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Editorial Comment

Debunking dogma and developing theses

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It is a challenge to write any brief commentary on the research, observations, speculations and theories promulgated by each of these authors individually, but when they are together the task may be just be hopeless! However, I will try to address just a few of the many ideas, observations and speculations presented in this issue [1] because this is an essay rich in important inferences and serves well to make us reconsider accepted paradigms. Nowhere is this more important in oncology than when considering breast cancer for it has been the study of this disease that has produced dogma regarding the aetiology, natural history and treatment of all types of cancer [2]. The term "dogma" is used with full appreciation of all its religious and authoritative connotations. Critical reflection on such strongly held beliefs is always a good thing, but it is especially true in medical science. We are indebted to the authors for their presenting information in a way that invites interpretation at variance to generally accepted theses. Their selective review of the history of our understanding of cancer is informative and enjoyable. However, the discussion of the natural history of untreated breast cancer seems beside the point. Despite the paucity of relevant data documenting the dire consequences of leaving breast cancer untreated, clinical observation confirms both the local growth and the metastatic spread of the disease leading to morbid symptoms and death. There are surely exceptions as the anecdote presented, but unfortunately they are rare indeed and surely nothing on which to base the management of a patient.

The authors reach into a rich lode when they discuss the possible deleterious influence of surgery. Not only have there been concerns about untoward effects of this treatment within the medical community, there is a common lay perception that surgical manipulation of cancer – if not successful – accelerates disease progression. The description of an increase in the hazard of relapse about 2 years after surgery in the control group of the Milan trial is important especially as the authors note that it is this that is ameliorated in the adjuvant treated patients. That this increased hazard rate is due to removal of the primary lesion – because of the release from inhibitors produced by the primary or because of some stimulation – is an interesting notion for which some experimental data are presented. This needs much more study. There have been many randomised trials as well as meta-analyses of adjuvant breast cancer treatment which can inform and enrich this observation. These should be used to verify the observation and, if it is confirmed, to shed light on its cause with particular attention to the hypothesis that it is surgery that is the cause of the transient increase in the recurrences seen.

With this important observation and its possible explanations it is unfortunate that we are presented with yet another rehearsal of the arguments about whether breast cancer is really curable. These concerns have been presented well before and no new light is shed here. The Halsted paradigm of orderly, centrifugal spread of cancer by invasion, lymphatic extension and then metastatic dissemination served as the prevailing dogma until the last quarter of the 20th century. It has been replaced by the thesis of predeterminism regarding metastatic spread that has been held tenaciously with similar certainty by some. However, both paradigms fail to explain all that we observe in breast cancer. Mammography in 50–70 year old women reduces breast cancer by 30%. This must be because the cancers were found before metastases had disseminated, but would have spread if

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the primary tumours had not been detected until they were clinically evident. Predetermination cannot be true for those 30%. Metastatic likelihood is a function of increasing tumour size, but at any size of invasive tumour there is some possibility of metastatic spread and even at the largest sizes there are some patients without metastases [3,4]. Of the long-term survivors of breast cancer treated with only local-regional methods, 30% had initially involved regional lymph nodes. This plus the correlation of tumour grade and oncogenic mutations with increasing tumour size all suggest a third and most likely paradigm for breast cancer; one that explains both contiguous spread and early dissemination as occurring within a continuum [5]. Breast cancer comprises a spectrum of disease proclivities extending from those that disseminate very early in their natural history to those that never do regardless of size. But for the great majority there is malignant progression as tumours grow. The tumour progression in the facility to produce metastases is very likely due to evolutionary mechanisms [6].

The authors damn by faint praise the benefits of adjuvant treatment. This is unfortunate. An increase of approximately 10% in absolute survival is a significant saltation in breast cancer treatment. And it can be built upon as shown by additional approximately 10% improvement in absolute survival produced by regional radiation reducing persistent local-regional disease. The bottom line of an approximately 20% improvement in cure is very important. Adjuvant chemotherapy was first developed by Nissen-Meyer to prevent a potential adverse effect of surgery; that of the haematogenous spread of cancer cells during the surgical procedure. Whether that was the mechanism of benefit seen in his studies or with any of the adjuvant regimens or whether it is that suggested by this essay by Baum and colleagues is still to be determined. The authors' interpretation is amenable to testing and I look forward to seeing what likely mechanism will emerge. Whatever it is, it will be arrived at inductively, by scientific methods and thus must be a conditional truth subject to continued testing for consistency with new information. Surely such tentative conclusions are not the stuff of dogma. If for no other reason than making me question my closely held beliefs, reading this essay has been useful and therapeutic as well as enjoyable.

Conflict of interest statement

None declared.

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