sures. The gastrointestinal symptoms focused our attention on colitis. No data were available in the literature at that time to justify systematic addition of G-CSF to the docetaxel-doxorubicin combination. Following the addition of prophylactic G-CSF in the GEICAM trial, the rate of febrile neutropenia associated with the docetaxel-doxorubicin-cyclophosphamide regimen fell below 10%.[2]

The controversial use of prophylactic antibiotics, favoring the emergence of resistant bacteria without lowering the risk of death,[3] did not achieve this level of protection, as found in the NSABP, GEICAM, BCIRG, and Eastern Cooperative Oncology Group (ECOG) trials. It may, however, explain the lower rate of febrile neutropenia in these studies as compared with ours, which did not include prophylactic antibiotic use (around 25% vs 41%).

The last fatal serious adverse event in our study in January 2003 triggered a detailed safety analysis that revealed a rate of febrile neutropenia above 40%, exposing patients to life-threatening complications unacceptable in the adjuvant setting. This urged us to close the trial and describe the observed toxicity.

High-grade toxicity and toxic deaths are unacceptable for a therapy given to reduce the risk of recurrence when this risk is both small and distant in time. In the RAPP-01 trial, we observed a rate of death without evidence of cancer of 0.63% in the docetaxel-doxorubicin group vs 0% in the doxorubicin-cyclophosphamide group. In comparison, in the BCIRG-001 trial the rates of death were 1.1% in the docetaxel-doxorubicin-cyclophosphamide group vs 0.5% in the fluorouracil-doxorubicin-cyclophosphamide group.[4] In the ECOG 2197 trial, the rates of death in the docetaxel-doxorubicin and doxorubicin-cyclophosphamide groups were 0.41% and 0.14%, respectively, with doses of 60 mg/m^2 each of doxorubicin and docetaxel instead of 50 mg/m^2 and 75 mg/m^2 as in the RAPP-01 trial.[5] The smaller studies of the Anglo-Celtic Cooperative Oncology Group (363 women)[6] and GEICAM (448 women)[2] do not report any deaths.

Some groups are advocating the use of G-CSF in patients with a 20% risk of febrile neutropenia instead of the standard threshold of 40%.[7] This needs to be evaluated in terms of cost and benefit since G-CSF is one of the most expensive cancer drugs. Another question is whether chemotherapy drugs need to be combined in the adjuvant setting. If we consider cancer in general, sequential monotherapy is not usually the accepted approach. However, in the PACS-01 adjuvant trial, docetaxel given after combined fluorouracil-epirubicin-cyclophosphamide provided a significant survival improvement compared with the same regimen without docetaxel and a safer profile than docetaxel-doxorubicin–like regimens (less than 10% incidence of febrile neutropenia).[8] This would support the use of a sequential schedule to integrate docetaxel in the adjuvant setting, but this needs to be interpreted with caution given less positive results from the NSABP B-27 neoadjuvant program, with 21% of febrile neutropenia in women sequentially given docetaxel following doxorubicin-cyclophosphamide[9] and a lack of survival benefit for those having received docetaxel vs those treated only with doxorubicin-cyclophosphamide.[10]

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Self-reported Sexual Function in Women and Androgen Levels

To the Editor: In their study comparing androgen levels with self-reported sexual function in women, Dr Davis and colleagues[1] refer to dehydroepiandrosterone (DHEA) and its sulfated ester (DHEAS) as androgens. This is not true because these steroids have little or no affinity for the androgen receptor, nor do they have any intrinsic androgenic effects. To date, only 2 DHEA receptors have been described in vascular endothelium[2] and murine T cells.[3] It is the peripheral conversion to androgens and estrogens that is thought to lead to their effects on peripheral tissues.

Moreover, the DHEA that is found within brain tissue is not derived from the peripheral circulation but is formed de novo from its steroid precursor, 17-hydroxypregnenolone, and then broken down to increase local levels of sex hormones.[4] Peripheral measurements of these hormones may thus not be representative of levels found within the areas of the brain responsible for sexuality and sexual function.

The authors may be correct in their statement that DHEA and DHEAS provide a large precursor pool for peripheral sex hormones, but their role and their effects on brain function remain undetermined.

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In Reply: Dr Dhatariya has pointed out that there is evidence for de novo biosynthesis of DHEA within the brain[1] and that peripheral levels of DHEAS may not reflect brain tissue concentrations. The intention of our study was to highlight that the biosynthesis and metabolism of C19 steroids is complex and that measurement of circulating androgens and pre-androgens does not necessarily provide an accurate guide to the hormonal milieu in different target tissues.

With respect to referring to DHEA and DHEAS as androgens, we acknowledge that there is still considerable uncertainty as to whether DHEA has any significant physiological androgenic actions independent of its conversion to other androgenic steroids. Dehydroepiandrosterone is a C19 steroid, as is testosterone, and in recent competition binding studies, Chen et al[2] demonstrated that DHEA exhibits affinity to the androgen receptor. Although we have included DHEA and DHEAS in the term *androgen* in our article, as is commonly done, we emphasized in the discussion the importance of DHEA and DHEAS as precursors for both estrogen and testosterone production.

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Long-term Outcomes for Extremely Low-Birth-Weight Infants

To the Editor: In their study of the long-term outcomes for extremely low-birth-weight (ELBW) infants, Dr Hack and colleagues[1] show that medical advances in perinatal care in the 1990s have decreased mortality, but ELBW children have very high rates of chronic conditions, functional limitations, and special health needs. The authors underscore the importance of providing a medical home and care coordination as part of long-term treatment. In their accompanying editorial, Drs Tyson and Saigal[2] describe the increase in the absolute numbers of impaired ELBW survivors as disappointing, and propose approaches for gaining a better understanding of the effects of perinatal treatment decisions and the long-term needs of these children for medical services. I believe that the recommendations for health services and planning by Hack et al do not look far enough into the future, and that Tyson and Saigal's questions about the long-term needs of these children have, in many important ways, already been answered.

There is a growing number of policy statements,[3] reports,[4] and studies[5] on health care transition (the movement of youth with disabilities and special health care needs from pediatrics to the adult care system). This literature shows that most adult health care professionals, facilities, and programs lack the requisite knowledge base and experience to provide quality primary and specialty care to young adults with childhood-onset chronic conditions and disabilities. Thus, preservice and in-service training of adult care clinicians are critically needed.

This literature also shows that ELBW children not only need a pediatric medical home, but that they will need a source of coordinated, community-based, person-centered care throughout the course of their adulthood. As articulated in a recent consensus statement on health care transition, endorsed by the American Academy of Pediatrics, the American Academy of Family Physicians, and the American College of Physicians,[3] the pediatric and adult care communities must work in a more coordinated and collaborative fashion to provide high-quality, developmentally appropriate health care services that continue uninterrupted as individuals with special needs move from adolescence to adulthood.

Hack et al have alerted the adult care community that ELBW children born in the 1990s will soon be joining the