There can often be confusion as to what we mean by rare or uncommon and whilst the dictionary may give a definition of what is meant by rare or uncommon, we have to take into account a number of modifying factors. These include the kind of practice that is run, the local geography, the part of the world where we work and local politics and arrangements. For example, clear cell cancers of the ovary are considered to be relatively uncommon in the Western world, accounting for only 3–5% of ovarian cancers, and yet in the Far East they may account for 15–20%. There are other examples where there are variations in the frequency of a condition on a global basis. From a different standpoint, an individual working in a small district cancer hospital seeing only 1,000 or 1,500 new cancers a year will see very few rare conditions, and yet those of us who work in major supra-regional or comprehensive cancer services will see a reasonable number of these so-called uncommon and rare cancers. Thus it is all relative to the kind of practice in which we work. In the introductory chapter we have already made reference to the fact that it may be argued that concentration of the care of these rare and uncommon cancers should be in the hands of a smaller number of regional or supra-regional centres, but of course there can be opportunities for shared care and networking between the smaller district hospital and the regional cancer centre. There is no “one size fits all” and it will be determined by local arrangements.

It is probably helpful at this point in time to list many of the types of tumours that we are discussing in this book. Firstly we are focusing on tumours of the ovary, uterine corpus, uterine cervix, vagina and vulva. We are concentrating mainly on tumours such as mucinous tumours, clear cell cancers, neuroendocrine tumours, sarcomas and sex cord and stromal tumours. Other less common cancers include serous uterine cancers, squamous cancers arising in ovarian dermoid tumours and melanomas of the vulva and vagina. We also cover uncommon situations like high grade borderline cancers which are worthy of merit not only because of their clinical infrequency but also because of their different biological behaviour. Fallopian tube cancers have not been specifically included as they are considered to be similar to ovarian cancers, and a recent provocative paper has suggested that Fallopian tube cancers may be the “mother of gynaecological epithelial tumours”. Given the strong similarity between serous epithelial ovarian and tubal cancers, there is no attempt to distinguish them. The topic of gynaecological cancers arising in pregnancy is also a challenging one and we are fortunate to be able to include a chapter from the team based in Leuven who have been addressing this important topic. We also are pleased to be covering the controversial topic of pseudomyxoma peritonei (PMP). In the UK we have developed a National Service in Basingstoke and the chapter has been written by their team.

What has been omitted? We have not covered some important areas such as gestational trophoblastic tumours and germ cell cancers mainly because the management of these is usually relatively straightforward and there are already well established referral pathways and guidelines for centralisation of care.
2.1 Rare and Uncommon Gynaecological Cancers

We have already alluded to the difficulties in trying to define a rare or uncommon cancer and one of the challenges is trying to establish just how infrequent these tumours are. Cancer registers are very variable in their quality around the world but often reflect the quality of the data recorded at the time of initial diagnosis, and particularly for rare tumours the subsequent management and review of the case may indicate that we are dealing with a different final diagnosis. This revised diagnosis is unlikely to be routinely picked up by cancer registries. Internationally, there is huge variation in the way that this data is collected and one of the issues that we would like to address is the setting up of formal registries for these rare tumours. The Gynaecological Cancer Intergroup (GCIG) attempted an initiative a few years ago to try and set up a web-based register but unfortunately this faltered, mainly because of issues of how to deal with confidentiality and security. Transferring data globally presents major challenges and many felt that this was not securely achievable at present. However, other initiatives have shown that this can be done at least within a nation. The presentation at ESMO 2007 by Isabel Ray-Coquard on behalf of the French Rare Tumour Registry has shown how this can be done working within one nation and using a defined framework. The reader is referred to their website http://ovaire-rare.org/. Although this was set up partly to provide advice on the management of these rare cancers it has led the way forward in establishing how to collect data on these rare cancers.

The GCIG Rare Tumour Working Group has tried to lead the way in resolving how to overcome the challenges of setting up these databases internationally. One initiative would be to have a series of national registries and databases which could then be linked once the data had been suitably anonymised. However, to do this it would be necessary to have a common dataset. This could be in the format of a core dataset where the basic registration details with some form of unique identifier are kept. We would then have add-on modules in which we would collect specific details for the specific tumour types.

The benefits of this kind of registry are not simply that we would be able to collect data on the frequency of these tumours and establish whether they are truly rare or uncommon, but also that we could have a fantastic valuable resource for clinicians and scientists wanting to develop clinical research or translational studies in these areas. Using virtual tumour and serum banks we do not necessarily need to have tissues and serum flying round the world but can use identifiable tagging processes. We must use every opportunity to take advantage of modern technologies and these kinds of initiatives will hopefully lead the way in developing and progressing care.

We can also see whether, over the course of time, there are changes in patterns of disease. For example, uterine sarcomas were considered to be very uncommon tumours and yet, more recently, carcinosarcomas have become more frequently documented. Is this a genuinely increasing incidence or is this better recognition by pathologists using modern immunocytochemical techniques? For example, is the incidence changing due to exogenous oestrogens and use of tamoxifen for breast cancer? These kinds of issues can be addressed. We have to work together but the modern world is getting smaller and smaller due to the expanding use of electronic technologies. Many of the so-called Third World or low-income countries now have access to technology to match those of us in the Western world and no longer need to be excluded from these initiatives.

2.2 Definition: What is Rare?

There can often be confusion as to what we mean by rare or uncommon and whilst the dictionary may give a definition of what is meant by rare or uncommon we have to take into account a number of factors.

How do we define rare? Is there a simple definition? One definition is “few in number and widely separated from each other (in space or time)” and another is “of a kind, class or description seldom found, met with or occurring: unusual, uncommon, exceptional”. This does not help as no numbers are given and it has already been commented that what is rare in a small centre may be seen more often in a big centre. Recently the National Institute of Health and Clinical Excellence (NICE) in the UK suggested that a cancer with less than 7,000 cases per annum would be proposed as uncommon. This would be considered generous by most standards and many intermediate incidence cancers like renal and oesophagus would be included. A reasonable proposal might be to suggest fewer than 50 cases per million population but the author has never seen such a figure
proposed and we have to start somewhere! This will include virtually all of the cancers listed below.

What kinds of examples can we consider? Listed below are some of the other rarer cancers.

### 2.3 Examples of Rare and Uncommon Cancers

- Ophthalmic cancers
- Thyroid cancers
- Neuroendocrine cancers
- Soft Tissue and Bone sarcomas
- Brain and CNS cancers

However, we are looking often at subsets of the more common gynaecological cancers as well as the rarer types; these have been listed below.

- Sub-sets of commoner gynaecological cancers
  - Small cell and neuroendocrine cancers
  - Clear cell cancers
  - Mucinous cancers
  - Serous endometrial cancers
  - Sarcomas/carcinosarcomas
  - Sex cord tumours

Having thus set the scene, it is now time for the reader to review the contents and it is to be hoped that we have done our best to address most of the issues likely to be raised. In the next section of the book we have brought together all the rarer types into sections as listed, but we recognise that there are differences between some of the tumour types. In each section we have attempted to have a template format of epidemiology, diagnosis, imaging and treatment with particular emphasis on the multi-modality and multi-disciplinary treatments. It will be noticed that the chapters and sections vary in their detail, but this reflects the amount of information that is known about a condition and the degree of controversy about their management and care. We have attempted to include not just the clinical aspects but the molecular pathology and the associated biomarkers as appropriate.

Whilst we accept that there are differences between mucinous or clear cell cancers within the ovary, uterus and cervix, it is felt that this commonality of approach is justifiable because there are similarities in their aetiology and in their clinical behaviour. The increasing use of molecular markers to diagnose tumours has indicated that the pathways to cancer development may be similar. This is increasingly being reflected in the use of cell signalling pathway inhibitors as part of the therapeutic armamentarium. It is very likely that by the time the book is published, our knowledge will have leapt further forward, but nevertheless, we hope that this is an accurate reflection of the state of the art at the time of writing.
Rare and Uncommon Gynecological Cancers
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