more than its effect. But this result is still informative, since the assertions that lifestyle change by definition works and that any lack of effect is therefore due to poor adherence constitute a tautology. Indeed, this is the essential, maddening conundrum of the epidemic of type 2 diabetes — collective failure to adhere to a lifestyle healthy enough to prevent the disease. A critical point is that the participants in the TODAY study were not adults, but youth immersed from a young age in a sedentary, calorie-laden environment that may well have induced and now aggravates their type 2 diabetes. Fifty years ago, children did not avoid obesity by making healthy choices; they simply lived in an environment that provided fewer calories and included more physical activity for all. Until a healthier “eat less, move more” environment is created for today’s children, lifestyle interventions like that in the TODAY study will fail.

Solace can still be found in the TODAY study, if its larger message transcends its worrisome findings. Illness from childhood overnutrition is a societal and cultural problem that current medicines treat but cannot resolve. For a substantial proportion of those millions of children at risk for largely preventable type 2 diabetes, the findings of the TODAY study reinforce the idea that medications and even procedures will not stave off a lifetime of illness. Furthermore, lifestyle changes for youth are undermined by immersion in an obesogenic world, in which personal responsibility appears to be invalidated by the limits of willpower with respect to overnutrition. The stark message from the TODAY study is that, tomorrow and beyond, public-policy approaches — sufficient economic incentives to produce and purchase healthy foods and to build safe environments that require physical movement — and not simply the prescription of more and better pills will be necessary to stem the epidemic of type 2 diabetes and its associated morbidity.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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This article (10.1056/NEJMe1204710) was published on April 29, 2012, at NEJM.org.


Hormonal Contraceptives and Arterial Thrombosis — Not Risk-free but Safe Enough

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The link between combined estrogen–progesterin oral contraceptives and venous and arterial thrombosis was made soon after these products were marketed, in the early 1960s. By 1970, the doses of estrogen in combined estrogen–progesterin oral contraceptives had already been lowered on the basis of epidemiologic data showing that formulations with higher estrogen doses were associated with increased vascular risks. Studies published in 1995 and 1996 showed that increases in the risk of venous thromboembolism were greater with newly marketed estrogen–progesterin oral-contraceptive formulations containing desogestrel and gestodene than with formulations...
containing levonorgestrel and other “older” progestins.\textsuperscript{5-8} Much attention has since been paid to estimating the comparative cardiovascular risks associated with hormonal contraceptives, with a focus on possible differences in risk among progestins.

In this issue of the \textit{Journal}, Lidegaard and colleagues report the results of their cohort study of hormonal contraceptives and arterial thrombotic events (thrombotic stroke and myocardial infarction).\textsuperscript{9} The study encompasses data from the entire population of Danish women, 15 to 49 years of age, for the period from 1995 through 2009. With more than 1000 strokes and almost 500 myocardial infarctions in current users of hormonal contraceptives, the study is 10 times as large as a recently reported study in the United States that also assessed the comparative risks of arterial thrombotic events among users of hormonal contraceptives.\textsuperscript{10}

The study by Lidegaard and colleagues showed that the relative risks of thrombotic stroke and myocardial infarction were increased by a factor of 1.5 to 2 among users of estrogen–progestin oral contraceptives with a low dose of ethinyl estradiol (30 to 40 \textmu g) for all the progestins studied (norethindrone, levonorgestrel, norgestimate, desogestrel, drospirenone, and cyproterone acetate). In a comparison of such low-dose formulations with different progestins, the relative risks of thrombotic stroke and myocardial infarction were statistically indistinguishable. For estrogen–progestin oral formulations containing a very low dose of ethinyl estradiol (20 \textmu g), the study showed that the relative risks of thrombotic stroke and acute myocardial infarction were increased by a factor of approximately 1.5 when formulations containing desogestrel and gestodene were used, as compared with nonuse. Among users of the vaginal ring and the transdermal patch, which are combined estrogen–progestin formulations, the relative risks of thrombotic stroke were 2.5 and 3.2, respectively. Although these relative risks are higher than the relative risks of thrombotic stroke among users of the other low and very low doses of ethinyl estradiol in the combined estrogen–progestin hormonal contraceptives studied, the increases are statistically indistinguishable. The relative risks of thrombotic stroke and myocardial infarction were not significantly elevated for any of the progestin-only formulations studied.

Among Danish women who did not use hormonal contraception, the absolute risks of cerebral thrombosis and myocardial infarction were low. Considering the absolute risks of cerebral thrombosis and myocardial infarction among nonusers of hormonal contraceptives and the relative risks among users, the number of “extra” arterial thrombotic events attributable to hormonal contraceptives is about 1 to 2 per 10,000 women per year or, equivalently, 10 to 20 per 100,000 women per year for the combined estrogen–progestin formulations that might cause arterial events. These are small numbers. For an individual woman, the probability of an event is quite small.

Venous thromboembolic disease is more common than arterial vascular disease in women of reproductive age. Arterial vascular disease is potentially a greater threat to an individual woman because the sequelae are more serious. Stroke in particular can lead to severe and permanent disability. Although not explicitly stated in regulatory and other discussions, a large excess in the relative risk of stroke in the comparison of one hormonal contraceptive with another could, and probably should, have an important influence on the conclusion about the overall risk–benefit ratio of the formulation, as compared with other formulations that have equal contraceptive effectiveness. None of the hormonal contraceptives studied by Lidegaard and colleagues were associated with an excess risk of stroke that was unacceptable, considering their contraceptive and noncontraceptive\textsuperscript{11} benefits.

Women, their physicians, and the public should be reassured not only by the Danish study but by the vast body of evidence from epidemiologic studies of hormonal contraception that have been done over the past five decades. This body of research documents the small magnitude of the problem of arterial thrombotic events in women using combined estrogen–progestin hormonal contraceptives. The research shows that the small risk could be minimized and perhaps eliminated by abstinence from smoking and by checking blood pressure, with avoidance of hormonal contraceptive use if blood pressure is raised.\textsuperscript{12} With the addition of the Danish data, evidence is now even stronger that progestin-only formulations of hormonal contraception have vascular risks that are undetectable with modern epidemiologic methods. Although hor-
monal contraception is not risk-free, the evidence is convincing that the low and very low doses of ethinyl estradiol (<50 μg) in the combined estrogen–progestin contraceptives studied by Lidegaard and colleagues — whatever the progestin and whether delivered orally or by means of the patch or the ring — are safe enough.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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