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Conference Report
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Breast Disease

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(Chairman of the Symposium)

This article reports the proceedings of the symposium. Some contributions have been considerably edited to select points raised in discussion, and overseas practice.

The speakers and their respective topics were:-

Genetics of Breast Cancer:	*Prof Alfred Cuschieri*
Pathology:	*Dr James Degaetano*
Management of a Patient with Breast Lump:	*Mr Gordon Caruana-Dingli*
Concepts of Surgical Management of Breast Cancer:	*Mr Charles Swain*
Breast Imaging:	*Dr Malcolm Crockford*
Adjuvant Therapy of Breast Cancer:	*Dr Victor Muscat*
Breast Reconstructive Surgery:	*Mr Francis Darmanin*
Functions of the Breast Care Support Group:	*Mrs Helen Muscat*

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Introduction

In common with other Western countries, breast cancer is the most frequent malignancy in Maltese women, and the commonest cause of death in women aged 40 to 55 years.

Although the incidence of breast cancer in Malta (about 1 in 12 women) appears to be higher than the European Average, it is lower than that of some north European countries and also lower than the incidence in the USA. However, the mortality from breast cancer in Malta is not only higher than in the USA, but is also the highest in Europe. Why we have the highest mortality, in spite of not having the highest incidence, needs looking into. Furthermore, Western countries report a rising incidence of breast cancer, and there is no reason to believe that ours is falling.

The genetics of breast cancer

Genetic analyses of families with a high incidence of breast cancer suggest that specific mutations within the genome are responsible for breast cancer. The BRCA1 and BRCA2 genes, when mutated within the germ line, are associated with an approximately 85% risk of breast cancer development in the lifetime of individuals with such a mutation. Those with the BRCA1 mutation are also at high risk for ovarian cancer. The BRCA1 gene encodes a large protein that may be excreted from cells and appears to control cell proliferation.

Whereas perhaps only 8% of all breast cancers can be attributed to these two genes, it is likely that other genetic defects will be found in families in which cancer of the breast and ovary are prevalent. Breast cancer in very young women without a family history of the disease is frequently not associated with mutations in the BRCA1 and BRCA2 genes. Screening of women and their children for the presence of mutations in the BRCA1 and BRCA2 genes poses important ethical, legal, and privacy issues that need to be addressed before screening becomes widespread.

Analyses of individuals with the Li-Fraumeni syndrome, a condition associated with development of multiple cancers (including breast) at a young age, indicate that germ line mutations in the tumour suppressor gene p53 are responsible for breast cancer in these individuals.

About 60% of breast cancers during their formation have acquired mutations in the p53 gene or other genes on chromosome 17. These acquired mutations, either alone or in conjunction with the overexpression of other oncogenes or the loss of tumour suppressor genes, are likely to play an important role in the progression of breast cancer.

There is presently no basis for some expressed fears that the Maltese population may have a higher incidence of breast cancer because of more inherited genetic defects due to in-breeding. Some north European countries with far larger populations than Malta have a higher incidence of breast cancer than Malta, and our present understanding is that differences in incidence within Europe, and between Japan and Western

countries, are not due to differences in genetics but differences in environmental factors, with diet possibly playing a dominant role. The important principle of reduced penetrance and variable expression in genetics, whereby individuals with the same gene mutation have different phenotypes, must be borne in mind, because it indicates that the phenotypic differences must be due to the effects of other "modifier" genes, to environmental interactions, or to chance. This is the explanation why researching environmental factors, and not simply finding mutated genes, is important in the study of causation of breast cancer, and why a modification of the relevant environmental factors may alter the risk of breast cancer development.

Pathology

Significant advances have been made in our understanding of breast premalignant epithelial changes and their clinical relevance, the microscopical features in invasive carcinoma which relate to biological behaviour and prognosis, the assessment of tumour hormone receptor status and other biological characteristics in tissue sections with immunohistochemical techniques, and the development of fine needle aspiration cytology diagnosis.

As with cancer in other organs, the development of breast cancer involves a progression of precancerous changes. These are of two broad biological types:-

i) atypical lobular hyperplasia (ALH) and lobular carcinoma in-situ (LCIS)

ii) atypical ductal hyperplasia (ADH) and ductal carcinoma in-situ (DCIS)

These premalignant changes have been estimated to be associated with between 4 and 10 times increased risk of development of invasive carcinoma, when compared to similarly aged women with no breast problems.

i) ALH is presumed to be an earlier stage of LCIS, and distinguishing between the two is rather arbitrary and of no proven clinical significance. They are both morphological markers of increased risk of invasive carcinoma development for both breasts, and the most recent genetic studies claim that the DNA abnormalities in ALH and LCIS are similar.

LCIS is typically discovered by coincidence in breast tissue removed for proliferative lesions that cause a mass or in apparently normal tissue surrounding a benign tumour such as fibroadenoma. Associated benign processes may cause mammographic abnormalities that lead to a biopsy in which LCIS is detected. Mammography is not an effective method for detecting LCIS and cannot be depended upon to assess multicentricity or bilaterality of the disease.

Both breasts are frequently affected by LCIS, often at the same time, but there are women with LCIS who do not have simultaneous bilaterality and may never have both breasts affected by LCIS or any other form of mammary carcinoma.

The majority of patients with LCIS not treated by mastectomy remain well. Subsequent ipsilateral invasive carcinoma has been estimated at about 20% at 15 years of follow-up. The risk increases with longer follow-up.

Three treatment choices are generally considered for LCIS:-

a) Clinical follow-up to detect subsequent invasive carcinoma, b) bilateral mastectomy, and c) ipsilateral mastectomy.

Clinical follow-up is a lifetime undertaking in view of the relatively high frequency of late-occurring invasive carcinomas. It is increasingly recommended for, or selected by, LCIS patients, but there is no consensus regarding the optimal follow-up programme. Mortality due to invasive carcinoma among untreated patients in one retrospective study of LCIS patients was nearly 11 times greater than expected. It remains to be seen whether mortality can be reduced by detecting subsequent invasive carcinomas through close clinical surveillance. Other data indicate that when detected, subsequent invasive carcinomas of 1cm or less have axillary metastases in about 15% of cases. In one series with no systematic follow-up of LCIS patients, about 50% had nodal metastases when invasive carcinoma was later detected. A study of more carefully followed-up patients showed axillary metastases in 26% and nearly 25% later developed systemic metastases.

Bilaterality of LCIS occurs frequently, but is unproven whether it occurs in every patient. Biopsy of the opposite breast may identify patients with the greatest risk of subsequent contralateral invasive carcinoma. There seems little justification for routine contralateral mastectomy without prior biopsy, although some patients may choose this approach.

There is little experience other than surgical with treatment of LCIS. Radiation therapy is not recommended. Trials employing Tamoxifen in patients with LCIS or other markers of high risk invasive carcinoma of the breast are under way.

ii) The other broad group of premalignant breast changes are ADH and DCIS. DCIS has been variously classified into "micropapillary", "cribriform", "clinging", "solid" and "comedo". The micropapillary, cribriform and clinging types are characterised by low grade cytological features, whilst the solid and comedo types exhibit high grade cytological morphology, the comedo type typically showing intraductal necrosis and calcification. Some cases of DCIS may have a mixture of low and high grade features and these have been referred to as of intermediate grade type. There is much practical merit in classifying DCIS into low, and high grade types. Calcification occurs less often in low grade DCIS, and mammography is therefore more likely to underestimate its extent than that of high grade DCIS which often has much microcalcification. Furthermore, high grade DCIS apparently progresses more rapidly to invasive carcinoma.

The importance of DCIS relates to its potential to progress to invasive ductal carcinoma. This has been assessed by several studies and it is evident that only a fraction of incompletely treated DCIS's progress to invasive carcinoma, these usually being of high grade type. Treatment of DCIS is variable, with mastectomy favoured by some and wide local exision, usually followed by irradiation, recommended by others. Although mastectomy has a cure rate of nearly 100%, and circumvents the issues of multicentricity, recurrence and occult invasive growth, there is an increasing trend toward breast conservation treatment. This requires rigorous long-term monitoring of the patient with regular physical examination and mammography as

often as every 6 months in the first 2 years and annually thereafter.

The local recurrence rate after wide local excision with postoperative radiation has been variously reported as anything between 10 and 30%. The likelihood of multicentricity and occult microinvasion in nonpalpable lesions has been shown to be greatest with high grade DCIS, whereas it is least likely with low grade DCIS presenting as incidental findings.

The assessment of adequacy of surgical excision margins may be inaccurate because of multicentricity of DCIS. Reliance upon mammographic microcalcifications to guide the extent of excision may overlook foci of low grade DCIS with no calcifications. Factors that must be considered in choosing therapy are the extent of the DCIS lesion, the ease of follow-up physical examination of the breast, the mammographic density of the breast, the family history, and the patient's ability to comply with a follow-up schedule. The patient's age and absence of grossly detectable neoplastic changes may also be factors to consider. The cumulative risk for development of invasive carcinoma is less in the elderly.

The presence of extensive DCIS in the grossly normal breast tissue adjacent to an invasive neoplasm in the excisional biopsy has to be related to the presence of DCIS in the remainder of the breast. The presence of multiple foci of DCIS in the grossly normal breast adjacent to an invasive neoplasm is a predictor of an increased risk of recurrence following wide local excision of the neoplasm and radiotherapy. This is especially true if the growth pattern is that of high grade DCIS. High grade features in DCIS have been shown to be a predictor of local recurrence after local treatment for DCIS.

Axillary node metastasis is unlikely with DCIS. However, microinvasive carcinoma is difficult to exclude with certainty in multifocal DCIS and when large regions are involved. In this situation low axillary dissection may be appropriate, but may be omitted if there is only a small area of DCIS which appears completely excised.

In contrast to LCIS, the risk of subsequent invasive carcinoma in the contra-lateral breast following a diagnosis of DCIS is relatively small, occurring in only about 3% of patients.

ADH is theoretically a precursor lesion of DCIS but in practice there are significant inter-observer subjective difficulties in distinguishing between ADH and low grade DCIS.

The diagnosis of ADH is employed to indicate that a patient has an increased risk of developing invasive carcinoma. This information must be utilised in combination with other factors to determine appropriate treatment. Other considerations include family history of breast cancer, age, ease of subsequent breast examination clinically and mammographically, extent of the microscopic abnormality, and the willingness of the patient to adhere to a rigorous follow up programme. ADH and a history of breast cancer in a first degree relative has a risk of subsequent invasive carcinoma comparable to that of DCIS.

Invasive carcinoma has potential to kill primarily because of its capability of blood-borne spread. Long term survival depends on whether blood-borne spread has occurred or not. The gist of pathological attempts at predicting which invasive carcinomas are more likely to have potential for blood-borne spread are the following prognostic factors:-

- Size: Tumour size correlates directly with survival. Invasive carcinomas up to 0.5cm diameter are not usually associated with axillary node spread, but careful axillary node dissections combined with "sentinel" node identification techniques have demonstrated nodal metastasis associated with about 15% of 0.5cm to 1.0cm diameter invasive tumours.
- Histological type: Some so-called special types of invasive carcinoma (tubular, cribriform, mucinous and papillary) are associated with a much better prognosis than cancers of no special type. Histological type is one of the best predictors of long term survival.
- Histological grade: Tumour grading based on differentation, nuclear pleomorphism and mitotic frequency correlates with tumour biology and prognosis.
- Vascular invasion: Tumour cells can be identified in lymphatic and blood vessels adjoining the primary neoplasm in up to 25% of cases, and is associated with a doubling of local recurrence rate after wide local excision or mastectomy, and with a high risk of short term systemic relapse.
- Hormone receptors and oncogenes: Presence of oestrogen receptors predicts a breast cancer's response to hormonal manipulation, much appears to be of some value in predicting early outcome but is of limited value in predicting long term survival. Tumours negative for both oestrogen and progesterone receptors will not respond to hormonal manipulation.

Tumours overexpressing c-erbB-2 (HER/2 neu) oncogene and associated with lymph node spread have a particularly poor prognosis, but c-erbB-2 seems of less value in delineating the prognosis of patients who are lymph node negative. Tumours expressing c-erbB-2 are more likely to be resistant to both chemotherapy and hormonal treatment.

In spite of these advances, the pathological assessment of invasive breast carcinoma still lacks the ability of accurately predicting which tumours are going to kill and which will not. Somewhat less than half of breast cancer patients are dead at 10 years post treatment and more than half are dead after 20 years follow-up. Patients presenting with disseminated tumour 12 or 15 years after initial therapy have obviously had blood-borne spread at the time of initial treatment. The biological reasons for these disseminated tumour clinically latent periods are not understood, and what exactly cytotoxic chemotherapy would have achieved in the cases that had not been given adjuvant chemotherapy (prolongation of tumour latent period, ?cure, ?no effect) is also unknown. Pathological research is currently engaged in attempts at identifying markers of metastasizing potential in breast carcinoma cells to more accurately predict which are the ones very likely to kill by blood-borne spread, in the short or long term, and which would therefore need aggressive chemotherapy.

Management of a patient with a breast lump

Only a small proportion of breast lumps are malignant, but still, breast cancer is a common and serious problem. About 180 breast cancers are reported in Malta every year and also half that number die of the disease

within the first ten years after initial treatment, and between half and two thirds after twenty years.

The first step is to ask about the symptoms and also the patient's history with particular reference to the menstrual and obstetric history. Details of risk factors, including family history can be obtained with a simple questionnaire, which is completed by the patient while waiting to be seen in the clinic. The duration of symptoms is important -- breast cancers usually grow slowly but cysts may even appear overnight.

A thorough physical examination follows the history, and should precede other investigations. It includes examination of both breasts and axillae for signs of primary cancer and local spread, and a thorough examination of the rest of the body for signs of distant spread.

Clinical assessment of axillary nodes is often inaccurate, palpable nodes are found in 30% of normal patients and 40% of patients with breast cancer and axillary nodal metastasis do not have palpable nodes. Always believe a woman who feels a lump in her breast.

At this stage the patient should be referred to a surgeon with a special interest in breast disease. Patients with the following signs and symptoms should always be referred for further investigation:

- lump,
- nipple discharge or eczema,
- skin or nipple tethering,
- any doubt.

In the hospital setting a so-called Triple Assessment is carried out. This consists of clinical examination, imaging and cytology. Used alone, all three methods have an appreciable error rate. However, when the trio of tests are used together the accuracy is very high.

Mammography delineates the extent of the tumour and is useful in pre-operative assessment. It also enables screening of the contra-lateral breast. Ultrasound is useful in young patients and distinguishes well between a cyst and a solid lump.

Up to 15% of tumours are not visualised by mammography or ultrasound. A clinically suspicious lump must be biopsied in spite of a normal mammogram.

Fine needle aspiration (FNA) cytology is quick and painless and can be performed in the clinic.

When a diagnostic FNA sample of malignant cells is obtained it may be possible to proceed directly to definitive surgery without a preliminary biopsy. This allows detailed discussion with the woman about surgical management and may permit a single stage surgical procedure. It is prudent to confirm a cytological diagnosis of malignancy with frozen section before performing a mastectomy, or axillary node dissection, particularly so in a relatively young woman. Even in the best of hands, FNA cytology has a false positive rate of about 2 per 1000.

If the triple assessment is not conclusive a biopsy can be performed, either using a Trucut needle or as a lumpectomy.

A baseline blood film and serum biochemistry should be carried out, but chest X-Ray, isotope bone scan and liver ultrasound have a low diagnostic yield. They should only be used when there are symptoms or signs, e.g., respiratory symptoms, a palpable liver or abnormal liver function tests, and bone pain or tenderness.

It is now recognised that only very small breast cancers, i.e., smaller than 1cm in diameter, can be cured by local surgery alone. Breast cancer is often a systemic disease which is controlled by systemic treatment and not major destructive surgery like the Halsted radical mastectomy. Spread to the axilla is an important prognostic factor reflecting systemic spread and usually indicating the need for chemotherapy.

Concepts of surgical management of breast cancer

A Specialist Breast Unit should have a defined protocol for the treatment of primary breast cancer. Surgical protocols help in the standardisation of treatment and the assessment of results. The following is our current suggested protocol:-

A. DCIS: <4cm : wide local excision
: re-excise if margins are histologically involved.
: consider postoperative radiotherapy if high grade.
: consider Tamoxifen

extensive : simple mastectomy

B. Primary Invasive Cancer

<3cm : breast conservative surgery

>3cm : mastectomy advisable
: axillary node sampling in all cases

C. Recurrent Breast Cancer

local : mastectomy

regional : axillary dissection

distant : excision when possible

Breast imaging

Most breast cancers are detected by the patients themselves when their average size is 2.5cm diameter and about half of them have already metastasized to lymph nodes. Mammography, however, can detect smaller breast tumours. Results of breast screening in Sweden show that the 10 year cure rate for invasive breast carcinomas of any grade, but no larger than 1cm, is close to 100%. More recent results of surgery in Britain show that 15% of invasive carcinomas of 0.5cm to 1.0cm diameter are associated with axillary nodal spread, whilst no axillary metastasis was detectable with invasive tumours of up to 0.5cm diameter.

Mammography therefore appears to have the potential of picking up invasive breast carcinomas before they acquire metastasizing potential, and also picking up neoplastic lesions in a premalignant preinvasive stage. Although breast self-examination should not be discouraged, there is no evidence that self or clinical examination can detect the smaller than 1cm diameter lesions that mammography can identify.

Ultrasonography is a useful adjunct to mammography.

There are lingering controversies about mammographic screening in young women, probably because the results of more recent studies using more modern equipment have not been fully appreciated. However, globally, a majority are of the opinion that mammographic screening on a large scale reduces mortality from breast cancer.

Over 70% of the target population must accept the invitation to participate if a screening programme is to significantly reduce mortality. If fewer participate, the costs per life year saved rises and, although some will clearly benefit, the cost effectiveness of the programme comes into question.

The best frequency for screening is probable between one and two years. Patients judged to have an important abnormality require further assessment to determine whether cancer or an unimportant abnormality is present. Assessment requires further imaging and sometimes also clinical examination and cytology. Assessments are best performed by a dedicated assessment team of experienced radiologist, surgeon, pathologist and breast care nurse.

About two thirds of abnormalities detected in screening are shown to be unimportant on further mammographic or ultrasound scanning. In patients with important lesions the aim is to achieve a specific diagnosis by FNA cytology or core needle biopsy. An open biopsy should be performed if there is a suspicion of malignancy on either radiological or clinical grounds even when the results of cytology or core biopsy are benign.

The risks of mammographic radiation exposure are considered to be negligible. MRI breast scanning is under evalutation in several countries.

Adjuvant therapy of breast cancer

Conservative surgery has at times led to inadequate staging of breast cancer cases, and one is then left in doubt as to which is the best adjuvant therapy for the particular patient. It is therefore possible that some of our patients have had inadequately aggressive therapy, which may at least partly explain our poor breast cancer mortality figures. Hence the need for more accurate grading of primary tumour, hormone receptor status assessment and determination of axillary nodal status.

Although radiation is now commonly used in the breast-preserving procedure of excision and irradiation, it is less commonly used after mastectomy. Postoperative radiation of regional lymph node areas and chest wall after mastectomy is not recommended as a routine measure, but is considered for patients who have extensive lymph node involvement (more than 4-7 positive nodes), tumours larger than 5cm, or extension of the primary tumour to the chest wall, nipple, or breast skin. In such cases the radiation is delivered to the chest wall, internal mammary and supraclavicular nodes because these patients are at high risk for relapse in these sites.

When the primary tumour is very large or fixed to the chest wall or when there is extensive lymphatic or skin involvement (e.g., "inflammatory" breast cancer), there is a high risk of uncontrolled local-regional disease, besides distant spread. In such cases, combined radiation and surgery are indicated, and some centres use neoadjuvant chemotherapy, i.e., a number of cycles of intensive combination chemotherapy before local therapy is initiated to enhance the technical feasibility of local-regional radiation or mastectomy.

There should not be a long delay between the completion of local-regional treatment and the initiation of adjuvant therapy. Ideally it should start within 14 days, but patients can benefit from it even if the delay is a matter of months. Once adjuvant treatment is started, it should be given for multiple cycles.

Adjuvant chemotherapy is indicated for premenopausal women with positive axillary nodes.

Adjuvant Tamoxifen alone, or chemotherapy plus Tamoxifen, is indicated for postmenopausal patients with positive axillary nodes and ER+ (estrogen receptor positive) cancers.

Adjuvant chemotherapy is indicated for postmenopausal patients with positive axillary nodes and ER- cancers. Chemotherapy plus Tamoxifen or Tamoxifen alone may produce comparable or greater benefit in this group. At this time, the best treatment for postmenopausal women who are node positive and ER- is not established.

Adjuvant chemotherapy is indicated for premenopausal and postmenopausal patients with negative nodes and ER- tumours greater than 1cm, but it is not clear what impact such therapy will have on mortality.

Adjuvant Tamoxifen in node negative premenopausal and postmenopausal patients, especially those with ER+ tumours, produces both an increase in relapse-free survival and a reduction in mortality.

The trend today in the adjuvant treatment of women with involved nodes is to increase dose intensity (amount of drug given per unit of time). Controlled trials at this time do not provide good evidence, except that in patients with c-erbB-2 positive tumours, standard to high doses produce differences in disease-free survival rates. Trials testing this hypothesis are under way using new agents such as paclitaxel in combination with cyclophosphamide and doxorubicin.

Some centres are using high-dose chemotherapy and peripheral blood stem cell infusion in patients with 10 or more involved axillary nodes. Peripheral blood stem cell infusions have completely replaced autologous bone marrow transplantation. Several cycles of standard-dose chemotherapy are given over 3 to 4 months, followed by a single or several large doses of chemotherapy, resulting in bone marrow aplasia. Stem cells harvested from the peripheral blood of the patient are then infused. We await results of controlled trials to show whether high-dose chemotherapy with stem cell rescue produces outcomes superior to conventional chemotherapy.

Breast reconstructive surgery

The female breast is a social and psychological symbol of femininity. Loss or absence of a breast is a potent precursor of psychiatric morbidity in women. A breast reconstruction can help in restoring some of this loss. Most patients are suitable for reconstruction but sensitive counseling and a detailed discussion about the type of procedure best suited to the patient's needs are essential pre-operatively.

Reconstruction commonly takes the form of a staged procedure starting first with reconstruction of the breast mound or volume. This is followed, possibly by a second

procedure on the breast mound or the opposite normal breast to obtain the right shape and symmetry. Finally reconstruction of the nipple-areolar complex completes the whole process of breast reconstruction.

There are many surgical options for breast reconstruction, ranging from the simple to the technically more complex procedures. Each case needs to be approached individually to tailor the procedure to the patient's desires and expectations, because the various procedure have different advantages, limitations and contra-indications.

The breast care support group

The group has a statute and a committee and its current aims are:

1. Support to women with breast disease
2. Education for lay people and for specialist nurses and
3. Promoting the role of the Breast Care Clinical Nurse Specialist.

The group wishes to be considered as a reliable source of help to the medical profession with regard to the further development of services for women with breast disease.

How can we reduce mortality, & possibly incidence, of breast cancer? -- Concluding remarks

1. It is now well established that no significant impact on breast cancer mortality can be made by variations in surgical techniques. What determines whether a breast cancer will kill or not is whether it has "killer" biological properties that will enable it to metastasize by the blood stream. The same can be said for radiotherapy. The "killer" biological properties of some breast cancers are probably not acquired "ab initio", but at a later stage in the evolution of the cancer. Invasive breast cancers probably have not acquired metastasizing potential until they are at least 0.5cm in diameter. Mammographic screening therefore offers the possibility of detecting and excising invasive cancers in this "window of opportunity" (invasive cancer diameter less than 1cm and preferably not larger than 0.5cm), when surgery alone could be genuinely curative.

2. Have we been, and are we still, underusing chemotherapy? Do a significant number of Maltese women suffer from an exaggerated fear of temporary hair loss resulting in many refusals of indicated chemotherapy? Have patients got enough family, nursing and medical support to appreciate that chemotherapy may improve their chances of long term survival? Do our oncologists have access to the latest, and possibly more expensive, chemotherapeutic agents? What are the chances that we might be using high dose chemotherapy and peripheral blood stem cell infusion in Malta in the foreseeable future? Is the importance of the Oncology and Haematology units sufficiently recognised by doctors in general and the Health Department in particular?

3. In our present state of knowledge, pathology cannot precisely identify all the operable breast cancer patients who will be alive, and all those who will be dead, 15 to 20 years after initial treatment. Between half and two - thirds of these patients have clinically occult blood-borne spread at presentation, but not all of them are offered chemotherapy because pathology is unable to precisely identify them. Research continues to try and find molecular characteristics that would reveal, under the microscope, precisely which tumours have metastasizing potential and which have not. The best marker of blood-borne spread has been axillary node metastasis, but up to 25% of node negative cases have blood-borne spread. Attempts at improving the precision of axillary nodal staging by sophisticated "sentinel" node identification imaging techniques are now the "rage" in many breast units overseas. Theoretically this would improve the accuracy of adjuvant radiotherapy and chemotherapy decision making.

4. The big difference in incidence and mortality from breast cancer between Japan and Western industrialised countries appears to be related to diet and not genetics. The Japanese eat mainly vegetables, rice and fish; many vegetables, and particularly soya beans, contain phytoestrogens which are thought to compete with endogenous oestrogens for oestrogen receptors on cell membranes, thus dampening the proliferative effect of endogenous oestrogens on breast epithelium and therefore diminishing the risk of development of breast cancer. It is claimed that Japanese and some other Asian women have much less of ovarian cycles in their fertile years than Western women, and that this is due to the high levels of phytoestrogens in the Asian diets. It is epidemiologically well established that breast cancer risk is directly related to the number of years between menarche and menopause, i.e., the number of ovarian cycles. Retinoids (vitamin A analogues) and some anti-oxidant minerals such as selenium, may also lessen risk of neoplasia. The future is likely to see many foods fortified by various plant derived substances, besides vitamins and minerals. Diet is potentially one of the most potent elements in causation of a number of important chronic diseases. Evidence is emerging that antioxidants and hormone-like substances in vegetables and fruit, essential fatty acids in marine and plant oils, and other minerals, may be related to disease prevention and longevity, and that a diet containing too much animal fats and proteins appears to have a detrimental effect.

5. There is much to recommend the setting up of a multidisciplinary breast cancer management team lead by a surgeon, radiologist, oncologist and pathologist, and also a specialist breast care nurse, on the lines developed overseas. Whether this is achievable within the Maltese medical scene, is another matter.