INDIAN ASSOCIATION OF SURGICAL ONCOLOGY
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ASSOCIATION OF SURGEONS OF INDIA

IASO NEWSLETTER

SEPTEMBER 2005, Vol. 19, No. 1

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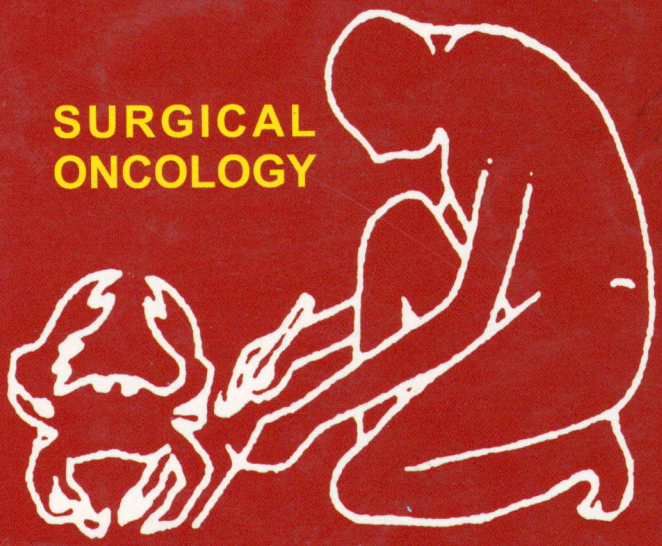
SURGICAL ONCOLOGY



Indian Association of Surgical Oncology

(A Section of The Association of Surgeons of India)

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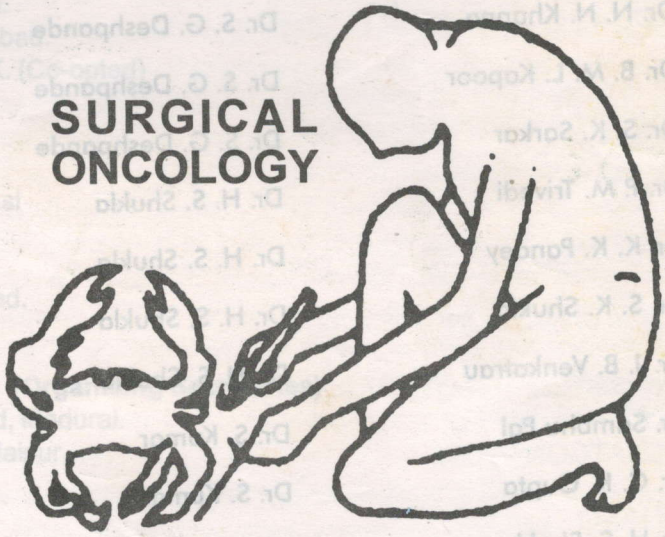

Indian Association of Surgical Oncology

(A Section of The Association of Surgeons of India)

INDIAN ASSOCIATION OF SURGICAL ONCOLOGY

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Dr. P. Subhas	Dr. K. Kothari	1999
Dr. K. K. Maudar	Dr. K. Kothari	2000
Dr. K. Panda	Dr. Ravi Kant	2001
Dr. R. I. Dave	Dr. Ravi Kant	2002
Dr. K. S. Gopinath	Dr. L. Sarangi	2003
Dr. K. Kothari	Dr. L. Sarangi	2004

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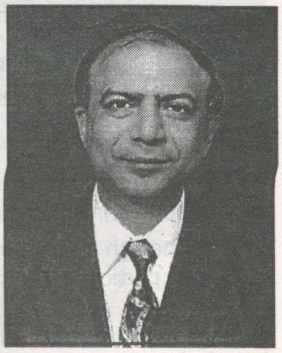
Message from the President



It is close to three decades now that Surgical Oncology emerged as an important specialty of surgical practice in India. It gained an identity of its own to build on – the Indian Association of Surgical Oncology. I have been keenly watching its progress and vigor for about two decades. It all started with creating a significantly more focused service to cancer patients and it developed into pleas for a multi-disciplinary, multi-modality approach. But, the more recent tendency to view Oncology as something altogether separate, is to my mind, a little misconceived. Such a concept could be justified in a single organ or a single region surgical specialty, like cardiac surgery or ophthalmology (no longer a subject in MBBS in some UK medical curricula). The argument that Surgical Oncology is an independent predictor of the outcome also seems to me biased. For, even within the realm of surgical oncology - breast and oesophagus, base of skull and melanoma, sarcoma and uterine cervix carcinoma, – continue to require entirely different surgical skills.

Furthermore, stress and burn out in pure oncological practice, deprives it of good humored health care delivery. It is not foreseeable that gastrointestinal surgeons will easily forego trans-hiatal oesophagectomy and thoracic surgeons will disown the lung lobectomies. The brand Surgical Oncology has not yet dared to cross paths with neurosurgeons. Incidental encounters with cancers by general surgeons during laparotomies will continue. How can then one afford not to capacity build the general surgeons in cancer resections, biopsies and palliative surgical procedures? How lame and innocuous would it be to think that a good radical colectomy is the monopoly of the brand surgical oncologist and gastrointestinal surgeons are unworthy of it? I am not pleading that surgical oncology as a specialty should wane and merge. Nor do I infer that surgical oncology hospitals and service units should just fade away. What I am suggesting is that general surgeons should indeed continue to be equipped with teaching and training of surgical oncology. The general surgeons with oncological bias will thus remain in the frontline of patient management. The Indian Association of Surgical Oncology (IASO) will provide a unique, but much-needed, forum and opportunity for these two parallel forward marches to the frontiers of surgical oncology.

I have been toying with fond visions of surgical oncology providing more masterly surgery, fewer surgical morbidity, more organ conservation, oncoplastic procedures, adoption of targeted therapies and radio and nuclear guided diagnostic and therapeutic adjuncts to surgery. The Association is an important instrument to forge these objectives.

While haloing the work and memories of our seniors, I look forward to our young, to carry on the cause of surgical oncology teaching and skill transfers. I thank the executives of the IASO who laid down a rich program during my tenure. My special thanks to Drs Rajendra Karwasra, Manmoy and Mohan Kumar.

SANDEEP KUMAR
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King George's Medical University,
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EDITORIAL

Dear Colleagues,

When I took over the mantle of responsibility for publishing this newsletter, from my illustrious predecessors, it was a time of introspection on many fronts and I would like to share these home truths with you.

The first newsletter of the IASO which started as a four page publication in 1979, has come a long way and presently is in the form of a newsletter cum journal (though not formally labeled as such yet). However the difficulties faced by my predecessors still exist and I hope they can be sorted out during my tenure as Editor.

Though our members are always eager to present papers and convene/ participate in symposiae at our IASO meets, there is a reluctance to convert their slides into papers which can be published in this newsletter cum journal. Hence the members who could not attend these meets, fail to benefit from the wealth of knowledge dissipated there (the primary purpose of these IASO confere It is my earnest request to all invited speakers, orators, conveners and symposium speakers, to send in/ hand over the salient features of their talks (in 1-2 pages, if not a full article), before or conference (since they forget later, inspite of reminders) to the Editor.

After these floodgates of information open, as hoped, the second deficit i.e the fisca needs to be addressed. Presently publishing and posting the journal (a considerable sum in mo terms, apart from time and energy spent) is the sole responsibility of the Editor. Being the mout of the IASO (and the articles contained within the unofficial voice, till the official guidelines for trea are finalised), it is felt that this endeavor should be funded by the association, perhaps out profits earned by the organisers of NATCONS, and other regional CME's held using the IASO b This will enable us to increase the quality and quantity of articles, as well as the number of issu fact my idea is to devote each issue to cancers affecting one particular part of the body or syste that it can be used as a ready reference, especially by our younger colleagues. This can o achieved with the cooperation of all members.

Today cancer cannot be treated by resection of the tumour alone. Hence there is a pr need for the general surgeon dabbling in oncology, or surgeons from other subspecialities res tumours, to not only understand the importance of nodal dissections and composite resection also the potential of various neoadjuvant and adjuvant therapies and the importance of multim treatment in the treatment of cancer. Only then can we achieve better survival figures, while ca out organ conservation, without compromising radical treatment of the tumour and its metas Therein lies the importance of the trained surgical oncologist and the IASO in propagating concepts.

Keeping the above in mind, it is my present endeavour to publish some articles by onco of other disciplines, as well as those on the cutting edge of research in oncology, on unusual tum apart from review articles by leading members of our association. Hence this issue carries a cou articles from ICON (our medical oncology colleagues have stolen a march over us by their collabo group), on GIST, IHC and the status of HRT in increasing breast cancer. Since I have not yet re the final program of NATCON it carries the tentative one (subject to changes) and the list o members.

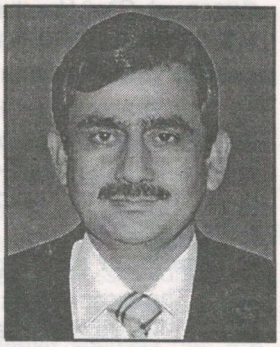
I request you all once again to send in your articles for our newsletter (you may follo standard instructions for authors, from the website www.icmje.org), current mail and e-mail add with telephone numbers, on the tearaway forms, for updating our directory and reply to Sax the enclosed prepaid inland letters. I also invite you to share your recent oncology related ac and achievements, as well as send in your comments and suggestions for further improvemer then I wish you useful reading, a Happy Dusshera and Diwali, Id mubarak and a merry Christmas f and your families, till the next newsletter, or our next meeting after NATCON, at ASICON.

MANOMOY GAN

Secretary's Report

Dear Colleagues,

Greetings.



Surgery is the principle mode of the therapy for most of the solid tumors which constitutes more than 95 % of the cancers but speciality of surgical oncology is yet to be established in this country and cancer management is still synonymous with the radiotherapy particularly in the Govt. Institutes. Surgeon not only provide surgical treatment of cancer but also plays crucial role in establishing the diagnosis, treatment planning and early detection of cancer and therefore leadership of surgical oncologist rather than radiotherapist is desirable for proper management of cancer. Though Indian Association of Surgical Oncology was started more than 25 years ago but majority of the medical colleges are still not having this department, which may be a reason for poor outcome of cancer patients in the country.

During **NATCON-2004** at Jaipur also it was clearly highlighted by various eminent speakers even from abroad, that surgeon plays key role in the management of cancer. This was obviously reflection of the global scenario, and therefore, it is high time for our association to take initiative to establish the speciality of surgical oncology and improve the situation of cancer management in India. Preparing the book of guidelines for appropriate surgical management of various cancers is already in progress. The association is also planning to start some form of **accreditation program** for surgeons, based on their qualifications, training and experience in surgical oncology, either independently or jointly, with organizations like MCI and Diplomat of National Board etc. because surgeon himself is now considered as prognostic factor in cancer management.

A very important symposium on **'surgical oncology in rural setting'** was held in association with the rural surgery section of ASI during **ASICON 2004** at Hyderabad to improve management of cancer patient at countryside. During **E.C meeting**, it was decided that treatment guidelines to be given at the end of the symposium, which will be helpful in preparing the book of guidelines and even consensus meetings may be held during conferences for this purpose.

Journal of Surgical oncology

The association was planning for subscribing some international journal for the members but cost is still an important factor coming in our way. Nonetheless quality of our own IASO newsletter is improving & we should concentrate on converting it into a journal in due course of time by findings the means of raising funds such as advertisements and contributions from annual conferences etc. for these journals during NATCON-IASO.

Membership and Directory of IASO

It was approved during E.C meeting that membership fees must be raised to Rs. 2000/- and new member should have at least two publications in indexed journal. I think simultaneously we should also revise the categorization of membership, depending upon qualification / experience & fixed the fees and voting rights accordingly. However final decision about these will be taken in the annual general body meeting, till then opportunity at low fees is available and I request all the members to encourage new membership.

We have planned to bring out **directory of IASO** with full details of the surgeon along with photo and I sent request to all the members to update their address, however the response is poor. I again request you all to kindly send me your updated details along with a coloured photograph & e-mail addresses.

Fellowships / Scholarships

The association awards two fellowships every year to young surgeons. Detroit visiting fellowship is to visit Detroit Cancer Center in USA while Baroda traveling fellowship is to visit any cancer center in India to enhance their skills. Another fellowship for UK now also available from this year and Dr. Sailesh

Chaturvedi from U.K is coordinating this. It will be an international technology transfer fell visit Aberdeen University, U.K.

Apart from this, one more fellowship will also be available from this year for minima surgery at Gem Hospital, Coimbatore, funds for which will be provided by Dr. R.I.Dave & Kothari out of the savings of their conference.

Awards and Orations

The association has three orations during NATCON and one during ASICON every y from this, the association recently started best presentation awards out of financial suppor by Dr. Gopinath and others to encourage the young surgeons. I request you all to kindly pr work and win the awards. Another important event during Natcon is the Oncoquiz which a position awards.

International Meetings

The association is represented every year in two International conferences abroad. Pas attends the **WFSOS** meeting while President & Secretary attends the **BASO** meeting by the expenditure at their own level.

CME programs

For the first time in the country our members held a video conferencing. On 16th Apri P. Jagnanath at Mumbai telecast a video on LAR and surgeons at 42 cities participated Rohtak I joined on behalf of IASO office.

Apart from this Dr Ajay Vidyarthi organized oncology update on 3rd April 2005 at Ran Sanjay Kapoor organized National Oncology update from 15th-17th April 2005 at R & R ho Delhi.

Social activities

On 31st May, World Anti Tobacco Day was celebrated and an 'Anti Tobacco Week' wa by IASO in association with medical students at PGIMS, Rohtak. The association should pa more and more social activities so that surgical oncology is highlighted as a leading speci management of cancer. I believe many of our members are also participating in various soci and I request them to kindly convey these to the IASO office.

The forthcoming **NATCON is at Kodaikanal from 23rd to 25th September** organizing committee has negotiated very good rates for boarding and lodging. A large international speakers will deliberate through orations and guest lectures apart from emine faculty. While your family will enjoy the natural beauty of this hill station, you will get a scientific feast and therefore, I request you all to avail a scientific holiday and plan to stay th all the three days at Kodaikanal.

Though in the GBM at Jaipur, it was decided to hold the **NATCON-IASO-2006** at V some members have requested to shift the venue for the 2006 annual conference becaus will also be venue for the **ASICON-2006** and as per our earlier decisions both IASO & AS not be held at the same place. In view of this, the matter will be taken up in the GBM at for final decision.

Looking forward to see you at Kodaikanal.

R.K. KA

HORMONE REPLACEMENT THERAPY & BREAST CANCER

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Classified Specialist (Surgery & Oncosurgery)
Command Hospital (Western Command),
Chandimandir

Introduction

The life expectancy of women in Western countries is rapidly approaching 90 years. Menopause, the cessation of ovarian follicular function, occurs at the age of 51 (average). This means that women are expected to spend nearly half their lifetime in the postmenopausal state. Menopause is a period in women's lives lasting for many years and characterized by profound positive and negative changes in many, if not all, areas of their lives: ageing with physical changes or even alterations, possibly diseases; psychological changes related to loss of fertility (maybe positive or negative), loss of appeal. possible decrease in sexual interest and ignorance of what the future holds in store; family changes with the loss of parents or other relatives, and departure of children from home; changes in the workplace; and many more possible changes at the individual level.

Menopausal transition is characterized by ovarian failure, during which a variety of symptoms may arise which can last tor several years. Among the most common are hot flushes, which affect about two-thirds of menopausal women (most of them have symptoms lasting for 1 year. but about 20% of women may suffer hot flushes for > 10 years) [1], possible changes in body composition and muscular performance [2, 3], decrease in bone density with an average annual bone density loss of 1-2% [4], changes in the skin [5], changes in all mucosae, particularly the vaginal mucosa [6, 7] with urinary incontinence [8,9], heart disease [10, II], Alzheimer's disease [12], possible metabolic changes [13], possible changes in sexuality [14, 15] and many more. Menopausal symptoms vary according to ethnic groups (apparently Asian women suffer fewer menopausal symptoms than their counterparts in the West) [16]. and hot flushes generally decrease spontaneously over time.

Different modalities and types of hormone replacement therapy

For many years hormone replacement therapy (HRT) with oestrogens, progestins or a combination of both (concomitant, sequential, alternating etc.) has been administered orally, intravaginally, intranasally, percutaneously, subcutaneously etc. to women in the perimenopausal period of their life mainly to treat the symptoms of menopause, to help prevent ageing, osteoporosis and coronary heart disease [17], and for possible additional beneficial effects. Oestrogens lower cholesterol levels, but recent studies do not show a reduction of cardiovascular events with HRT in women at increased risk [18-20]. Oestrogen alone and in combination with progestins has been shown in a meta-analysis to decrease the risk of Alzheimer's disease by 34% but a number of psychocognitive functions were not improved by the use of HRT [21] and the relationship with Alzheimer's disease or other forms of dementia is not yet conclusive.

HRT and risk of developing breast cancer

The effect of HRT on breast cancer risk has been a controversy for several years. Laboratory findings have clearly shown the role of oestrogen (and progesterone) in mammary tumour cell growth, but the translation of these findings in epidemiological observation was only possible with a metaanalysis [22]. Data from 51 epidemiological studies including more than 52,000 women with breast cancer and more than 1,08,000 women without the disease, show that the relative risk of breast cancer is significantly increased (relative risk, 1.35) for current users of HRT or women who ceased HRT in the past 1-4 years and that the risk increases with longer duration of HRT. Five years or more after cessation of HRT an excess of breast cancer can no longer be observed.

The data from the Women.s Health Initiative (WHI) which compared the combination and progestin with placebo, and which was stopped prematurely, showed a 24% increase cancer incidence, coronary heart disease, stroke and pulmonary emboli [23]. In addition, the of breast cancer by mammography was more difficult and cancers were at a more advanced HRT users [24]. The WHI also conducted a study in hysterectomized women compared consisting of oestrogen alone with placebo [25]. More than 10,000 women between 50 and of age were included in the trial, but the interventional phase was stopped because of safety The data showed an absolute excess risk of 12 additional strokes per 10,000 person-years absolute risk reduction of six fewer hip fractures per 10,000 person-years. Coronary heart which was the main endpoint of the study, was not influenced by the use of equine oestrogens

The Million Women Study [26] also showed an increase in breast cancer risk for (relative risk, 1.66); however no increased risk for past users was observed in this study. The increased with all types of HRT (including tibolone), but the magnitude of risk was greater oestrogen-progestin combinations than for other types of treatment.

The Danish Nurse Cohort Study also showed that the risk of developing breast cancer for patients treated with continuous combined oestrogen and progestin,

In addition to oestrogens and progestins, tibolone, a synthetic steroid with androgenic and progestogenic properties. has been widely used for the treatment of menopausal symptoms. The safety of the compound has been described as excellent (no increase of endometrial cancer), but recently new data seem to challenge this claim [27].

Ursin etal [28] showed that the use of HRT is increasing breast cancer risk, and that not limited to subgroups of women with specific cofactors.

HRT in a special population (BRCA mutation carriers)

Available data suggest that oestrogen exposure in BRCA mutation carriers influences cancer incidence in a similar way to that in the general population without mutation [29].

Patients with mutations of BRCA 1 and 2 are at elevated risk (about 70% at the years) of developing breast and ovarian cancer compared with the general population. Recommendations have been issued for these women, including bilateral mastectomy [30, 31] and oophorectomy which substantially reduce the risk of developing breast and ovarian cancer. The question of HRT replacement is paiticularly relevant for this subpopulation, as generally oophorectomy will be performed at a relatively young age and will lead to the serious problem of early menopause. HRT may be warranted but is very controversial. Careful decision analysis will be required in cases. The short-term use of HRT after prophylactic oophorectomy in this population does not to be related to a significant decrease of life expectancy. However, the use of HRT until an age of 50 years (assumed age of natural menopause) seems to be related to a substantial decrease expectancy and therefore should probably be discouraged [33].

HRT and risk of recurrence in patients previously or currently treated for breast

Again, the information available today on the use of HRT in patients who have been diagnosed and treated for breast cancer is controversial. In some of the reports recurrence mortality due to breast cancer were similar or even lower in patients treated with HRT than controls who did not receive HRT [34, 35].

Recently the HABITS study (Hormone Replacement Therapy after Breast Cancer-Is which included 434 women who were relapse free after breast cancer and who had menopausal symptoms, was prematurely closed because of an elevated risk of breast cancer relapses [36] and of serious adverse events (8 versus 4) for patients treated with HRT compared with

receiving non-hormonal therapy for menopausal symptoms [36]. A similar study from Stockholm yielded different results, but the pooled analysis of the two trials showed significant differences. As a consequence of these findings, both studies were closed to further accrual.

Outlook

HRT has been a subject of discussion during recent decades and continues to remain an extremely important topic in our society where, in general, a 'natural' menopause will need to be rediscovered by women, patients, partners and physicians. HRT obviously remains the best short-term therapeutic option for women who suffer severe menopausal symptoms, but its use for severe menopausal discomfort in patients who have had breast cancer needs to be carefully weighted with the patient against possible harm in terms of recurrence.

Based upon currently available data, HRT as practised in the cited studies cannot be recommended for the prevention of chronic conditions such as coronary heart disease or Alzheimer's disease. Further studies are needed for the assessment of the risks and benefits of different types of HRT, including lower doses of oestrogen-only HRT (as released by some transdermal patches).

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IMMUNOHISTOCHEMICAL APPLICATIONS IN DIAGNOSIS OF TUMORS

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Over the turn of the century, the technique of immunohistochemistry (IHC) came of age. For the uninitiated, it is simply the marriage of the twin disciplines of immunology and histopathology. In more scientifically lucid terms, it implies that the presence or absence of an antigen can be directly visualized under the microscope at its recognizable cellular location by applying appropriate antibodies to the tissue and recognizing the union of antigen-antibody as a coloured product.

The discourse that follows is designed to demystify the subject in simple terms for clinicians engaged in treating malignancies who read histopathology reports incorporating immunohistochemical results; and fellow pathologists not routinely engaged in tumor diagnosis who can use it as a ready reckoner to know where this technique will come in handy in the occasional diagnostic dilemma they encounter. It will also provide a guideline on how to consolidate a differential diagnosis before sending on the material to a reference centre for this investigative tool.

(As a corollary, it is not meant for my subspeciality colleagues who may find it an oversimplification of ground realities in immunophenotyping).

What is the aim of the technique in tumor pathology?

It serves to identify structural, functional or growth related proteins within cells which are antigenically distinct and hence will selectively be demonstrated by an antibody applied to them. In the case of **structural antigens** most of these are present in the normal cells: when a tumor cell displays them it can be deduced that the histogenetic origin of the tumor is from a particular type of tissue eg actin present in tumors of smooth muscle lineage or the tumor at that point of time is exhibiting that particular lineage. By identifying **functional proteins/secretions** the functional status and in some cases 'true to tissue type' secretion can be recognized (examples are hormones like calcitonin and enzymes like prostate specific antigen). **Growth-related proteins** may be receptors receiving growth signals (eg. Estrogen receptor present even in normal tissues) or altered or enhanced growth promoting/suppressing protein products of growth controlling genes (eg. Her2neu or p53). The ultimate objective is providing greater accuracy in diagnosis when morphology alone reaches its limits of resolution. This ultimately translates in deciding the appropriate therapy.

How is it performed?

Tumor markers have been detected in serum long before IHC came about. But these were restricted to selected tumors which do have a dedicated product which spills into the blood eg. βHCG, AFP, PSA etc. IHC, however, not only identifies the antigen under the microscopic eye in its parent localization within the tumor but also has a wide range of antigens to choose from. The majority of antigens can be detected in paraffin sections (routinely processed tissues). Some need to be performed on frozen sections (eg CD1a, kappa or lambda) or cytologic preparations (especially fluorescent tagged anti-CD antibodies in leukemias). The basic procedure is sequential application to the tissue section of a chosen antibody (against the antigen desired to be demonstrated) followed by a link antibody, and then a sensitive detection system (like avidin-biotin complex) with an attached coloured product, that will be appreciated by the eye, at its localization site, on the tissue under the microscope.

What antibodies are used?

While hundreds of antibodies are available in catalogues of numerous manufacturers, t is a representative selection of some that would form a reasonable list to maintain on the a laboratory actively engaged in oncologic diagnosis:

1. Epithelial markers:

a. Broad spectrum (mark most epithelial cells):

   i. Cytokeratin (cocktail of various weights) broad spectrum marker.

   ii. Epithelial membrane antigen

b. Subsets: 34ße12 for basal cells of prostate, CK 7&20 TCC. CK20 Colon, CK 7 Lung etc

2. Mesenchymal markers: Vimentin (broad spectrum), actin (smooth muscle), desm myogenin (skeletal muscle), CD 31, 34 (endothelial), CD 68, CD XIIIa (fibro-histio (GIST).

3. Neural/neuroendocrine markers: Vimentin, S-100, neuron-specific enolase (NSE), G acidic protein (GFAP), synaptophysin, neurofilament, MIC-2 (CD 99), chromogra hormones (pituitary-GH, PRL etc, pancreas-Insulin, glucagons etc.)

4. Haematolymphoid markers: CD markers eg Leucocyte common antigen (LCA-CD spectrum for most lymphoid cells) CD 3, 5, 7, 43, 45RO (T cells), CD 19, 20, 79a, ka (B cells), CD 15, 30 (Hodgkins), CD 57 (Monocytes), CD 1a (Langerhans cell Histio (Anaplastic large cell lymphoma), bcl-2 (follicular lymphoma), CD11c (Hairy cells).

5. Specific organ markers: PSA (prostate), calcitonin (medullary ca thyroid), thyroglobu carcinoma thyroid), calretinin (mesothelioma), melan-A (melanoma), GCDFP-15 (bre (ovary).

6. Receptors: Estrogen and progesterone receptor, Her2-neu (breast).

7. Miscellaneous: p53 (Mutated tumor suppressor gene), MIB-1 (proliferation astrocytomas) if affordable

When is this technique needed ?

The broad categories of tumors where morphologic diagnosis can be improved resolved are as follows:

1. Poorly differentiated tumors

In these tumors the appearance cannot be traced to their histogenetic origin on alone. Examples include tumors of epithelial origin that look sarcomatoid viz. spindle cell ca oesophagus, urinary bladder – by demonstrating cytokeratin or EMA (with coexpression of mesenchymal marker) the problem can be solved. Similarly gliosarcomas in the CNS can from other soft tissue sarcomas by coexpressing Vimentin with GFAP.

It must be remembered that lymphomas and melanomas can appear at odd site they are kept in mind in the D/D of a poorly differentiated tumor the appropriate antibod included in the panel for their exclusion.

2. Metastatic tumors for primary site

The correct identification is significant, in the context of diagnosis of primary on where specific diagnosis not only directs limited, money and time-saving search for the

the nature of the disease may be biologically indolent despite presentation with metastases. For example specific recognition of PSA staining in metastatic prostatic adenocarcinoma that does not necessarily mean a short survival unlike any other Stage IV malignancy. Identification of medullary carcinoma metastases (by calcitonin) helps plan radical surgery of the neck which is the only chance the patient has for disease extirpation. Other tumors that may typically remain occult with extensive metastases are melanoma (melan A, HMB-45 and S-100 are useful), follicular carcinoma thyroid presenting as bone metastasis (thyroglobulin is diagnostic), choriocarcinoma (âHCG), small cell carcinoma lung (NSE, chromogranin, synaptophysin) or even breast (GCDFP).

3. Soft tissue tumors for histogenetic subtyping or a non soft tissue tumor appearing at a soft tissue location.

Soft tissue tumors have always posed the toughest challenge to a diagnostician. The surgeon's concerns are largely of size and grade of the tumor to plan the extent of excision. This is now modified with availability of chemo-radiotherapy protocols that 'shrink' the tumor prior to surgery changing an amputation into a compartmental excision: a good example is childhood rhabdomyosarcoma that has well-defined chemotherapeutic protocols. The histologic diagnosis also predicts expectancy of local recurrence/distant metastases. While synovial sarcomas and malignant peripheral nerve sheath tumors uniformly carry a poor prognosis with early, distant metastasis, epithelioid sarcomas are locally recurrent. This has been the area of greatest success in use of IHC. A number of specific markers are available for determining smooth and skeletal muscle origin or nerve sheath histogenesis (as detailed above). The approach to diagnosis rests on identifying the predominant pattern of cells: round, spindle, epithelioid or pleomorphic and then choosing a suitable panel of antibodies. Round blue cell tumors of childhood have thus become easy to separate out with each having a completely different treatment protocol. For example a childhood small round cell tumor could have a differential diagnosis of lymphoma, PNET, rhabdomyosarcoma and neuroblastoma. In an adult it would include lymphoma, PNET, neuroendocrine carcinoma and small cell variant of synovial sarcoma (at a bony site one would also consider small cell variant of osteosarcoma). Rarely melanoma can also have a round cell variant. Thus choice of panel of markers would be based on age, site and morphology.

4. CNS Tumors

In CNS tumors diagnostic dilemmas lie in four areas. Firstly, in poorly differentiated tumors a primary high grade CNS tumor and metastases have to be separated (and both occur in the elderly): here using a combination of neural markers like GFAP and synaptophysin with epithelial markers would resolve the issue. Secondly, common cytologic appearances as in clear cell tumors may cause confusion between different primary tumors eg.oligodendroglioma, neurocytoma and clear cell ependymoma. Thirdly, it is difficult to pick up patterns on small tissues ie stereotactic biopsies. Lastly, lymphomas do occur in the CNS and need to be identified and separated from other small round cell tumors for appropriate therapy. For all these reasons IHC plays an important role.

5. Typing of haematolymphoid malignancy

The panel of lymphoma markers has been detailed previously. Leukemia typing is not within the scope of this review. Illustrative indications of use of IHC include separating hyperplasia from follicular lymphoma (bcl2), separating the morphologic range of diffuse small cell lymphomas (follicular centre cell, mantle and marginal zone), differentiating Hodgkins lymphoma and T cell lymphomas and identification of an anaplastic lymphoma in nodes or extranodal sites (where it may be confused with an anaplastic carcinoma)

6. Benign and malignant:

IHC is never touted for this distinction but in special situations may come in h demonstration of loss of basal cells (by HMWCK) in atypical prostatic acinar proliferations whic difficult to interpret in a trucut biopsy or loss of myoepithelial cells (by smooth muscle a suspicious ductal proliferation in the breast.

7. Miscellaneous

a. Detection of receptor status for adjuvant therapy: ER/PR and Her2neu for breast c for tamoxifen therapy and prognosis.

b. Identification of organ involved: This happens when the parent organ may be ru tumor cells as in MALTomas in thyroid or salivary glands or thymoma versus lymphoma in a m mass.

c. Atypical proliferations in the vicinity of tumors eg. neuroendocrine proliferations in lung and GIT or C-cell hyperplasia in thyroid.

d. Detection of micrometastases in lymph nodes eg in breast cancer: the utility in therapy remains a debatable issue.

e. Others: Study of tumor microvasculature, demonstration of genetic aberrations e

How is it interpreted?

It is obvious that the lab performing the technique must keep a stringent chec quality of the technique with appropriate internal and external controls. However the ultimate of the technique lies in the hands of the pathologist who, in the first place, prioritises his markers as a composite panel based on a sound morphologic eye that narrows down the di relevant tumors. In the second step it is the logical correlation of the findings of this tech the entire clinicopathologic assessment that leads to refinement of the original morphologic

Key to successful use of immunohistochemistry:

1. A good morphologic diagnosis and differential diagnosis. If the primary diagnosis is wrong choice of antibodies will be ordered and create more diagnostic confusion.

2. Selection of appropriate antibodies related to the above as a panel and not a singl (except occasionally eg. Demonstration of basal cells in prostate by HMWCK or staining fo breast).

3. Quality control and standardisation of technique for optimal results.

4. Logical interpretation keeping in mind the morphologic diagnosis and the clinical pr site) as well as aberrant immunoreactivity, and known cross-reactions.

Cross reactions :

Keratins (Melanomas, PNET, leiomyosarcomas, GIST'S) EMA (plasma cells, synovial mesothelioma, meningioma) Vimentin (Renal cell ca, endometrial ca, follicular ca thyroid)

S-100 (melanocytes, adipocytes, chondrocytes, skeletal muscle, breast, apocrine gland, dendritic cells, Langerhans cells, myoepithelial cells).

When the morphologic diagnosis entertains entities with known antigenic cross additional antibodies for the same tissue types should be included to clarify the issue eg being used to separate a nerve sheath tumor from others add a second neural marker.

5. When immunoreactivity is confusing or misleading revert to morphologic diagnosis and give the nearest, best, group diagnosis like 'high grade spindle cell sarcoma: further typing not possible' for a soft tissue sarcoma or 'high grade round cell tumor NOT a lymphoma' for a paediatric tumor.

Immunohistochemical applications in the laboratory dealing with cancer diagnosis, have opened the flood gates for the beginnings of a more scientific 'Final Diagnosis'. With accumulating knowledge on the subject, discovery of more specific markers and hindsight of cross-reactions and technique related problems, we are heading towards an era of increasing refinement and accuracy. The cost more than justifies the benefits accrued. The ultimate beneficiary will be the cancer patient for whom tailor-made therapy can be devised and prognosis better understood.

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HEPATOCELLULAR CARCINOMA

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Opinion Statement

Early detection of hepatocellular carcinoma (HCC) is feasible, particularly in patients known to be at risk from chronic hepatitis and chronic liver disease. The optimal surveillance strategy is unknown. HCC usually presents as an incurable disease even when detected on surveillance. Surgical resection is the treatment of choice, but the coexistence of chronic liver disease and the insidious nature of HCC make it unresectable in most patients. Orthotopic liver transplantation for selected patients or ablative techniques may offer an opportunity to render patients disease-free even if the tumor is unresectable.

There are numerous therapies offered to patients with unresectable HCC, including chemotherapy, hormonal therapy, and regional intra-arterial treatments. While potentially palliative, none of these approaches has been demonstrated to prolong survival in these patients. If possible, the treatment of patients with HCC should be done on clinical trials.

Introduction

Hepatocellular carcinoma (HCC) is one of the most common malignancies in the world, although it has accounted for less than 20,000 cases per year in the United States during the 1990s [1]. This incidence is rising rapidly, however, with the increasing role that chronic hepatitis C viral disease is playing in the causation of chronic liver disease and cirrhosis of the liver in the western hemisphere [2].

Although this change in epidemiology of the cancer may lead to earlier recognition of HCC as patients with chronic liver disease undergo surveillance, the coexistence of chronic liver disease with the cancer makes it incurable in most patients. Even in a group of patients with chronic hepatitis B who were screened aggressively, the 10-year survival of the few patients who were initially resectable for cure was less than 15% [3]. This reflects the risks of tumor metastases prior to diagnosis but also the lifelong risk of developing another primary HCC in the diseased liver.

Improvements in surgical technique make more patients eligible for operations than in the past, and the advent of alternative ablative technology (cryosurgery or radiofrequency thermal ablation) may offer a patient a curative opportunity not previously available. Orthotopic liver transplantation is the best approach for selected patients and offers the only chance to eradicate both the cancer and the underlying liver disease [4], but the utility of this strategy is limited by organ availability and cost.

Following surgical extirpation of HCC, adjuvant treatment has historically been ineffective. Recent studies using a semisynthetic oral retinoid, polyprenoic acid [5], or internal radiation into the hepatic artery [6] in the postoperative setting have demonstrated improvements in survival. These results need to be confirmed in larger studies, and neither therapy is routinely available.

For most patients, however, HCC is unresectable, and the goal of therapy is palliation. Many disparate approaches have been tested in these patients, including hormonal treatments, systemic chemotherapies, intra-arterial chemotherapy, and tumor embolization. Although numerous treatments

can produce tumor responses in some patients with HCC, most of the data suggest that no approach offers meaningful benefit to the average patient with HCC. This reflects inher resistance to treatment as well as the inevitable progression of the underlying liver disease

Given these circumstances, patients with unresectable HCC should be considered trials testing new combinations of chemotherapy or novel agents directed at tumor biolog

Treatment

The treatment of patients with HCC is based on the extent of cancer and its rese general schematic approach to decision-making is demonstrated in Figure 1.

Surgery

Surgery is the first choice for the management of patients with early stage HCC. technically resectable, ablative techniques may be appropriate in selected patients.

Partial hepatectomy

Standard procedure - Resection of tumor and neighboring hepatic tissue to achieve a cle margin. Details of appropriate techniques for hepatic surgery are beyond the scope of thi

Contraindications - Cirrhosis of the liver, portal hypertension, comorbid illnesses.

Complications - Bleeding, infection, hepatic failure.

Special points - Numerous studies have demonstrated that the outcomes of patients u major hepatic resections for malignancy are superior when the surgery is done at centers wit experience in the field [7].

Cost effectiveness - In that this is the gold standard for curative therapy, there is no effective approach. However, the cure rate is less than 30%.

Cryoablation

Standard procedure - Laparotomy followed by insertion of nitrogen-cooled trocar into hep multiple freeze thaw cycles under ultrasound guidance [8].

Contraindications - Portal hypertension, tumors abutting major vessels or biliary tree, comorb

Complications - Bleeding, liver cracking, infection, myoglobinuria, renal failure.

Special points - Indicated particularly in patients with resectable HCC, but there is inadeq reserve to spare the extent of hepatic resection. Not less invasive than conventional resect tumors are harder to freeze.

Cost effectiveness - This procedure is more costly than hepatic resection on average b multiple freeze-thaw cycles take a long time in the operating room and the equipment n perform the cryosurgery is very expensive.

Percutaneous ethanol injection

Standard procedure - Injection of ethanol into tumor with ultrasound guidance. Repeat m for maximum effect.

Contraindications - Tumors larger than 3 to 4 cm in diameter are too large for this proce in the periphery of the liver may also be less favorable due to risk of bleeding and ru hepatic capsule.

Complications - Bleeding, pain, risk of tracking tumor cells from HCC to percutaneous tra

Special points - Although tumors can be individually treated, the size of the lesions amen

treatment and the limited number suggest that good long-term results may reflect patient selection rather than the efficacy of the modality [9]. Although not proven, there is a theoretic concern for spread of tumor cells into the needle track, making this a potential problem if done as definitive therapy.

Cost effectiveness - Because laparotomy is not required, this is far less expensive than the previous two options, but the patient selection criteria and limitations of the therapy make it of less certain benefit.

Radiofrequency ablation

Standard procedure - A probe, introduced either at laparotomy, laparoscopy, or percutaneously, is introduced into the HCC lesion, and radiofrequency waves are used to heat and destroy the tumor [10].

Contraindications - Similar to percutaneous ethanol injection, there is a limit to the size and location of lesions, although this modality may be able to handle tumors in the 5- to 6-cm range. HCC lesions located near major blood vessels or bile ducts are not favorable.

Complications - Bleeding, pain, infection, risk of tumor cell tracking (when done percutaneously or laparoscopically). Cracking of the cirrhotic liver is less of a problem because the instrument is much thinner than the cryoprobe.

Special points - Although much effort has gone into demonstrating the ability to ablate multiple lesions with this approach, it remains to be seen whether such intervention is of any benefit to a patient requiring it.

Cost effectiveness - If this technique becomes readily available for percutaneous usage, it will probably be far more cost effective than either ethanol injection or cryosurgery for patients with lesions that are within reach of the probe and can be visualized by ultrasound.

Orthotopic liver transplantation

Standard procedure - Total hepatectomy and transplant. Most centers perform chemoembolization or another procedure to control HCC while awaiting an available liver. In selected patients, the results are as good as transplantation for patients without HCC [4, 11].

Contraindications - Patients with any evidence of metastatic disease, more than three hepatic tumors, or portal vein involvement or any tumor larger than 5 cm in diameter are generally not considered for this approach. Hepatitis B viral disease is a relative contraindication.

Complications - Complications include all of the complications of organ transplant and immunosuppression as well as the risk of HCC metastasizing to other sites or back to the donor liver. Patients with chronic hepatitis B or C are also at extremely high risk for reinfecting their new liver.

Special points - The excellent results reported in transplant series reflect patient selection. The results were obtained when the median wait for a liver was a few months. The average patient now waits more than 1 year for a liver to become available, so this approach may not be as effective as it first appeared.

Cost effectiveness - This may be the preferred treatment for all resectable patients because it successfully controls both HCC and underlying liver disease. However, organ availability and cost make it impractical and extremely expensive.

Pharmacologic treatment

Chemotherapy is mostly ineffective in the management of HCC. Numerous trials have failed to

consistently demonstrate any advantage to systemic chemotherapy. Doxorubicin [illegible] chemotherapy, and newer combinations are being tested.

Specific drugs

Doxorubicin

Standard dosage - 60 mg/m² every 3 weeks.

Contraindications - Hepatic dysfunction, cardiac disease with cumulative dosing.

Main drug interactions - The principal concern remains altered drug clearance in patient[illegible] dysfunction.

Main side effects - Myelosuppression, which may be increased due to underlying liver [illegible]

Special points - Although doxorubicin is the standard therapy for HCC, data show that [illegible] active [12] compared with supportive care.

Cost effectiveness - Although doxorubicin is inexpensive, the relative lack of activity [illegible] inadequate treatment.

Cisplatin, Interferon-á, Doxorubicin, 5-fluorouracil (PIAF)

Standard dosage - Cisplatin 20 mg/m² days 1-4; doxorubicin 40 mg/m² day 1; 5-fluoro[illegible] m² days 1-4; interferon-?, 5 MU/m² days 1-4. Repeat cycle every 3 weeks.

Contraindications - Hepatic dysfunction, cardiac disease.

Main side effects - Myelosuppression, anorexia, diarrhea.

Special points - This combination of chemotherapies is the first to demonstrate a signi[illegible] rate and the ability to induce complete pathologic remissions [13] in HCC. Most patients [illegible] study tested positive for the hepatitis B virus, and these data may not apply to other [illegible] HCC.

Cost effectiveness - A comparative trial of PIAF versus other therapies or best supportive [illegible] been conducted.

Tamoxifen

Standard dosage - 10 mg twice daily.

Contraindications – None

Main drug interactions – None

Main side effects – None

Special points - Although tamoxifen is mostly without side effects, no objective responses [illegible] and data are inconsistent on any survival advantage seen with this drug [14, 15], [illegible] because of its relative cost and ease of administration.

Cost effectiveness - In that there is no evidence of efficacy; cost effectiveness has not [illegible]

Sandostatin (octreotide)

Standard dosage - 250 ?g subcutaneously twice daily.

Contraindications - None known.

Main drug interactions - None known.

Main side effects - Bloating, hypoglycemia.

Special points - Although no objective responses were observed, a randomized study [illegible]

octreotide to supportive care in patients with advanced HCC demonstrated a significant improvement in survival for the treated patients [16]. This finding may reflect a treatment effect on underlying liver disease rather than an anti-tumor effect, and it needs to be validated in a larger study.

Cost effectiveness - Until verified by further studies, the cost of octreotide argues against the standard use of this treatment in this disease.

Interferon-á

Standard dosage - Interferon-á, 5 MU/m², 3 days a week.

Contraindications - Poor performance status.

Main drug interactions - None.

Main side effects - Symptoms consistent with viral syndrome, including aches, chills, fever.

Special points - As with other systemic treatments, there have been mixed results with interferon-á in the management of HCC. For patients with advanced cancer, at least one study has demonstrated a modest survival advantage for the treated group [17]. Other studies do not show that advantage. The most promising role for interferon-á is probably its effect on chronic liver disease caused by hepatitis C and the potential role it plays in preventing new HCCs in cirrhotic patients [18].

Cost effectiveness - Given the marginal, if any, benefit to this treatment, it is not considered cost effective in patients with advanced HCC.

Radiation therapy

The role of radiation therapy in the management of primary liver tumors has always been limited by the inability of liver tissue to tolerate doses of radiation. Because HCC is often multifocal, there is inevitable damage to the surrounding liver parenchyma. Innovative methods of delivering conformal or "focal" radiation make some patients candidates for radiation treatment [19].

Radiation therapy

Standard regimen - Dose and field are modified by a special "conformal" technique that focuses the radiation to the specific tumor site and avoids harm to surrounding tissues.

Contraindications - Multifocal liver tumors compromised hepatic reserve.

Complications - Radiation hepatitis in the setting of chronic liver disease.

Main side effects - Nausea, emesis, progressive manifestations of liver disease.

Special points – Although this new technique is promising, it is one of a number of regional treatment options for patients with HCC. Very few centers around the world are equipped to deliver this kind of treatment.

Cost effectiveness - No comparative trial of this radiotherapy technique versus other treatments has been conducted.

Regional Intrahepatic treatments

Hepatic intra-arterial chemotherapy

Infusional chemotherapy

Standard procedure - Either a percutaneous catheter is inserted into the common hepatic artery or an infusion device is implanted with a catheter feeding into the hepatic artery via a branch of the hepatic artery. Chemotherapy is administered into the device on an intermittent basis. Various chemotherapy combinations have been tested. The best results may come from infusing the combination of floxuridine,

leucovorin, doxorubicin, and cisplatin [20].

Contraindications - Compromised liver function, thrombosis of the portal vein, ascites, metastatic disease.

Complications - Hepatic decompensation and its resultant effects. Patients with HCC are particularly vulnerable to toxic effects from hepatic intra-arterial chemotherapy [21]. not exclude the possibility of systemic side effects from the chemotherapy, based on the of the chemotherapies that are administered. Surgical placement of the catheter is ass the morbidities of a laparotomy but diminishes the risk of misperfusion of chemotherap bladder or other intestinal sites.

Special points - Because many patients with HCC have compromised liver function benefit from this approach may reflect patient selection as much as efficacy of the th only the healthiest patients are suitable for this treatment.

Cost effectiveness - This is a costly therapy. If done via a percutaneous route, it requires stays and repeated procedures. When administered via an implanted device, it requires

Infusional chemotherapy with Lipiodol

Standard procedure - Involves the coadministration of chemotherapy with Lipiodol France) into the hepatic artery via a percutaneous catheter [22].

Contraindications - Compromised liver function, thrombosis of the portal vein, ascites metastatic disease.

Complications - Hepatic decompensation, systemic toxicities depending on chemother

Special points - Lipiodol is a highly lipophilic contrast agent that selectively concentrates the liver.

Cost effectiveness - Less costly than infusional intra-arterial approaches because it is a single sitting. It is not clearly superior to infusional chemotherapy given alone.

Chemoembolization

Standard procedure - Percutaneous access to the hepatic artery, infusion of a mixture and vaso-occlusive particles until cessation of antegrade blood flow through the tum The optimal chemotherapies and particles to be used are uncertain [23].

Contraindications - Marked impairment of liver function, ascites. Most investigators do with thrombosis of the portal vein, although others believe it can be done safely.

Complications - Pain, fever, worsening ascites, pleural effusion, infection, nausea and of hepatic failure is a function of the underlying liver disease, as is the risk of varicea

Special points - The radiographic changes following chemoembolization often sugges without tumor shrinkage. The significance of this finding is uncertain. No adequate st of life have been conducted with chemoembolization.

Cost effectiveness - Efficacy in terms of tumor necrosis or shrinkage has been shown advantage or palliative improvement has been demonstrated.

Lipiodol chemoembolization

Standard procedure - The procedure is the same as for chemoembolization with Lipiodol to the chemoembolization mixture.

Contraindications - Same as for chemoembolization.

Complications - Same as for chemoembolization.

Special points - Lipiodol chemoembolization has been compared to best supportive care in prospective randomized trials. The best study failed to demonstrate a statistically significant improvement in survival for the treated patients [24]. Although the trial methodology may have been the reason, this study suggests that this treatment should not be considered the standard for HCC.

Cost effectiveness - Relative efficacy for this approach has not been shown compared with other therapies or best supportive care.

Postsurgical adjuvant therapy

The risk of recurrence of HCC following curative hepatic resection is very high. Following surgery, two therapies have been demonstrated to improve survival by diminishing tumor recurrences or by reducing the risk of developing new primary HCC. One, polyprenoic acid [5], is an oral semisynthetic retinoid that is not commercially available.

Hepatic intra-arterial radio-labeled Lipiodol

Intra-arterial injection

Standard procedure - A single dose of Lipiodol labeled with radioactive iodine-131 is administered into the hepatic artery within 6 weeks of a curative operation on primary HCC [6].

Contraindications - Poor hepatic function.

Complications - Myelosuppression; requires hospitalization due to radiation effects.

Special points - Although this procedure can technically be done by equipped nuclear medicine facilities, it is extremely cumbersome and has not been done in the United States. The data supporting this approach are from a single institution in Hong Kong and need to be validated before this can be generally considered an appropriate treatment.

Cost effectiveness - One study [6] suggests that this therapy improves patient survival. This needs to be validated in a larger trial.

Newer Chemotherapeutic Drugs

The search for new active drugs is mandatory. Several phase II trials have tested new single agents for treatment of Stage IVa and IVb disease. Gemcitabine, an active agent in biliary tract cancer, was tested in patients with Child A or B cirrhosis and performance status of 0 to 2 and yielded response rates from 0% to 18%. Gemcitabine was also tested in combination with doxorubicin but produced only modest activity. Modulated 5-FU/eniluracil was tolerated well but displayed only minimal activity. Oral doxifluridine gave responses in four of 25 patients, but four patients had Grade 3 & 4 diarrhea. The combination of 5-FU with IFN-á was tolerated well even in cirrhotic patients and partial responses were documented for an overall response rate of 25% and a median overall survival time of 15.5 months. Liposomal doxorubicin was tested at doses of 30 to 45 mg/m^2 and showed no advantage compared with doxorubicin, with response rates from 0% to 10% and severe toxicity. A phase II study of paclitaxel showed no activity and severe toxicity. Irinotecan was not proven useful, with one in 14 patients having a partial response and substantial toxicity, leading to dose reduction in all patients.

One phase II trial tested the drug combination topotecan and oxaliplatin, only one of 13 patients had a partial response, and severe hematoxicity occurred in cirrhotic patients. The epirubicin, cisplatin, and 5-FU combination was tested in 2 trials and displayed low response rates of 14% and

Contraindications - Same as for chemoembolization.

Complications - Same as for chemoembolization.

Special points - Lipiodol chemoembolization has been compared to best supportive care in prospective randomized trials. The best study failed to demonstrate a statistically significant improvement in survival for the treated patients [24]. Although the trial methodology may have been the reason, this study suggests that this treatment should not be considered the standard for HCC.

Cost effectiveness - Relative efficacy for this approach has not been shown compared with other therapies or best supportive care.

Postsurgical adjuvant therapy

The risk of recurrence of HCC following curative hepatic resection is very high. Following surgery, two therapies have been demonstrated to improve survival by diminishing tumor recurrences or by reducing the risk of developing new primary HCC. One, polyprenoic acid [5], is an oral semisynthetic retinoid that is not commercially available.

Hepatic intra-arterial radio-labeled Lipiodol

Intra-arterial injection

Standard procedure - A single dose of Lipiodol labeled with radioactive iodine-131 is administered into the hepatic artery within 6 weeks of a curative operation on primary HCC [6].

Contraindications - Poor hepatic function.

Complications - Myelosuppression; requires hospitalization due to radiation effects.

Special points - Although this procedure can technically be done by equipped nuclear medicine facilities, it is extremely cumbersome and has not been done in the United States. The data supporting this approach are from a single institution in Hong Kong and need to be validated before this can be generally considered an appropriate treatment.

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16.8%. In one trial, IFN-á was also administered, and responses were observed in the pa cirrhosis.

The most promising trial is the combination of Gemcitabine and Oxaliplatin us which shows a response rate of 42% and clinical benefit of 61%. Another rationa chemotherapy would be combining Gemcitabine with 5-FU and IFN-á.

Emerging therapies

Early diagnosis continues to be a focus of much effort; improving radiologic new serum assays for unusual proteins are being studied. Much effort is ongoing in the HCC, particularly through hepatitis B vaccination and the management of active hepati therapies. These hold the greatest hope for this disease.

Numerous other therapies are currently being evaluated. Some are directe ablation, including intralesional injections, new embolizing particles, and internal radiation artery. Although these are more convenient or cleverer than existing therapies, they a potential benefit. As with any other new treatment, the role of each of these requi comparing treatments with survival and quality of life endpoints.

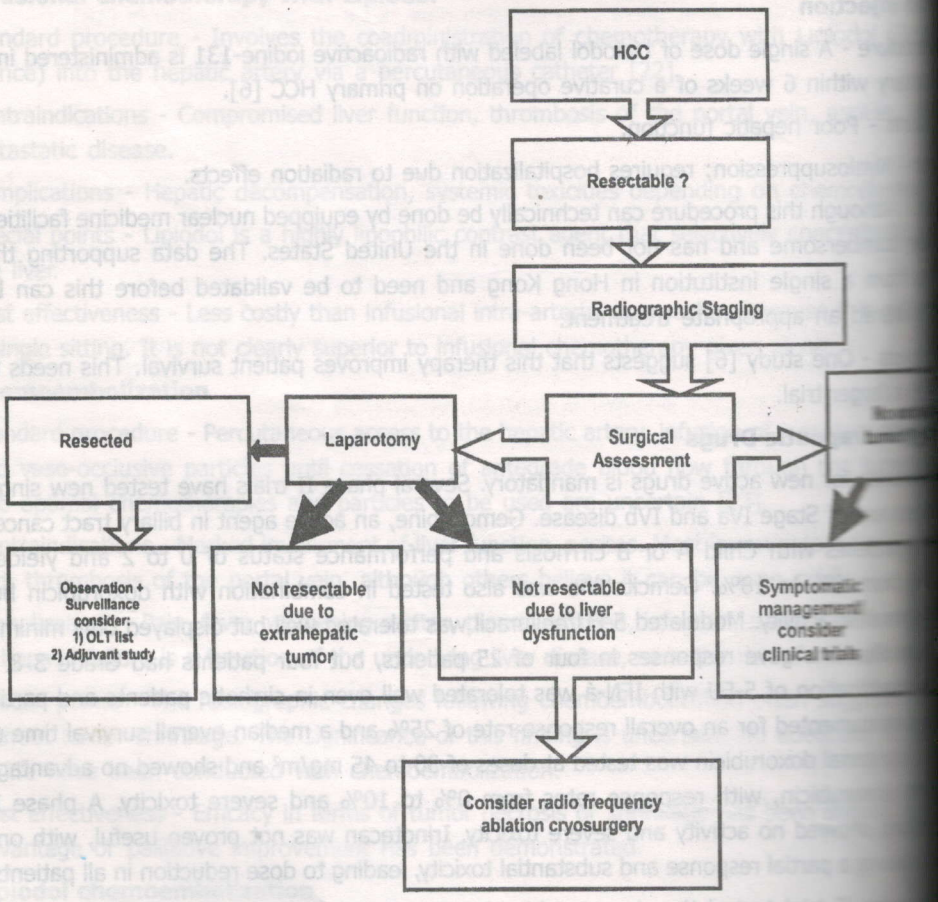

Figure 1
The treatment of patients with HCC is based on the extent of cancer and its resectability. A general approach to decision-making is demonstrated.

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MANAGEMENT OF GASTROINTESTINAL STROMAL TUMOURS

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Ch

INTRODUCTION

Gastrointestinal stromal tumours (GIST) are rare neoplasms originating from the tissue of the digestive tract and constitute most of the non-epithelial primitive digestive tu a percentage incidence of less than 1%. They were only recently recognised as a distinct entity, with the tumour cells derived from cells in the wall of the GI tract (interstitial cells They are believed to arise from the interstitial cells of Cajal, the pacemaker cells of the tract.They can be life-threatening soft tissue tumours and are located generally in gastrointestinal tract, mesentery and omentum.. Approximately 60% of GIST cases o stomach, 30% in the small intestine and 10% in other locations along the gastrointestinal GISTs are asymptomatic, but may cause abdominal pain or bleeding from ulceration of t mucosa. US endoscopy and fine needle aspiration with subsequent immunohistochemical study of c-kit gene mutation afford the best diagnostic accuracy. Surgical resection appea best option with little role for radiotherapy and chemotherapy. These tumours can metasta to other organs, including the liver, as well as spread throughout the abdomen. In such c as in irresectable tumours, Imatinib Mesylate or STI 571(brand name Glivec), is one of the which have showed promising results. Glivec is not a chemotherapy drug but a tyrosine kin which means it blocks a chemical (an enzyme) that the cancer needs in order to grow.

Incidence

GISTs are the most common malignant form of sarcoma (tumours arising from c blood, bone, muscle and connective tissue) of the gastrointestinal tract, but are still re Worldwide, there are approximately 12,000 new cases each year.. The incidence is highe aged 30 to 60 years.The estimated annual incidence is 10 to 20 cases per million .Clinical, histo ultrastructural and molecular-biological findings, have made clear that GIST is completely se leiomyoma and leiomyosarcoma.

DIAGNOSIS

1. ***On* endoscopic examination**, there may be a smooth protrusion of the bow with mucosa, which can also show signs of bleeding and ulceration. Most GIST are su grow endophytically, which decreases the likelihood that a tissue diagnosis can be o operatively.

2. **Endoscopic ultrasonography** may show a hypoechoic mass, which is contigu muscularis propria of the normal gut wall.

3. **CT Scan & MRI** are essential in assessment of primary tumour extension and th metastases. CT is used in staging and surgical planning. ***MRI*** provides better information in pre-operative staging work-up,for those with known or suspected rectal GIST

4. **Percutaneous fine-needle aspiration** has been suggested as an initial diagnos if feasible, but it is not universally recommended because intra-abdominal tumour spillag

5. **Positron emission tomography (PET) scanning** evaluation of fluorodeoxyglucose (FDG) uptake is recommended when an early detection of tumour response to imatinib treatment is required, e.g., for consideration of surgery after imatinib cytoreduction in rectal tumours. PET scanning may also be useful in cases of equivocal images suspected of being metastatic.

7. **Pathology - Immunohistochemically** most GISTs are positive for CD34 and c-kit protein CD117, a cell surface antigen on the extracellular domain of KIT; the latter is quite specific for GISTs among mesenchymal tumours. Genetically GISTs commonly show DNA losses in the long arm of chromosome 14, and c-kit gene mutations occur at least in some cases. Evaluation of malignancy of GISTs is based on mitotic count, tumour size and extra-gastrointestinal spread

Prognostic Features (which determine use of adjuant therapy)

1. The main features consistently predictive of biological behaviour are size and mitotic rate. Small GISTs (less than 5 cm in diameter) with fewer than five mitotic figures per 50 high-power fields (HPF) may safely be considered benign, whereas those with size larger than 5 cm or mitotic count greater than 5 to 10 mitoses/50 HPF or more than 10 mitoses/50 HPF should be classified as potentially malignant or malignant

2. **Location** – tumours arising from the small bowel, colon, rectum, omentum, or mesentery are generally associated with a less favourable outcome than those arising in the stomach.

3. **Incomplete surgical resection** and tumour **rupture** at surgery

4. **Infiltration** of tumour to other structures;

5. Presence of **necrosis**

6. A **high S-phase fraction** and DNA **aneuploidy**

7. A **high Ki-67** scores;

8. Proliferating cell nuclear-antigen expression; and

9. Presence of telomerase activity.

TREATMENT:

1. Surgery - Radical extirpative surgery with clear resection margins is deemed to be curative. However, recurrence rates are high, all GISTs are considered to have some degree of malignant potential, and there has been no effective systemic treatment for unresectable GIST or metastatic disease. They are unresponsive to standard chemotherapy and to radiotherapy. Thus for patients with metastatic or unresectable disease, GISTs represent an incurable malignancy with a median survival of approximately ten to twelve months.

2. Imatinib has been approved for the treatment of patients with advanced GIST, in which KIT, a tyrosine kinase receptor, is abnormally expressed. Imatinib mesylate (Glivac) is an orally administered 2-phenylaminopyrimidine derivative that is a competitive inhibitor of the tyrosine kinases and selectively inhibits the tyrosine kinase activity associated with KIT. Glivec (imatinib) induces tumour shrinkage and can be used for the treatment of patients, with Kit (CD117) positive unresectable (inoperable) and/ or metastatic malignant GISTs

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Gallbladder and Biliary Tract Carcinoma: A Comprehensive Management Update

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Gallbladder carcinoma and cholangio-carcinoma—carcinoma of the bile duct—are rare cancers in the Western World, but a common disorder in India, where it has a predilection, but have long been associated with a dismal prognosis. Although complete resection is the only hope for cure in both diseases, advances in diagnostic imaging techniques have improved diagnosis and have led to improved survival in recent years. The search for appropriate adjuvant or adjuvant treatments to improve survival and decrease recurrence rates is ongoing.

In this review, we address the expanded treatment options available in terms of surgery, radiation therapy, and palliative care, all of which are improving the outlook for patients with these cancers.

Adjuvant Treatment

Gallbladder Carcinoma

Few prospective randomized trials have assessed adjuvant therapy in this disease. The available data derive from small phase II trials in which patients undergoing surgery have been compared with historical controls.

The only phase III trial of **adjuvant chemotherapy** included 508 patients with gallbladder (n = 140), bile duct (n = 139), ampulla of Vater (n = 56), and pancreas (n = 173). [1] Patients were randomized to surgery alone or with MF (mitomycin [Mutamycin] and [5-FU]). The MF group received mitomycin, 6 mg/m2, at the time of surgery and 5-FU at 310 mg/m2 × 5 days in the postoperative period followed by oral 5-FU, 1,200 mg/m2, postoperative week 5 until recurrence. The 5-year disease-free survival rate (for gallbladder patients) favored adjuvant chemotherapy (20.3% vs 11.6%, $P = .02$), and the 5-year survival rate was also improved (26% vs 14.4%, $P = .03$). There were no significant differences in disease-free survival rates in the other cancer groups. A meta-analysis of published data on the role of radiation therapy in gallbladder carcinoma from 1974 to 2000 reported a benefit in survival after adjuvant or palliative radiotherapy. [2] The strongest benefit was seen in patients with only microscopic residual tissue. This report recommended an intraoperative boost to the residual lesion or tumor bed with additional postoperative external-beam radiation to a dose of 45 to 50 Gy.

Adjuvant chemo-radiation consisting of concurrent 5-FU plus EBRT in patients with gallbladder carcinoma was associated with a 5-year survival rate of 64% in the R0 (negative-margins) group, compared with 33% associated with surgery alone in the R1 group. Although confirmatory results from large randomized prospective trials are lacking, we offer patients with advanced gallbladder disease postoperative radiotherapy given the efficacy of radiation compared with the high local recurrence rates and poor survival associated with surgery alone. Adjuvant chemotherapy with 5-FU and mitomycin may be recommended for patients with cancer. [1]

Cholangio-carcinoma

Only 20% to 30% of patients with hilar cholangio-carcinoma are eligible for potentially curative (R0) resection. The median survival associated with an R0 resection is significantly better (22 months) than that of a palliative resection (10.7 months). [4] Small studies suggest that neo-adjuvant therapy consisting of chemotherapy, radiation, chemo-radiation, or photodynamic therapy may increase rates of curative resection. However, the small size of these experiences precludes any definitive conclusion.[4,5] Cameron et al reported the Johns Hopkins experience with 96 proximal cholangio-carcinoma patients undergoing either curative or palliative surgery and 66% receiving postoperative radiotherapy. No survival advantage was associated with postoperative radiotherapy in the group undergoing curative resection; however, radiation improved survival in those undergoing palliative surgery (R1 or R2 resection). [6] Table 1 summarizes some of the adjuvant and neo-adjuvant treatment experiences in gallbladder and cholangio-carcinoma. [1,3,4,7-10]

Liver Transplantation for Biliary Tumors

The prospect of liver transplantation as a cure for cholangio-carcinoma is appealing given encouraging results of transplantation in primary sclerosing cholangitis with incidental, small (< 1 cm) cholangio-carcinomas (Table 2) [11-16]. Unfortunately, the recurrence rate is high within the first few years after transplantation. Using life table analysis, projected 1-, 2-, and 5-year survival estimates of 72%, 48%, and 23% were reported for 207 patients who underwent liver transplantation for unresectable cholangio-carcinoma.[11,12] The poor long-term survival rates were secondary to high postoperative mortality and a high incidence of recurrence (51%). The majority of recurrences (85%) occurred within 2 years of transplant. Sites of recurrence were most commonly in the allograft (47%) and in the lung (30%). No prognostic markers were identified that could help with patient selection. To decrease the rate of post-transplant recurrence, preoperative chemo-radiation with 5-FU has been attempted. In a small series, 11 patients successfully completed this therapy, and at a follow-up of 44 months, only 1 had relapsed. [17] Transplantation for hilar cholangio-carcinoma after neo-adjuvant chemo-radiation with infusional 5-FU and biliary brachytherapy has been evaluated in 17 patients. [18] Five patients had tumor progression during the neo-adjuvant phase, precluding transplantation. Among the 11 who completed the protocol, 45% were alive without tumor recurrence at a median follow-up of 7.5 years. The high risk of recurrence of cholangio-carcinoma after transplantation precludes recommending this procedure as a routine treatment for biliary tract tumors. That said, it seems reasonable to consider liver transplantation for patients with cholangio-carcinomas less than 1 cm. [11,18,19]

Palliative Treatment

Biliary Decompression

Malignant biliary obstruction results in much of the morbidity of biliary tract and gallbladder carcinomas. Relief of biliary obstruction palliates symptoms including jaundice and associated pruritis, pain, and weight loss. Quality-of-life parameters have been evaluated in 50 patients undergoing endoscopic biliary drainage for malignant biliary obstruction. Weight loss and hyperbilirubinemia were strongly predictive of poor quality of life. [20] Successful biliary drainage was associated with improvement in quality of life, although less so in those with baseline bilirubin over 13 mg/dL. Patients with malignant biliary tract obstruction attain significant improvement in emotional, cognitive, and global health scores after endoscopic stent placement. [21] Biliary decompression can be achieved with equivalent efficacy by operative biliary-enteric bypass or endoscopic or percutaneous stenting of the biliary tree. [22, 23] Surgical decompression is recommended during an unsuccessful attempt at curative resection or in

patients in whom nonsurgical decompression is not feasible.

Self-expanding metallic stents produce a longer duration of patency—8 to 10 mon with 4 to 5 months using polyethylene endoprostheses. [24] Survival expectations ma used to guide stent selection. Reocclusion is usually secondary to tumor ingrowth or With improvement in radiologic techniques, the results of percutaneous stenting are superior to endoscopic stenting. [26] Percutaneous procedures may be preferable in cholangiocarcinomas, as endoscopic drainage in these cases is often difficult and results cholangitis due to inadequate drainage. [27,28]

To improve the duration of stent patency and overall survival, adjuvant chemotherapy has been tried. In a study in 32 patients, intraluminal brachytherapy wi 192 along with stent insertion was found to yield 2-year survival rates of up to 27% Klatskin's tumor and up to 50% in those with carcinoma of the ampulla of Vater, alon patency duration of more than 1 year.[29] Another study in 22 patients had similar resu stent patency duration of 19.5 months after treatment with Ir-192.[30] The signific findings is unclear given the potential patient selection bias associated with small sam

Palliative Chemotherapy

Patients with cholangio-carcinoma or gallbladder carcinoma typically present la of their disease and often are not candidates for curative surgical resection. In case intervention is not warranted, palliative chemotherapy has been used to diminish possibly to extend survival.

Only one large randomized trial has addressed the role of palliative chemother biliary tract cancer. Glimelius et al randomized patients with pancreatic cancer and bilia a regimen of 5-FU/leucovorin with or without etoposide, or best supportive care, and strategies for disease response and quality-of-life indicators. Of 90 enrolled patients, biliary tract carcinoma. Marked, although short-term improvements in survival (6.5 quality of life (measured with the European Organization for Research and Treatm [EORTC] QLQ-C30 instrument) were noted in the treatment group, establishing a treatment in unresectable disease. [31,32]

Several phase I and II trials, as well as numerous case and series reports, ha efficacy and toxicity profiles of various chemotherapy regimens in the palliative trea tract tumors. A variety of single-agent and multiagent chemotherapy regimens have results in palliating patients with advanced carcinomas. Response rates have ranged fr No consensus has been reached regarding standard of care.

Many drugs including 5-FU/leucovorin, cisplatin, oxaliplatin (Eloxatin), carbopla mitomycin C (Mutamycin), doxorubicin, interferon-alfa 2b (Intron A), gemcitabine (Gem (Ellence), capecitabine (Xeloda), irinotecan (Camptosar), and docetaxel (Taxotere) evaluated alone and in combination for the treatment of advanced biliary cancer. Wh these phase II trials do not permit conclusive recommendations for a particular re indicate that progression of advanced carcinoma of the biliary tract can in many cas controlled. Partial responses consistently ranging from 10% to 30% and disease stabiliz 10% to 50%, as well as improving median time to progression and median overa indicate that investigation of palliative treatment warrants continued attention. This sec recent phase I and II trials in the management of biliary tract tumors. Small sample

and the small number of trials preclude the development of statistically significant findings in cross-study analyses. Furthermore, studies seldom examine identical dosing and delivery schedules, making cross-study comparison difficult. However, analyzing the results of these trials can provide guidance in the clinical management of patients and suggest new avenues for investigation.

5-FU/Leucovorin

Either in combination or as a single agent, 5-FU has been used in the management of biliary carcinomas for almost 30 years. Single-agent studies have met with variable success. From 1974 to 1994, four small studies (enrolling between 7 and 30 patients) investigated the efficacy of single agent 5-FU. Response rates ranged from 0% to 24% in a total of 78 patients. [31]

Table 3 summarizes the results of the Glimelius et al randomized trial and three additional 5-FU/leucovorin trials. [32-35] Response rates in these trials appear better than those reported for 5-FU alone. [32] The toxicity of 5-FU/leucovorin regimens is tolerable and easily managed. Grade 3/4 toxicities have included mucositis, diarrhea, hematologic toxicity, asthenia, and abdominal pain.

5-FU Combination Regimens

Given the poor responses with 5-FU/leucovorin alone, investigators have evaluated 5-FU–based combinations in a number of phase I and II clinical trials. These trials are summarized in Table 4. [36-47] Outcomes have been mixed, with partial response rates ranging between 0% and 64% and disease stabilization rates from 0% to 50%. Complete responses have been rare. Reported median time to progression ranges from 3 to 10 months, while reported median survival ranges from 5 to 32 months.

5-FU and Mitomycin

Single agent mitomycin has been used in several trials, with response rates ranging from 0% to 47%. [31] The FAM regimen (5-FU, doxorubicin [Adriamycin], mitomycin) demonstrated a disease control rate (complete and partial responses plus disease stabilization) of 81%. [36] Unfortunately, other mitomycin-based trials have shown unacceptable toxicity. A trial of mitomycin, 10 mg/m2 every 8 weeks, together with weekly 5-FU at 2,600 mg/m2 plus leucovorin at 150 mg/m2 was stopped after treatment-related deaths exceeded 10% in the first 25 patients.[48] Given the potential toxicity of mitomycin and the availability of other agents, further investigation of mitomycin regimens is probably not warranted.

5-FU and Platinum

Cisplatin has minimal activity as a single agent against biliary tract carcinomas. [31] The combination of 5-FU and cisplatin has been assessed in several trials with variable success. An over- all response rate of 24% was attained in a 25-patient trial evaluating 5-FU, 1,000 mg/m2 intravenous infusion daily for 5 days, plus a 1-hour infusion of cisplatin, 100 mg/m2 on day 2. [37] The PIAF regimen (cisplatin, interferon alfa-2b, doxorubicin, 5-FU) produced response rates of 35% and 9.5% in 19 gallbladder carcinoma patients and 22 cholangio- carcinoma patients, respectively. Although the median survival of 14 months was encouraging, the significant toxicity profile of PIAF, which included grade 3/4 neutropenia (41%), nausea and vomiting (34%), thrombocytopenia (20%), and anemia (15%), precludes future use.[38] In addition, it is impossible to discern the contribution, if any, of interferon in this regimen.

Gemcitabine as a Single Agent

Gemcitabine is a deoxycytidine analog related to cytarabine with demonstrated success in

the palliative treatment of patients with advanced pancreatic cancer. [49] Hence, clinic
were eager to develop this agent in the treatment of biliary tract neoplasms. A number
trials summarized in Table 5 have examined the palliative effects of gemcitabine on biliary tra
[42,50-57] In general, gemcitabine therapy has produced moderate disease-control
progression, and median survival. These trials have shown objective response rates
disease-control rates ranging from 50% to 93%. [42,57,58] Clinical benefit with relief
symptoms and weight gain has also been attained in more than 60% of evaluable pa
unique schedule consisting of larger gemcitabine doses (2,200 mg/m2 as a 30-minute
weeks for 6 months) was administered to 30 patients with biliary tract tumors. The
and disease stabilization rates were 22% and 44%, respectively. Median time to
median overall survival were 5.6 and 11.5 months. [57] The tolerance was excellent
myelosupression despite the increase in dosage. These results with gemcitabine are
better than, those achieved with 5-FU/leucovorin. Single-agent gemcitabine treatments
well tolerated and result in encouraging progression-free and overall survivals. Grade
toxicity is rarely observed, with thrombocytopenia the most common event, affecting
patients.

Gemcitabine in Combination Regimens

Table 6 summarizes the dosing schedules and outcomes of 12 phase II trials
based combinations. [55, 59-73] Gemcitabine has been combined with 5-FU, docet
cisplatin, and capecitabine. The efficacy of combination treatments has varied, but
phase II trials have shown encouraging activity as compared with single agent Gemcit
these trials have been associated with improved survival outcomes of 11 months. How
for these regimens to be acceptable in clinical practice, they need to demonstrate
profiles and reproducible survival benefits.

Gemcitabine and Cisplatin

Gemcitabine/cisplatin regimens have been well tolerated with few grade 4
rates have ranged from 47.6% to 57% and disease stabilization rates from 28% to 4
efficacy of this combination needs to be further assessed in larger randomized trials.

Gemcitabine and Capecitabine

Single-agent capecitabine at a dosage of 2,000 mg/m2/d has been evaluated
patients with biliary and gallbladder cancers. [74] A 50% response rate and 1-year
of 70% was attained. These encouraging outcomes prompted studies of
combination regimens. In one such trial, gemcitabine at 1,000 mg/m2 on days 1 and
at 650 mg/m2 po bid on days 1 to 14 was administered every 21 days.[63] Of 15
for response, 33% attained a partial response and 33% had stable disease. The
tolerated, with less than 5% of patients developing grade 3/4 toxicity.

Gemcitabine and Irinotecan

The combination of gemcitabine at 1,000 mg/m2 and irinotecan at 100
and 8 every 21 days has been evaluated in a small trial including 13 patients.[64]
were observed in 18.2% of patients, with stable disease in 54.5%. Grade 3/4
tolerable. The regimen appears to be feasible in the treatment of biliary cancers,
whether irinotecan adds appreciably to treatment with gemcitabine alone. [64]

Gemcitabine and 5-FU

Two trials have examined the efficacy of gemcitabine/5-FU combinations for the treatment of biliary tract tumors. Gemcitabine at 1,000 mg/m2 followed by 5-FU at 500 mg/m2 once a week for 3 weeks on a 4-week cycle has been evaluated in nine patients; three experienced a partial response. [59] Gemcitabine at 1,000 mg/m2 in combination with 5-FU/leucovorin has been evaluated in 42 patients. [65] Patients were treated on days 1, 8, and 15 of 4-week cycles, and partial responses were attained in 9.5% of patients. Median time to progression and median overall survival were 3.8 and 6.8 months, respectively. The combination was well tolerated, with few grade 3/4 toxicities. Based on these data, however, the combination of 5-FU and gemcitabine appears to have little benefit.

Gemcitabine and Docetaxel

On the basis of the activity and safety profile of gemcitabine plus docetaxel in non–small-cell lung cancer, a phase II study of this combination administered weekly was conducted in 43 patients with unresectable biliary tract cancers.[66] A 9% partial response rate, 53% disease stabilization, and median overall survival of 11 months were attained with this well tolerated combination. The regimen is undergoing further investigation in a randomized multicenter study.

Gemcitabine, 5-FU/Leucovorin, Irinotecan, and Cisplatin

The novel combination known as G-FLIP (gemcitabine, 5-FU bolus plus infusion, leucovorin, irinotecan, and cisplatin [Platinol]) makes use of clinical evidence of known sequence-dependent synergy among these four drugs, while avoiding known sequence-dependent toxicity.[75] A phase I study included five patients with gallbladder cancer; three achieved a partial response.[67] The regimen was well tolerated, with largely hematologic toxicities consisting of anemia (9%), thrombocytopenia (9%), neutropenia (19%), and neutropenic fever (14%). These results require further evaluation in a phase II study in gallbladder cancer patients.

Other Gemcitabine-Based Combinations

Some multidrug combinations, especially those with cisplatin and gemcitabine, show improved activity compared with single-agent gemcitabine. Most combinations have been well-tolerated and have produced improved response rates, but survival outcomes from randomized multicenter trials are lacking. Thus, while activity and survival outcomes are encouraging, definite confirmatory randomized trials are warranted be fore they can be recommended outside of a clinical trial.

New Anticancer Agents

Table 7 shows the results of clinical trials with several new anticancer agents being studied in advanced biliary and gallbladder cancers.[74,76-78] Dowlati et al reported an 11.1% partial response and 33.3% disease stabilization in 27 patients treated with the antitumor antibiotic rebeccamycin

analog.[76] Rebeccamycin analog has both topoisomerase I and II activity and DNA intercal properties. The 6-month survival rate in this study was 76%, with a median survival of 10 mo Grade 3/4 toxicity consisted of neutropenia (52%), thrombocytopenia and anemia (28%), neutropenic fever (11.1%).[76] An ongoing study by Philip et al involves 30 patients with adv biliary carcinoma being treated with the epidermal growth factor receptor inhibitor erlotinib (Tarc To date, only toxicity data are available and only 4% grade 3/4 toxicity with nausea/vomiting has noted. Efficacy data are pending.[77] Ueno et al recently reported preliminary data on the use 1 in 19 patients with advanced biliary and gallbladder cancers.[78] S-1 is a new oral anticancer that contains tegafur (a prodrug of 5-FU), 5-chloro-2,4-dihydroxypyridine (dihydropyrim dehydrogenase inhibitor), and potassium oxonate (orotate phosphoribosyl transferase inhibit total of 21% of patients treated with 40 mg/m² bid for 28 consecutive days in 6-week cycles exper a partial response and 47.4% had disease stabilization, with few grade 3/4 toxicities. Median survival was over 8 months. S-1 seems to be well tolerated and active in this disease and w examined in a larger phase II trial.

Conclusions

Complete surgical resection is the only hope for cure in both gallbladder and chola carcinomas. While a simple cholecystectomy is usually curative for T1 gallbladder tumors, cholecystectomy is required for T2 and more invasive lesions. Radical resection should be cons for stage I–III gallbladder carcinomas. Complete tumor resection for cholangiocarcinoma, inclu partial hepatectomy for hilar carcinomas, is necessary to achieve long-term survival. Adjuvant radiot with or without concurrent 5-FU and mitomycin may improve survival, especially in gallbladder tu resected with microscopic residual disease.

Large randomized prospective studies on the use of adjuvant therapy are lacking, and recommendations are based on small studies and meta-analyses. Liver transplantation can pro long-term survivals for cholangiocarcinomas less than 1 cm in diameter but cannot be recomm routinely for all biliary tract tumors due to the high rate of recurrence and postoperative mo Although advances in imaging techniques have improved preoperative diagnosis, most patient diagnosed late and are not candidates for curative resection. Palliation in these patients includes of biliary obstruction with endoscopic or percutaneous stent placement as well as palliative chemoth which improves both survival and quality of life. Gemcitabine probably offers the most favorable agent profile with respect to disease response and toxicity. Trials of gemcitabine/ cisplatin combin offer encouraging results and a tolerable toxicity profile. Other combinations including gemc plus capecitabine or docetaxel seem promising but await confirmatory data from larger trials. conclusive disease-specific phase III data become available, single-agent therapy with gemcitabi reasonable standard of care for palliation of biliary tract tumors.

Table 1
Adjuvant Radiation/Chemoradiation in Gallbladder/Biliary Tract Carcinoma

Study	Number of Patients	Schedule	Radiation Dose	Chemotherapy	5-yr Survival
Kresl et al, 2002[3]	21 GBC	Postop (includes residual disease)	54 Gy	Concurrent 5-FU	64%
Todoroki et al, 1999[8]	85 GBC	Postop IORT/EBRT	20–30 Gy IORT, 36.4Gy EBRT	None	8.9%
Takada et al, 2002[1]	140 GBC 139 BDC	None	None	Surgery + (mitomycin/5-FU) vs surgery alone	26% vs 14.4% (P = .03)
de Aretxabala et al, 1999[9]	27 GBC	Preop	45 Gy	5-FU	7% 1-yr survival
Mahe et al, 1994[10]	11 GBC	Postop	30–50 Gy	None	36%
McMasters et al, 1997[4]	9 BDC 21 BDC	Preop Postop	45–50.4 Gy	Infusional 5-FU	Resection rates 100% vs 54%
Urego et al, 1999[7] + interferon	23 BDC	Postop	49.5 Gy	5-FU/leucovorin	53%

Table 2
Liver Transplantation for Biliary Tumors

Study	Number of Patients	Site of Cancer	5-yr Survival
Meyer et al, 2000[12]	207	Cholangiocarcinoma	23%
Pichlmayr et al, 1997[13]	53	29 PBDC 24 IBDC	18.4% 0%
Sudan et al, 2002[14]	17	Cholangiocarcinoma	45% (7.5 yr)
Iwatsuki et al , 1998[15]	38	Hilar cholangiocarcinoma	25%
Hassoun et al, 2002[16	NA	Hilar cholangiocarcinoma	87%

Table 3
Trial of Fluorouracil/Leucovorin Treatments

Study	Regimen	Number of Patients	Disease	Response Rate	Time to Progression	Overall Survival
Glimelius et al, 1996[32]	FELV or FLV alone in elderly vs best supportive care	37	BDC	Not reported	Not reported	6.5 vs 2.5 mo (best supportive care)
Chen et al, 1998[33]	Infusional 5-FU/LV weekly X 6 q8wk	18	BDC	PR = 33% SD = 39% DCR = 72%	4 mo	7 mo
Choi et al, 2000[34]	Mayo regimen, bolus 5-FU/LV days 1–5 q3–4wk	28	BDC	CR = 7.1% PR = 25%	Not reported	6.0 mo
Malik et al, 2003[35]	Mayo regimen	30	GBC	PR = 7% SD = 33%	4.7 mo	14.8 mo

Table 4
Fluorouracil Combination Regimens

Study	Regimen	Number of Patients	Disease	Response Rate	Time to Progression	Overall Survival
Harvey et al, 1984[36]	FAM	14	BDC	PR = 31% SD = 50% DCR = 81%	Not reported	Not reported
Kajanti et al, 1994[39]	FEM	17	11 EHBDC 6 GBC	No objective response	Not reported	9 mo
Ellis et al, 1995[40]	ECF	20/25 evaluable	BDC	PR = 40% SD = 25%	10 mo	11 mo
Gebbia et al, 1996[41]	5-FU/LV + hydroxyurea	30	GBC	PR = 30% SD = 27%	6.5 mo	8 mo
Ducreux et al, 1998[37]	Infusional 5-FU + cisplatin	25	BDC	ORR = 24%	5 mo	10 mo
Raderer et al, 1999[42]	Bolus 5-FU/LV + mitomycin q28d	20	BDC	PR = 25% SD = 30% DCR = 55%	4 mo	9.5 mo
Eckel et al, 2000[43]	CLFT	30	23 BDC 7 GBC	No objective response	Not reported	BDC = GBC =
Chen et al, 2001[44]	Infusional 5-FU/LV + mitomycin q8wk	25	BDC	PR = 26% SD = 42% DCR = 68%	3 mo	6 mo
Patt et al, 2001[38]	PIAF	41	19 GBC 22 CGC	GBC = 35% BDC = 9.5%	Not reported	GBC = BDC =
Melichar et al, 2002[45]	Regional 5-FU/LV + cisplatin	32	17 BDC 15 GBC	Not reported	Not reported	Palliative alone:
Taieb et al, 2002[46]	Infusional 5-FU/LV + cisplatin q2wk	29	BDC	CR = 3% PR = 31% SD = 38% DCR = 72%	6.5 mo	9.5 mo
Nehls et al, 2002[47]	FOLFOX	16	BDC	PR =19% SD = 37.5%	4.1 mo	9.5 mo

Table 5
Trials of Gemcitabine as a Single Agent

Study	Schedule	Number of Patients	Disease	Response Rate	Time to Progression	Overall Survival
Metzger et al, 1998[50]	1,000 mg/m2/wk × 7 wk, then weekly × 3 q4wk	13	BDC	PR = 8% SD = 85%	7.0 mo	16 mo
Raderer et al, 1999[42]	1,200 mg/m2 × 3 q5wk	19	BDC	PR = 16% SD = 21%	2.5 mo	6.5 mo
Valencak et al, 1999[53]	1,200 mg/m2 × 3q4wk	24	BDC	PR = 17% SD = 33%	3.5 mo	6.8 mo
Dobrila-Dintinjana et al, 2000[52]	1,000 mg/m2/wk × 7 wk then wkly × 3 q4wk	18	BDC	PR = 60%	Not reported	6.3 mo
Kubicka et al, 2001[51]	1,000 mg/m2/wk × 7 wk then wkly × 3 q4wk	23	BDC	ORR = 30%	Not reported	Not reported
Arroyo et al, 2001[54]	1,000 mg/m2/wk ×3 q4wk	39	BDC	PR = 36% SD = 28%	Not reported	6.5 mo
Penz et al, 2001[57]	High-dose 2,200 mg/m² infusion q2wk	32	BDC	PR = 2 2% SD = 44%	5.6 mo	11.5 mo
Gebbia et al, 2001[55]	1,000 mg/m2/wk × 3 q5wk	18	12 GBC 6 BDC	PR = 22% SD = 28%	3.4 mo	8 mo; 22% 1-yr survival
Lin et al, 2003[56] × 3 q4wk	1,000 mg/m2/wk	24	BDC	CR =4.2% PR = 8.4% SD = 33.3% DCR = 45%	2.5 mo	7.2 mo

Table 6
Trials of Gemcitabine in Combination Regimens

Study	Regimen	Number of Patients	Disease	Response Rate	Time to Progression	Overall Survival
Gebbie et al, 2001[55]	Gemcitabine$_a$ + infusional 5-FU/LV	22	10 GBC 12 BDC	PR = 36% SD = 23%	4.1 mo	11 mo
Carraro et al, 2001[60]	Gemcitabine$_a$ + cisplatin wkly × 3 q4wk	10	BDC	PR = 50% SD = 40%	5.5 mo	11.3 mo
Doval et al, 2001[61]	Gemcitabine$_a$ + cisplatin	17	BDC	PR = 53% SD = 41%	Not reported	Not reported
Andre et al, 2001[68]	Gemcitabine$_a$ + oxaliplatin q2wk	31	BDC	PR = 29% SD = 26%	5.8 mo	11.3 mo
Kuhn et al, 2001[69]	Gemcitabine$_a$ + docetaxel wkly × 3 q4wk	43	BDC	PR = 9.3% MR = 2.3% SD = 55.8%	Not reported	11 mo
Kornek et al, 2002[70]	Gemcitabine at 2,200 mg/m^2/wk + mitomycin q4wk	18	BDC	PR = 28% SD = 44%	5.0 mo	> 8.0 mo
Murad et al, 2003[59]	Gemcitabine$_a$ + bolus 5-FU q4wk	9	BDC	PR = 33%	Not reported	Not reported
Stieler et al, 2003[64]	Gemcitabine$_a$ + irinotecan wkly × 2 q3wk	11	6 GBC 7 BDC	CR = 9.1% PR = 9.1% SD = 54%	Not reported	9.5 mo
Reyes-Vidal et al,2003[62]	Gemcitabine at 1,250 mg/m^2 + cisplatin wkly × 2 q3wk	42	GBC	CR = 9.5% PR = 38.1%	Not reported	7 mo
Baluch et al, 2003[71]	Gemcitabine$_a$ + cisplatin q3wk	7/14 evaluable	BDC	PR = 57% SD = 28%	Not reported	Not reported
Jacobson et al, 2003[65]	Gemcitabine$_a$ + bolus 5-FU/LV wkly × 3 q3wk	42	BDC	PR = 9.5%	3.8 mo	6.8 mo
Knox et al, 2003[63]	Gemcitabine$_a$ + capecitabine (650 mg/m^2) po bid q3wk	15/17 evaluable	10 BDC 7 GBC	PR = 33% SD = 33%	Not reported	Not reported
Kuhn et al, 2002[66]	Gemcitabine$_a$ + docetaxel wkly × 3 q4wk	40/43	BDC	PR = 9% SD = 53%	5.3 mo	11 mo
Malik et al, 2003[72]	Gemcitabine$_a$ + cisplatin	11	BDC	CR = 9% PR = 55%	7 mo	10.5 mo
Morizane et al, 2003[73]	ECF	37	32 GBC 5 BDC	PR =19% SD = 54%	Not reported	Not reported
Rachamalla et al, 2004[67]	G-FLIP	5	GBC	PR = 60%	5.8 mo	9.2 mo

Table 7
New Anticancer Agents Being Studied in Advanced Biliary and Gallbladder Cancers

Study	Regimen	Number of Patients	Disease	Response Rate	Time to Progression	Overall Survival
Dowlati et al, 2003[76]	Rebeccamycin analog (165 mg/m$_2$/d × 5 d q3wk)	27	BDC	PR = 11.1% SD = 33.3%	Not reported	10 mo
Philip et al, 2003[77]	Tarceva (150 mg) × 28 d	30	BDC	Not reported	Not reported	Not reported
Lozano et al, 2000[74]	Capecitabine (2,000 mg/m$_2$/d) × 14 d q21d	55	BDC	ORR = 18%	6.3 mo	1-yr survival: 70%
Ueno et al, 2003[78]	S-1 (40 mg/m$_2$) bid × 28 d q6wk	19	BDC	ORR = 21.1% SD = 47.4%	Not reported	8.4 mo

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IASO BYE LAWS

IASO has been registered under society of registration at Varanasi (UP) in the year 2004-05 bearing registration number 627. The income tax PAN number is AAAT14187N issued on 27th August 2004.

The bye-laws of the IASO have been adopted at one of the general body meetings held in December 1997, Mumbai and amended time to time.

These bye-laws supercede all previous bye-laws of the IASO.

1. In these bye-laws, unless there is anything repugnant in the subject or context,

(a) **IASO** means "Indian Association of Surgical Oncology". -This will remain a section of the ASI.

(b) **ASI** means "Association of Surgeons of India.

(c) **Memorandum and Ruies and Regulations** mean Memorandum of the Association and Rules and Regulations of the ASI which came into force in 1985.

2. **Name:** The name of the Association is IIIndian Association of Surgical Oncology: -A section of ASI.

3. **Address:** The office of IASO is the place from where the Secretary functions.

4. **Objectives:** IASO is formed as per guidelines set in schedule II of memorandum of ASI and was approved as a section in 1977. The objectives of IASO are same as stated in schedule III of memorandum of ASI. Further to that, IASO will encourage and advance the study and practice of the science and art of surgical oncology and allied organisations concerned with cancer problems.

5. Membership :

(a) **Life Membership:** A life member should be a full member (Annual/life) of the parent body IIThe Association of Surgeons of Indiall. All persons, being surgeons with sufficient interest in cancer surgery/practicing cancer surgeons/completed an acceptable training in cancer surgery pursuing research in Cancer surgery or related subject, are eligible for becoming life member.

(b) **Associate Membership**: Those who are under training in cancer surgery or those who are interested in surgery but belong to other specialties, such as Radiology, Pathology, Biochemistry and who may not be in the member of the ASI. Subscription of membership will be as decided from time to time by the general body of the IASO. Generally all members will be inducted as life members.

6. **Termination of Membership:**

(a) If a member of IASO ceases to be a member of ASI, he/she will cease to be member of IASO.

(b) If a member fails to pay subscription by due date or resigns, he/she will cease to be a member of IASO.

7. **Year:** The year of the IASO will be same as of ASI -Ist. January to 31 st December.

8. **Management:**

(a) IASO will be manged by an Executive Committee consisting of following office bearers, members and ex-officio members:

i. President

ii. Vice President: 2

iii. Secretary

iv. Editor

v. Associate Editor

vi. Members: usually 8 members will constitute the executive committee.

(b) All past Presidents will be invitees to Executive Committee meetings.

(c) Organizing Secretaries of both immediate past and future NATCON will be co-opted members of Executive Committee of IASO for the year.

(d) Only those members and life members who have put in minimum 5 years of membership are eligible to election to Executive Committee.

(e) Save and except President, the tenure of all office bearers and members will be for two years.

(f) The president shall hold office for one year. Senior Vice President will be the President after expiry of his term unless he/she has resigned, indisposed or disqualified otherwise.

9. Election

(a) Election of the vacant posts as notified by the Secretary of IASO will be conducted in the Annual General Body Meeting of IASO to be held during the annual conference of IASO in NATCON every year.

(b) Every eligible member shall be proposed and seconded by two full members of IASO in the meeting after the proposed member has consented for the election.

(c) If there is no contest, the President shall declare the member elected for the post. Otherwise the election shall be by show of hands or secret ballot as decided by the President.

(d) A full member of IASO who has completed at least one term as executive member is eligible to contest for the post of Vice- President.

e) If a poll is demanded by at least 25% of the members of IASO present in the meeting and President are satisfied that such demand has been carried out by majority of members present in the meeting, the vote shall be taken by ballot.

10. **Power of Executive Committee:** Shall be same as that of the Governing Council of ASI.

11. The function and responsibility of different office bearers of IASO will be same as that of ASI. The secretary will maintain and present the audited accounts each year at the annual conference.

12. Meeting and Conference:

(a) IASO shall hold Annual General Body Meeting every during the Annual conference of NATCON and transact the business stated in bye-law 15(b). Other meetings, be it of Scientific, Social/ Executive Committee/General Body in nature, may be held as per the requirements of IASO.

(b) IASO shall endeavor to organize Mid-term conference at least once every year and appoint an organizing secretary for the conference in its Annual General Body Meeting. The dates of the conference will be fourth weekend of September.

13. **Annual Report:** An annual report stating the activities of the year shall be prepared by the Secretary for Annual General Body Meeting, a copy of which is to be sent to headquarters of ASI.

14. **Accounts of the year:** Accounts of the year of IASO shall be prepared by Secretary and audited by an auditor appointed by General Body within six months of the closing of the year.

This should be placed in the General Body Meeting and after adoption, a copy sent Headquarters of ASI

15. **Annual General Body Meeting:**

(a) Annual General Body Meeting (AGM) shall be held once every year as stated in Bye- laws.

(b) The following business will be transacted in the AGM.

i. Annual Report.

ii. Audited accounts of the previous year.

iii. Programme and budget of the next year.

iv. Recipients of various orations for the next year.

v. The venue of Mid-term conference and appointment of Organizing Secretary.

vi. Election of the office bearers and members of the executive committee.

vii. Any other business with the permission of the President. Topics of the symposia and conveners, theme of CME, workshops and programme outline should be discussed in the General Body Meeting.

16. **Journal:** IASO shall publish its own Newsletter and shall elect Editor for the same. He will the sectional editor of the Indian Journal Surgery.

17. **Income:** Income of the IASO shall be derived from:

(a) Admission fees and subscription from members, life members and associate members.

(b) Excess of income over expenditure in Mid-term conference.

(c) Donations.

18. **Investment:** IASO shall have account with nationalized or reputed bank to be operated persons authorized by General Body Meeting. The surplus fund after meeting statutory and expenditure shall be invested in fixed deposits of such banks and approved securities or in other manner to be decided in the General Body Meeting.

19. **Utilisation of Funds:**

IASO shall have account with nationalized or reputed bank and shall invest funds not required for its regular day to day activities in fixed deposits of such banks or approved securities as been decided by the General Body Meeting. The accounts will be operated as per provisions memorandum of ASI. The proceeds of income from various deposits and investments shall strictly spent for specific purpose for which such fund/funds are created.

20. **Representation:** IASO shall be represented as per Memorandum of ASI.

21. **Amendment of Bye-laws:** Any of the bye-laws of IASO may be altered or rescinded new bye-laws may be made at General Body Meeting by majority vote. The amendment shall come into force after it is circulated to all members and provided objection to such amendment of IASO is not received from ASI and 50% of valid members of IASO within three months the date of circulation. A copy of such amendment is to be sent to Headquarters of ASI.

22. **Schedule:** IASO secretariat shall maintain a schedule comprising the various orations, fellowship research grant or any other grant for scientific works with rules and regulations for awards and management.

23. **Orations, Fellowships & Awards :**

(a) **Radha Devi Oration** will be delivered by the outgoing President at the annual meeting of ASI. Rs. 5000/- have been donated for the oration by the family of Dr. S.~ Join. The orator will get a plaque, a cheque for Rs. 2000, certificate and a medal.

(b) **Motibhai Oration** will be delivered by an orator selected by the executive committee, and endorsed by the GBM. The oration will be delivered at the Annual meeting of IASO- NATCON. Rs. 50,000/ -have been donated for the cause by Dr. D. D. Patel and family. Only interest is to be used. 50% of interest is to be reinvested to generate same amount of money even in the era of falling interest rates. Thus, only 50% of interest should be available in the year to award the orator a plaque, a cheque for Rs. 2000, a certificate and a medal. Local hospitality by the organizing secretary NATCON.

(c) **Dr. N.C. Misra Oration:** Will be delivered preferably by an eminent foreign speaker selected by a panel consisting of the President IASO, Secretary IASO and the Organizing Secretary of the NATCON. In case of selection of eminent speaker from India, consultation will be held with the nominee of "The Student of Dr. N.C. Misra", who have donated Rs.three lakhs as endowment. Only interest is to be used. 50% of interest is to be reinvested to generate same amount of money even in the era of falling interest rates. Thus, only 50% or less of interest should be available in a year to award the orator a plaque, a cheque for Rs. 5000 or more/less (subject to calculation of interest), a certificate and a medal. Local hospitality by the organizing secretary NATCON.

(d) **Silver Jubilee oration in ASICON** -Will be delivered by national or international faculty. The orator shall receive a medallion, citation and Rs. 2000.

(e) **Detroit Visiting Fellowship** -A fellowship to visit Detroit will have local hospitality included by the host institution, excluding the travel cost to and from USA. The candidate should be less than 40 years of age (the cut off date is 31 st of December of the year of application), a full member of IASO, and permanently employed. Selection is based on CV and paper presentation during NATCON meeting. The paper must be on the work done in India only. Selection panel includes Dr. KK Moudar, President and Secretary of IASO. In case Dr. KK Moudar is not available than a person nominated by him or in case nominee is not available, than senior Vice President will be member of the panel.

(f) **Baroda travelling fellowship:** Rs. 5000 will be awarded to a young surgeon for visiting to a research or therapy oriented cancer center. No person can be awarded the prize again. Frequency of award -Once a year. Selection Panel: President, Secretary IASO & Dr. G.N. Shukla, Eligibility of applicant -young surgeon, full member of IASO, selection based on CV.

(g) **Best paper presentation** will be awarded Rs. 1000 towards complimentary Associate Membership of the IASO. Eligibility: Post-graduate student.

(h) **Best poster presentation** will be awarded Rs. 1000 towards complimentary Associate Membership of the IASO. Eligibility: Post-graduate student.

(i) **WFSOS :** The official representative of IASO in WFSOS will be immediate past president or his nominee. It will be the responsibility of President to generate $ 500 for yearly membership of WFSOS.

(j) **Dr. K.S. Panda - Dr. Gopinath Quiz Award :** During NATCON meeting winner will be awarded Rs. 700 and runners up to Rs: 300. Dr. K. Panda & Dr. Gopinath donated Rs. 10,000 each

towards the seed money for the Quiz award. Eligibility -all the delegates of NATCON. In case prize being won by a person who is not a member, the winner will get an additional Rs. 3 from the IASO towards his life membership dues, and cash award will be adjusted towards life membership of IASO.

24. **Guidelines of invitation for NATCON -**

(a) Organising secretary or his representative must be present in AGM to present his proposal.

(b) Rs. lOO per delegate must be deposited in IASO account. Besides this a opart of the savi may be donated to IASO.

(c) Audited accounts to be presented by next NATCON or circulated in the Newsletter. (d) It been decided that on request, a loan of Rs. 25000 may be given to the organizing secretary NATCON as seed money to start preparation, repayable within 6 months of the conferenc

25. Use of IASO banner in CME programs, Workshops & Conferences -It was decided that in C where delegation fee was charged, a token amount of Rs. 5000 or Rs. 50 per delegate for o day event of Rs. 75 for two days event which ever was more must be deposited to use IA banner.

ANNOUNCEMENT

The International Cancer Syposium of the Israel Society of Surgical Oncology - ISSO, Israel Surgical Association

in Conjunction with the

World Federation of Surgical Oncology - WFSOS

NOVEMBER 30th - DECEMBER 3rd, 2005

The Royal Beach Hotel, North Beach, Eilat, Israel

Congress Secretariat :

Dan Knassim Ltd., P.O. Box 1931, Ramat-Gan 52118, Israel

Tel : +972-3-6133340 Ext 212, Fax : +972-3-6133341

E-mail : team3@congress.co.il

Web site : www.congress.co.il/isso05

List of New Members of IASO in the year – 2005

(Subject to confirmation by Governing Body)

Dr. Abhinav Arun Sonkar
Asstt Provosts Bungalow, TG Hostel
Near Puccapul, Sitapur road
Lucknow-226003

Dr. Ajay Saha
North west of bodhjung girls school
Banamalipur, P.O Agartala,
Tripura-799001

Dr. Gupta Hanuman Prasad
Sanjeevan B-9, Talwandi, Kota-324005
Rajasthan

Dr. Wans Navinchandra Kanhajyalal
Dr. N.K.Wani, Ashwini Hospital
Parula Road, Dhule-424004

Dr. M.N. Kamaludeen
Abbaw House, 582 K.K.Nagar
Madurai – 625020

Dr. Muthu Chidambaram
No. 58, Nakkeerar Street,
Sivagangai Road
Madurai – 625020, Tamilnadu.

Dr. Sada Nand Mehta
CI/13, AIIMS Campus, Ansari Nagar
New Delhi – 110029

Dr. S. Vijayalakshmi
185, North veli street
Madurai- 625006

Dr. Satinder Singh Minhas
Set-21, Block 3, U.S.Club
Shimla – 171001

Dr. Subhash Khanna
Kalyani Hospital
Gurgaon – 122001

Dr. Surendra Prakash Chouhan
A-2, Sadur Ganj,
Bikaner – Raj - 334003

Dr. Vinay B. Bahl
Bahl Hospital,Hanumangarh Road
SriGanganagar-335001

Dr. Ram Kumar
309 Sec. 21, Panchkula-134109
Haryana.

Dr. Shaitan Singh Rathore
2-J-43, Nandanvan, Chopasni
Housing Board, Jodhpur – 342003

Dr. Shailender Kumar
King Geoorge's Medical University,
Lucknow

Dr. Harish Kumar
NC Jindal Inst. of Medical Care &
Research Centre Hisar, Haryana

Dr. Satpal Bhanot
Regional Cancer Centre
PGIMS, Rohtak.

Dr. Mithlender Kumar
Bikram Surgical & Maternity Centre
Malgodam Road, Bhagwan Bazar
Chapra, Bihar

Dr. M. Kalyansundram
Madurai Medical College,
Madurai

Prizes & Awards of NATCON-IASO- 2004 at Jaipur

1.	Detroit fellowship 2004–05	- Dr. Manoj Pandey	Trivendrum
2.	Baroda traveling fellowship 2004–05	- Dr. Pawan Gupta	N. Delhi
3.	Free paper awards 2004	- 1st Dr. Vikas Sharma	Varanasi
		- 2nd Dr. M.S.DeshpandeTMH	Bombay
4.	Poster presentation awards 2004	- 1st Dr. J.P Singh	
		- 2nd Dr. Pawan Kalra	
5.	Oncoquiz prizes	- 1st Dr. Arun Kumar Goel	Delhi
		- 2nd Dr. Jitender Poddar	Kolkatta
		- 3rd Dr. Sanjai Mandal	Delhi
		Dr. Kapil Kumar	Delhi

IASO -Baroda Travelling Fellowship

Application are invited for IASO-Baroda Travelling fellowship for the year 2005-6 Rs. 50001- only will be provided to a young surgeon who is aspirant to and has arranged attachment I observership with a Surgical Oncologist I Centre in India for 4 to 5 weeks.

An application on a plain paper enclosed with the Curriculum Vitae, place of attachment, acceptance from the centre, short objectives of the reasons for attachment and forwarding letter from the 2 members of the Indian Association of Surgical Oncology (IASO) should be sent to the office of the Secretary, IASO. The applicant must be MS in Surgery and citizen of India.

Detroit Fellowship

Detroit Medical Centre, Wayne State University, USA has instituted a visiting fellowship for four weeks at their centre for a young member of IASO, The fellow has to arrange his own passage. He will be provided free accomodation and sustenance allowance.

Those members desirous to apply for 2006-2007 may do so by sending their bio-data, research papers and publications to Secretary IASO. The candidate must be below 40 years (on 31-12-2005) and he is required to present a research paper during NATCON 2006 at Kodai Kanal, as a part of selection process.

Application must reach Secretary, IASO by 30th June' 2005

Scientific Programme NATCON IASO 2005 - Revised

Timings	Session	Event	Topic	Speaker
			23 / 09 / 05	
08.00 onwards			Registration & Display of Posters	
			Hall - A	
08.30 - 10.00	Session - I	Symposium - I	Oral Cancers	Dr. S Sadasivam, Coimbatore
10.00 - 10.20			**Tea / Coffee Break**	
10.20 - 11.15	Session II	Plenary Lecture I	Implications of Imaging in the management of Breast Cancer	Dr. K S Gopinath, Bangalore
		Plenary Lecture II	Multidisciplinary management of Breast Cancer	Dr. Tom Bates, UK
11.15 - 12.00	Session - III		Moti Bhai Oration	Dr. Rhys Evans, UK
12.00 - 01.00	Session IV	Invited Lecture I	Are Doctors responsible for Delay in Cancer Management	Dr. R K Karwasra, Rohtak
		Invited Lecture II	New Strategies in the Management of Sarcomas	Dr. Anurag Shrivvastava, UK
		Invited Lecture III	Transmandibular apporach to advanced Maxillary tumors and Maxillectomy	Dr. R M Tiwari, Bangalore
01.00 - 02.00			**Lunch Break**	
02.00 - 03.30	Session V	Symposium - II	Practice of Evidence Based Medicine (EBM) in Surgical oncology	Dr. Arun Chaturvedi, Lucknow
03.30 - 04.00			**Tea / Coffee Break**	
04.00 - 0600			**Inaugural function**	
06.00 onwards			**Cultural program followed by Dinner**	
			Hall B - 23/09/05	
02.00 - 03.30		Free Paper Session I	Total 9 papers will be presented. Each paper will be given 8 minutes for presentation and 2 minutes for discussion	
			Hall C - 23/09/05	
02.00 - 03.30		Free Paper Session II	Total 9 papers will be presented. Each paper will be given 8 minutes for presentation and 2 minutes for discussion	
03.30 - 04.00			**Tea / Coffee Break and Executive Body meeting**	
			End of the Programme	
			24 / 09 / 05	
08.00 onwards			Registration & Display of Posters	
			Hall - A	
08.30 - 10.00	Session VI	Symposium - III	Nonsurgical Interventional Technologies in Cancer management	Dr. L S Vohra, Dr. Somesh Chandra
10.00 - 10.20			**Tea / Coffee Break**	

10.20 - 11.15	Session VII	Plenary Lecture III: Laproscopicaly assisted miniadrenalectomy for Adrenal Tumors	[redacted]
		Plenary Lecture IV: G I Cancers - Where are we ?	[redacted]
11.15 - 12.00	Session VIII	N C Mishra Oration	[redacted]
12.00 - 01.00	Session IX	Invited Lecture IV: Something Old, Something New, Something Blue	Dr. Raghu Pillarisetty, Uk
		Invited Lecture V: Quality of life beyond cure - Changing Philosophy in local treatment of Breast Cancer	[redacted]
		Invited Lecture VI: A National Oncology Group - The Need of the Hour	[redacted]
01.00 - 02.00		**Lunch Break**	
02.00 - 03.00	Session X	Detroit Fellowship: Papers	
03.00 - 04.00	Session XI	Oncoquiz	[redacted]
04.00 - 04.20		**Tea / Coffee Break**	
04.20 - 05.30	Session XII	Video Symposium: Lap Management of Gynae Cancers	
		Intraoperative RT for Recurrent solid tumors	
		Reconstructive Microsurgery	Dr. Asok Gupta, Mumbai
		Hepatic Resection	Dr. Lileshwar Kaman, Chandigarh
		D-2 Gastrectomy	Dr. T D Yadav, Chandigarh
		Lap Total Proctocolectomy	Dr. G S Maheshkumar Coimbatore
05.30 - 06.30		**Annual General Body Meeting**	
07.30 onwards		**Banquet Dinner**	

Hall B - 24/09/05

02.00 - 03.00	Free Paper Session III	Total 6 papers will be presented. Each paper will be given 8 minutes for presentation and 2 minutes for discussion
03.00 - 04.00	Free Paper Session IV	Total 6 papers will be presented. Each paper will be given 8 minutes for presentation and 2 minutes for discussion
04.00 - 04.20		**Tea Coffee Break**
04.20 - 05.30	Free Paper Session V	Total 5 papers will be presented. Each paper will be given 8 minutes for presentation and 2 minutes for discussion

Hall C - 24/09/05

02.00 - 03.00	Free Paper Session VI	Total 6 papers will be presented. Each paper will be given 8 minutes for presentation and 2 minutes for discussion
03.00 - 04.00	Free Paper Session VII	Total 6 papers will be presented. Each paper will be given 8 minutes for presentation and 2 minutes for discussion
04.00 - 04.20		**Tea Coffee Break**
04.20 - 05.30	Free Paper Session VIII	Total 5 papers will be presented. Each paper will be given 8 minutes for presentation and 2 minutes for discussion

25 / 09 / 05

08.30-10.00		Symposium III	Gastric Cancer	Dr. Raja Raman, Chennai
10.00 - 10.20			**Tea / Coffee Break**	
10.20 - 11.00	Session XIV		Radha Devi Oration	[redacted]
11.00 - 01.00	Session XV	Guest Lecture I	Transanal Endoscopic Microscopic Surgery - TEMS	[redacted]
		Guest Lecture II		[redacted]
		Guest Lecture III	Surgical Oncologist - A prognostic factor or not ?	[redacted]
		Guest Lecture IV	Paediatric Tumors	[redacted]
		Guest Lecture V	Chemotherapy for Surgeons	[redacted]
01.00 - 01.30			**Validictory Function**	
01.30 onwards			**Lunch Followed By Departure**	

Hall B - 25/09/05

11.00 - 12.30	Free Paper Session IX	Total 9 papers will be presented. Each paper will be given 8 minutes for presentation and 2 minutes for

Hall C - 25/09/05

11.00 - 12.30	Free Paper Session X	Total 9 papers will be presented. Each paper will be given 8 minutes for presentation and 2 minutes for discussion

End of the Sessions & Conference

Announcement for IASO directory

All member are requested to kindly handover personally (at NATCON 2005) or send by mail, your updated address with telephone nos. and email i.d., alongwith attached photographs in the tearaway form enclosed, to the IASO Secretariat, by 30th Sep 2005 at the latest, for the IASO Directory.

Vijay Kant Jain
CHARTERED ACCOUNTANT

PHONE : 2364496
2228321

PARAS BHAWAN
21, JOBNER BAG
JAIPUR - 302

IASO NATCON 2004

HELD AT JAIPUR FROM 24th SEPTMBER TO 26th SEPTEMBER 2004

DATE.....

RECEIPT AND PAYMENT ACCOUNT FOR THE PERIOD ENDED ON 31st MARCH 2005

Receipts	Amount	Payments	Amount
By Opening Balance			
Cash	0.00	To Aid to Rajasthan Cancer Society	5,06,64
Bank of Rajasthan Ltd.	0.00	" Bank Expenses	1,75
" Advertisement,Sponsorship & Stall Booking	17,53,000.00	" Salary/Honorarium	34,18
" Delgate Fee	5,36,141.00	" Accomodation & Conference Expenses	9,87,33
" Interest	7,984.00	" Misc. Expenses	9,18
" Seed Money from IASO	25,000.00	" Printing & Stationery	1,19,57
" Seed Money from Rajasthan Cancer Society	50,000.00	" Momento & Compliment Expenses	46,65
		" Postage,Curier & Fax	64,79
		" Audio Visual Exp.	40,88
		" Telephone & Internet Expenses	30,36
		" Travelling Expenses	24,15
		" Donation to Dept. of Surgery, Jaipur (For IASGCON)	3,77,88
		" Donation to IASO (Parent Body)	30,88
		" Return of Seed Money to IASO	25,88
		" Return of Seed Money to Rajasthan Cancer Society	50,88
		" Tax Deducted at Source	5,94
		" Closing Balance Cash	
		Bank of Raj. Ltd. (Reserved for IASO, Parent Body)	20,88
	23,72,125.00		23,72,12

AUDITOR'S REPORT

I have checked the above "Receipt and Payment" Account of IASO-NATCON 20 for the year ended on 31.3.2005 with books of accounts and vouchers produced before me and found the same in agreement with them.

Date: 1st May 2005
Place: Jaipur

For IASO-NATCON 2004

Organising Secretary

VIJAY KANT JAIN
JAIPUR
Chartered Accountant

(VIJAY KANT JAIN)
Chartered Accountant
Memb. No. 70600

DEV ANAND GUPTA & CO.
CHARTERED ACCOUNTANTS

Vidya Complex, Kabir Road
Varanasi - 221 001.
Phone No. 9336910091

INDIAN ASSOCIATION OF SURGICAL ONCOLOGY
RECEIPTS & PAYMENTS ACCOUNTS FOR THE PERIOD FROM 1-1-2004 TO 31-12-2004

RECEIPTS	AMOUNT	AMOUNT	PAYMENTS	AMOUNT	AMOUNT
	Rs.	Rs.		Rs.	Rs.
Opening Balance :			Salary		12,000.00
Opening Cash Balance		36,218.00	Purchase of Medals, Cition & Certificates		5.855.00
FDR with Bank of India :			Stationary Expenses & Postages		7.611.00
FDR No. 1460620 Dt. 12-12-03 To 12-12-06	50,000.00		Tsunami Relief Fund		5,000.00
FDR No. 1460621 Dt. 15-12-03 To 12-12-06	50,000.00		Seed Money for NATCON, 2004		25,000.00
			Audit Expenses		2,000.0
FDR No. 1460622 Dt. 16-12-03 To 16-12-06	50,000.00		Registration & I. Tax Filing Exps for Yr. 2003-04 & 04-05		4,600.00
FDR No. 2159541 Dt. 30-4-03 To 30-4-06	125.000.00		Oration Award & Quiz		11.000.00
FDR with Bank of Maharastra :			Bank Charges		1.230.00
FDR No. 677486 Dt. 7-9-02 To 7-12-05	150.000.00		Closing Balance :		
FDR No. 677828 Dt. 1-11-02 To 1-11-09	50.000.00		FDR with Bank of India :		
FDR No. 154776 Dt. 11-2-03 To 11-2-2010	20.000.00		FDR No. 1460820 Dt. 15-12-03 To 15-12-06	50.000.00	
FDR No. 764044 Dt. 16-12-03 To 1-9-08	273.293.00		FDR No. 1460821 Dt-12-03 To 12-12-06	50.000.0	
FDR with Central Bank :			FDR No. 1460822 Dt. 15-12-03 To 15-12-06	50.000.00	
FDR No. 981997 Dt. 23-12-99 To 23-12-04	75,000.00		FDR No. 2159541 Dt. 30-4-03 To 30-4-06	125.000.00	275.000.00
TDS	6.716.00	880.009.00	FDR with Bank of Maharastra :		
			FDR No. 677486 Dt. 7-9-02 To 7-12-05	150.000.00	
Return o Seed Money		25,000.00	FDR No. 677828 Dt. 1-11-02 To 1-11-09	50.000.00	
Contribution from NATCON. 2004 Jaipur		30,000.00	FDR No. 154776 Dt. 11-2-03 To 11-2-2010	50,000.00	
Membership Contribution		60,800.00	FDR No. 764044 Dt. 16-12.03 To 1-9-08	273.293.00	523,293.00
Receipt from Praful Desal Oration		200,000.00	FDR with Central Bank :		
Saving Bank Interest		1,533.00	FDR No. 981997 Dt. 23-12-99 To 23-12-04	75.000.00	
Contribution from Dr. N.C. Mishra Oration, Allahabad		50.000.00	TDS	8,064.00	83,064.00
Receipt from NATCON, 2003 Lucknow		100,000.00	FDR with Allahabad Bank, Lucknow		
			FDR No. TD-409651, DT. 20-9-04 To 20-9-06		50.000.00
Balance c/d		1,383,560.00	Balance c/d		1,005,653.00

Date : 16-3-2005
Place : VARANASI

For Indian Association of
Surgical Oncology

Sd-
(L. Sarangi)
SECRETARY

For Dev Anand Guptal & Co.
Chartered Accountants

Sd-
(Dev Anand Gupta)
Proprietor

CHARTERED ACCOUNTANTS

Varanasi - 221 001
Phone No. 9336910091

INDIAN ASSOCIATION OF SURGICAL ONCOLOGY
RECEIPTS & PAYMENTS ACCOUNTS FOR THE PERIOD FROM 1-1-2004 TO 31-12-2004

RECEIPTS	AMOUNT	AMOUNT	PAYMENTS	AMOUNT	AMOUNT
	Rs.	Rs.		Rs.	Rs.
Opening Balance :		1,383,560.00	Balance b/d	1,005, 653.00	
			FDR with Union Bank of India, Varanasi		
			FDR No. 6473027 Dt. 31-12-04 To 31-12-07	60,000.00	
			FDR No 6473028 Dt. 31-12-04 To 31-12-07	60,0000.000	
			FDR No. 6473031 Dt. 31-12-04 To 31-12-07	40.000.00	
			FDR No. 6473071 Dt. 28-01-05 To 28-01-08	40,000.00	
			FDR No. 6473025 Dt. 31-12-04 To 31-12-09	60,000.00	
			FDR No. 6473026 Dt. 31-12-04 To 31-12-09	60,000.00	
			FDR No. 6473030 Dt. 31-12-04 To 31-12-07	30,000.00	350,000.00
			Cash at Bank of India		10,271,00
			Cash in Hand		17,636,00
		1,383,560.00			1,383,560.00

Note : The above Receipts & Payment Account has been compiled on the basis of papers & datas as produced before us and infomation as given to us.

For Indian Association of
Surgical Oncology

Sd-
(L. Sarangi)
SECRETARY

For Dev Anand Guptal & co.
Chartered Accountants

Sd-
(Dev Anand Gupta)
Proprietor

Date : 16-3-2005
Place : VARANASI