantages in general outweigh the advantages - but may be used CAUTIOUSLY, with extra COUNSELLING, with CAREFUL balancing against the alternative contraceptive options, other risk factors, woman's autonomy, etc.
4. The COC IS ABSOLUTELY CONTRAINDICATED, risks unacceptable in context of alternatives, = DON'T USE!

NB The most useful thing here is categorisation of so-called 'relative' risks as nos. 2 and 3.

2. Summation Principle: If the COC itself can independently cause a condition which is more likely at high altitude (HA), then some form of contraindication must be assumed (ie = WHO 2, 3 or 4 anyway, not 1).

3. Individualisation Principle: the woman's own circumstances, risk factors (both chronic and acute), acceptability for efficacy and safety of alternative contraceptives, must all be put into the decision.

4. Autonomy Principle, a critical part of individualisation. Relevant here is that rock-climbing is several orders of magnitude more dangerous than any risks modifiable by different choices of hormonal contraception! Person is entitled to take further risk of a COC if fully informed. But prescriber has autonomy too, to not put their name to a prescription, if s/he feels the risks are really in categ. 4.

5. Assessment of all associated risk factors: These are either venous alone, arterial alone , or can increase risks of both kinds of thrombosis. And both types seem important here, as in AMS it seems that the risk of both venous and arterial thrombotic events goes up.

VENOUS RISK FACTORS
a) Near Family History (sibling or parent with thrombophilia, such as activated Protein C Resistance, or just the history they had a DVT/PE under age 45)
b) Obesity, BMI > 30
c) Severe varicose veins
and more acutely:
d) Immobility, especially relevant to HA being stuck in tents during blizzards, but also LEG fractures put in splints or plaster (remember to advise stopping the pill!!)
e) Dehydration
f) Haemoconcentration, exacerbated by heavy exercise, sweating, alcohol and caffeine
g) Long-haul aeroplane flights, combining above!

ARTERIAL RISK FACTORS

a) Near FH (sibling or parent with acute myocardial infarction, thrombotic stroke under 45)
b) Cigarette smoking
c) Diabetes mellitus
d) Obesity
e) Hypertension
f) Migraine with focal neurological AURA (relates to cerebral thrombosis risk, specifically)

BOTH

Obesity appears in both lists; but more relevant to HA medicine (yet still rare) is acquired antiphospholipid antibodies which appear in connective tissue disorders and increase both venous and arterial disease risk.

PROPOSED (DRAFT) PRESCRIBING ADVICE FOR HIGH ALTITUDE COC USE

Circumstances	Advice based on World Health Organisation (WHO) criteria
If altitude to be >4500 metres for more than 1 week	**WHO 4, DON'T** (Could be WHO 3 if she is sure and free of all other risk factors)
Shorter time, or never reaching 4500 m	**WHO 3 CAUTION/Counselling** (Could be WHO 4 HOWEVER if she has one other risk factor from above. BEWARE: if more than one such risk factor,standard teaching is DON'T use even at sea-level)
All others, including most trekkers	**WHO 2, BROADLY USABLE** after assessing other risks (But still all should be informed of potential small added risk of arterial/venous thrombosis)

Always reassess in light of any new risk factors such as immobilisation/trauma

ALTERNATIVES

a) All non-hormonal methods could be used: but of course no benefit then with menstrual bleeding control
b) INJECTABLES such as Depo-Provera, implants, the progestogen-only pill, all no added risk (known or anticipated)
c) EMERGENCY CONTRACEPTION also usable as so short term (12 hours)

Guillebaud J, Contraception. IN: Women's Health, Oxford General Practice Series 39, eds A McPherson & D Waller. Oxford: OUP, 1997: pages 128-216. Contains most relevant refs, including 3rd generation controversy and re risk factors.

Guillebaud J Contraception Today. A Pocketbook for General Practitioners. London: Martin Dunitz, 1998: 1-98. Useful for ready reference and consideration of all reversible alternatives to the COC.

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