DG MEMORANDUM : EARLY DIAGNOSIS OF CANCER

1. The overall number of patients diagnosed with cancer is on the increase worldwide. This is largely due to improved awareness as also to the availability of better diagnostic facilities and methodology.

2. The objective of this memorandum is to heighten awareness of the possibility of cancer in the minds of all MOs. It lays down guidelines for the optimal utilization of clinical and investigational facilities in the Armed Forces Medical Services towards this end.

3. Entitlement for treatment of cancer is as given in para 306 of RMSAF 1983. A list of Oncology Centres in the Armed Forces is as follows:

a) Command Hospital (SC) Pune

b) Army Hospital (R & R) Delhi Cantt

c) Command Hospital (EC) Kolkata

d) Command Hospital (AF) Bangalore

e) INHS Asvini, Colaba, Mumbai

4. On diagnosis, or mere suspicion of cancer by a Specialist Medical Officer, an entitled patient will be transferred on Govt expense to the nearest Oncology Centre. (*Auth*: AHQ letter No 10021/Gen/DGMS-5(b) dt 09 Jan 1990) There is no need to ask for bed availability prior to transfer.

5. Early detection of cancer in symptomatic and asymptomatic individuals should be our objective. "*Early diagnosis equals good prognosis*". The objectives of early detection are:

a) To detect and remove / arrest all premalignant lesions

b) To provide patients the best available treatment

c) To reduce the morbidity and mortality of this disease

d) To help spread awareness among MOs and patients

6. A high index of suspicion of malignancy by the MO will enable early diagnosis in many situations. Very often the diagnosis of cancer is inordinately delayed on account of incomplete clinical examination, misdirected investigations or empirical / symptomatic treatment, e.g. antitubercular / antiamoebic treatment.

7. The symptoms and signs that arouse suspicion of cancer would vary with the site of lesion, and this awareness is essential on the part of the MO. A carefully elicited history with regard to nature, onset and duration of the complaint, and personal, family history must be accompanied by thorough clinical examination. Nearly half of all cancers are strongly related to tobacco abuse and another one-third related to dietary factors and are hence preventable.

8. The most common cancers among males arise in the head and neck, lung and GI tract, whereas in females, they are in the uterine cervix, breast and head & neck. Increasing number of cancers are being diagnosed at much younger ages than may be expected.

9. The imperatives of good clinical examination and appropriate investigations in the early detection of cancer at various sites are described in the subsequent paragraphs.

10. HEAD AND NECK CANCER

Majority of head and neck cancers being tobacco-related arise in easily accessible areas. The oral cavity i.e. the buccal mucosa, lips, tongue, floor of mouth, palate and oropharynx can be easily examined with the aid of a simple tongue-depressor and torch. Other common sites such as nasopharynx, hypopharynx and larynx can be well evaluated with an indirect mirror-examination. These very basic methods of examination must be widely and frequently used by all MOs. Dental Officers must carefully examine the oral cavity at the time of annual dental examination of serving personnel. Leukoplakia and erythroplakia are the common remalignant lesions, and can have a variety of clinical appearances.

The common symptoms of the cancers of the head and neck are:

(a) Hoarseness of voice lasting over two weeks

(b) Nonhealing ulcer in the oral cavity

(c) Unexplained bleeding from the mouth or nose

(d) Otalgia, odynophagia or dysphagia

The presence of any swelling in the region of the thyroid, parotid or any enlargement of cervical lymph node should prompt a complete ENT examination and further investigations like ultrasound (USS), fine needle aspiration cytology (FNAC), barium swallow and upper GI endoscopy. Staining of suspicious lesions with Toluidine blue by Dental Surgeons is a quick and in expensive method to evaluate a pre-malignant lesion.

11. LUNG CANCER

The two major types of lung cancer are: small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). Majority of NSCLC are related to smoking. Although lung cancer can have protean manifestations, the following are the common symptoms and signs:

(a) Persistent cough

(b) Haemoptysis

(c) Pain chest

(d) Breathlessness

(e) Unilateral wheeze

(f) Pleural effusion

(g) Non-resolving pneumonia

(h) Cervical lymph node enlargement

Uncommonly lung cancer can present with extra-thoracic manifestations. Though rare, it is good to remember them as possible pointers to the diagnosis:

(a) *Skeletal*

i) Clubbing;

ii) Pulmonary hypertrophic osteoarthropathy

(b) Cutaneous

i) Dermatomyositis

ii) Acanthosis nigricans

(c) *Neurologic*

(i) *Myesthenic syndrome*

(ii) *Peripheral neuropathy*

(iii) *Cortical cerebellar degeneration*

(iv) *Mental changes- psychosis*

(d) *Cardiovascular*

(i) *Thromboembolism*

(ii)*Non-bacterial thrombotic endocarditis*

(e) *Hematological*

(i) *Anemia*

(ii) *Serum protein abnormalities*

(iii) *Polycythemia*

(iv) *Purpura*

(f) *Metabolic manifestations*

(i) *Cushing's syndrome*

(ii) *Renal loss of sodium*

(iii) *Hypercalcemia*

(iv) *Gynecomastia*

(v) *Syndrome of Inappropriate ADH secretion (SIADH)*

A standard X-ray chest PA view is very informative and should be done as the first investigation. On suspicion of lung cancer the patient should be referred to the Oncology Centre where he / she will be evaluated by means of bronchoscopy, sputum cytology, USS, CT scan and FNAC. All cases of pul kochs not responding to ATT, or progressing while on ATT should be re-evaluated for CA Lung before labeling them as MDR – TB

12. CARCINOMA STOMACH

Carcinoma of the stomach was termed "Captain of the Men of Death" by Lord Moynihan in the last century and yet continues to be a lethal disease. While it is more common in those over 50 years, no age is exempt. Any dyspepsia lasting over two weeks merits investigation. Common symptoms and signs are:

(a) Unexplained weight loss / cachexia /anemia

(b) Anorexia

(c) Vomiting

(d) Hematemesis/ malena

(e) Epigastric lump

(f) Left supraclavicular lymph node

There is paucity of symptoms and signs in early gastric cancer and any clinical sign denotes advanced disease. Hence screening offers the only hope of early diagnosis in cancer stomach. In Japan, where the disease is very common a population based endoscopic screening programme is in place and has contributed in a major way towards early diagnosis and radical treatment with markedly improved results.

In India endoscopic screening is not feasible or cost-effective, yet wider use of fiber-optic endoscopy in the evaluation of patients with dyspepsia or anemia should yield increasing number of cases in earlier stages than hitherto possible. All patients with dyspeptic symptoms not responding to Ranitidine / Omeprazole after six weaks therapy should definitely be evaluated by endoscopy and biopsy

13. COLORECTAL CANCER

Cancers of the colon and rectum are eminently curable when detected early. Over half of these cancers occur in the rectum and sigmoid colon and can be easily detected by a careful per-rectal (PR) examination and proctosigmoidoscopy. It merits emphasis that no examination of the abdomen is complete without a PR examination. A proctoscope is available in all MI Rooms and it should be used in any patient who reports bleeding per rectum or alteration of bowel habits.

Patients with rectal cancer usually present with bleeding PR or a sense of incomplete evacuation of stool. Sigmoid lesions present with bleeding or obstructive features and /or lump. Any patient above age 40 with microcytic hypochromic anemia should be evaluated for this possibility. Double contrast Ba enema with Fibre-optic endoscopic evaluation are useful for early diagnosis . Fibre-optic endoscopic evaluation of the colon and rectum is very accurate and is well tolerated by patients.

Fecal occult blood test (FOBT) is very useful as a screening method and also to investigate a patient of altered bowel habit/ weight loss/ anemia in whom the possibility of colorectal malignancy is entertained. It is important to observe the following precautions for FOBT to obtain optimal results:

(a) Avoid consumption of meat, green vegetables or iron preparation for 3 days

(b) Avoid hard brushing of teeth, exclude bleeding gums

(c) Avoid contamination with menstrual blood

14. GALL BLADDER CANCER

Carcinoma gall bladder is more common in the northern and central parts of India. Unless it is diagnosed and treated at an early stage, the disease has a dismal prognosis. Very often it arises in patients who have gallstones. However it can also arise de-novo. There are no symptoms/ signs peculiar to carcinoma gall bladder making early diagnosis difficult. Hence most cases often get diagnosed at very late stages, after development of jaundice or hepatic/ lymph node metastases. Widespread availability and use of USS has resulted in increasing the diagnoses of gallstones and gall bladder polyps. The following guidelines may help in improving the outcome in this otherwise dismal disease:

(a) All cases of gallstones even if asymptomatic should be counseled regarding the long-term risk of malignancy. With the easy availability of laparoscopic cholecystectomy, gall bladder surgery has become much more acceptable.

(b) Any patient diagnosed to have gall bladder polyp must undergo cholecystectomy.

(c) Any gall bladder removed at surgery must be opened for naked-eye examination by the surgeon to look for any mucosal abnormality. On suspicion of cancer if the surgeon is trained, he must proceed to perform radical *cholecystectectomy*.

If facilities are lacking or the surgeon is not trained, it is best to transfer the patient to the Oncology Centre at the earliest for performance of radical cholecystectomy. This operation, if performed timely gives a definite survival advantage.

15. HEPATOCELLULAR CARCINOMA

Primary Hepatocellular carcinoma is etiologically related to Hepatitis B virus Carrier State, as also alcohol abuse and diet containing grains and peanuts contaminated with aflatoxins. Clinical presentations include right upper quadrant pain, fever, jaundice and findings of hard, irregular enlargement of liver with or without a bruit. Clinical signs of cirrhosis often co-exist and complicate treatment decisions. USS and CT scan are good imaging modalities and elevation of serum tumor marker alpha-fetoprotein above 500 ng/ml is virtually diagnostic. FNAC should not be done if surgery is deemed feasible on imaging because of the risk of tumor implantation in the needle track. A very small number of cases are potentially curable with liver resection surgery. For the majority, palliative chemotherapy is the only therapeutic option. Hepatitis B vaccine which has high sero conversion protects against hepatitis B and also shown to eliminate carrier state

16. CARCINOMA BREAST

Carcinoma breast is the prime example where the benefits of a screening programme coupled with heightened public awareness has resulted in early detection of a large number of cases. It is as yet unclear whether this translates into improved overall survival. The disease is associated with certain well-known risk factors. These are:

(a) Age above 30 years

(b) Family history (mother / sister)

(c) Obesity

(d) Early menarche, late menopause, late first pregnancy and nulliparity

The methods available for early detection are Breast Self Examination (BSE), Clinical Breast Examination by a physician (CBE) and mammography.

Breast Self Examination

All women must check their breasts once a month about one week after their period. They must look for any changes in the mirror and then feel carefully for any lump/ thickening or any other changes in the breasts / armpits.

The American Cancer Society recommends Monthly BSE for all women 20 years and older; CBE every three years between 20 – 39 yrs and annual CBE and Mammography for women above the age of 40 yr.

In our context given the large population , widespread lack of awareness and meagre public health resources BSE should be taught at all FWCs and Antenatal Clinics and appropriate cases referred for CBE and Mammography.

It is emphasized that the majority of lumps detected at BSE are in fact benign. Mammography is not recommended as a screening procedure in India and is indicated only in high-risk women or where an abnormality is suspected in CBE.

17. PROSTATE CANCER

Cancer of the prostate is among the common cancers in males. Above the age of 40 years, the incidence increases with each passing decade. The disease is eminently curable in it's early stages but metastatic disease has no known cure. Prostate cancer detection has been accomplished using Digital Rectal Examination (DRE), Serum Prostate Specific Antigen (PSA) and Transrectal Ultrasound (TRUS) or a combination of these three techniques.

On DRE, the finding of a normal prostate gland does not exclude prostatic cancer, however the finding of a hard nodular enlargement of the prostate usually denotes locally advanced cancer. Serum PSA is a sensitive marker of disease and is best used in combination with DRE. Serum PSA may also be raised in presence of prostatitis, after urethral instrumentation, recent ejaculation and after prostatic biopsy.

TRUS is an expensive investigation and adds little value to the diagnosis. It's main utility is in guiding the clinician in obtaining representative tissue at needle biopsy among patients who have an elevated Serum PSA, an abnormal DRE or both.

18. CANCER UTERINE CERVIX

It is the commonest cancer among women in India. It accounts for 25-30% of all malignancies in females. Due to lack of awareness and other socioeconomic reasons, 80% of all patients with cancer cervix present in advanced stages of the disease and have survival figures of < 2 years. The long pre-invasive stage of cervical cancer, the high prevalence of disease in unscreened population and the high sensitivity of cytological screening makes cervical cancer an ideal target for cancer screening.

The main risk factors are :

a) low socio-economic status

b) sexual promiscuity

c) early age at first childbirth

d) Human Papilloma Virus (HPV) infection

The common presenting features of invasive cancer are bleeding per vaginum, often after coitus and clear or foul-smelling vaginal discharge. Pelvic pain is a sign of late disease. The aim of screening is to diagnose the disease in the pre-invasive stage when the patient is asymptomatic.

PAP smear examination is a simple out-patient test that can be carried out by any trained Health Care Worker. It is aimed at obtaining surface epithelial cells from the cervix uteri which can be smeared onto a slide which is then examined by a cytopathologist.

The experience of the cytopathologist is of paramount importance. Dysplasia or carcinoma-in-situ can be diagnosed by this method. By itself a properly performed PAP smear cytology is fairly reliable to diagnose pre-invasive squamous cell carcinoma of cervix (sensitivity 80%), but is limited in detecting adenocarcinoma-in-situ, which tends to arise higher up in the endocervix.

Should a PAP smear be "*suspicious*" but there is no gross abnormality in the cervix the patient should be subjected to further evaluation by colposcopy and directed biopsy. Acetic acid (3%) staining of the cervical mucosa is used to identify suspicious areas for biopsy. In order to exclude adenocarcinaoma-in-situ an endocervical curetteage is desirable.

19. LEUKAEMIA / LYMPHOMA

Leukaemia & lymphoma together account for 12-15% of all cancers and are highly amenable to treatment. With modern treatment, cure is an expectation rather than an exception. Patients with leukaemias and lymphomas are usually immunocompromised. Leukaemias usually present with fever, pallor, sternal tenderness and/or infections.

Lymphomas commonly present with enlarged lymph nodes and hepatosplenomegaly. On any clinical suspicion of leukaemia, a complete haemogram and a peripheral blood smear examination must be done. Blood transfusions cause a change in the blood picture and may mask the diagnosis for several weeks. It is recommended that blood transfusion be avoided until the cause of anemia can be established. FNAC of enlarged lymph node is the usual first investigation to diagnose lymphoma though a biopsy is necessary to type the disease. A clinical suspicion of leukaemia / lymphoma should prompt immediate transfer to a service oncology centre.

20. PEDIATRIC CANCERS

A high percentage of childhood cancer is now curable: more so the hematological variety. However they must be diagnosed in time, before life-threatening complications develop. Leukemia and lymphoma account for over a third of pediatric cancers. While the general presentations are the same as in para 18, clinical features like joint pains, nodal enlargement are encountered more frequently in children who are eventually diagnosed to have leukemia. Juvenile rheumatoid arthritis is therefore a differential diagnosis.

Solid tumors like neuroblastoma, rhabdomyosarcoma, Wilms' tumor or retinoblastoma occur at characteristic sites in children. Significant prolongation of survival or cure is achieved in a majority of these children if they are recognized in a non-metastatic stage. It bears emphasis that mere large size also confers a poor prognosis in otherwise curable subsets of pediatric solid tumors e.g. Ewing's sarcoma.

21. CARCINOMA OVARY

Broadly speaking, these are of 2 types: *Epithelial Tumours and Germ Cell Tumours (GCT)*. All ovarian cancers are highly chemosensitive, While epithelial cancer tends to recur and have a worse outcome, the germ cell variety are highly curable in the majority.

GCT commonly occur in younger women and present as abdomino-pelvic masses, while epithelial cancers have protean manifestations. Elderly women who complain of abdominal distension, altered bowel habits and have an exudative ascites should undergo per-rectal and per-vaginal examination and a pelvic USS.

Several patients with above symptoms are often diagnosed clinically as abdominal tuberculosis and given varying periods of empirical ATT, leading to avoidable delay and allowing progress of disease. It is to be emphasized that the diagnosis of abdominal tuberculosis must not be empirical and ATT should not be started without the exclusion of ovarian carcinoma by pelvic USS in a female patient.

In any patient with a *complex ovarian cyst*, two useful investigations are Transvaginal Ultrasound and Colour Doppler Study. With the use of these tools a very specific diagnosis of malignancy can be made in high percentage of patients.

Cancers of the ovary have very reliable tumour markers. Serum CA-125 is the gold standard for tumour markers in the evaluation of pelvic masses particularly ovarian cancers. Besides ovarian cancers many other conditions can be associated with elevated CA-125 levels. They include cirrhosis liver, peritonitis, pancreatitis, endometriosis, uterine leiomyomata, benign ovarian cysts and pelvic inflammatory disease. Serum AFP and Beta-HCG have been helpful in recognizing pre-operatively the presence of ovarian GCT. The chief value of markers is to monitor the response of disease to therapy and to help during follow-up for early detection of recurrence.

22. TESTICULAR TUMOURS

Testicular tumours are uncommon but their importance stems from the fact that this disease strikes our soldiers in the prime of their youth and has a major impact on their long-term health and fertility. The usual clinical presentation is with painless testicular enlargement. Often it is clinically mis-diagnosed as hydrocele or epidydimo-orchitis, and variable delay occurs before proper diagnosis. The important clinical findings that should alarm the MO are that of "*heaviness*" of the enlarged testis and *absence of testicular sensation*. Should these be present, patient must be referred to a surgical specialist who is competent to perform *Retrograde Orchidectomy* as the primary treatment.

It must be emphasised that scrotal violation e.g. surgery for hydrocele / testicular biopsy must never be done when there is a possibility of testicular tumor. In all cases of painless testicular swelling, serum AFP and Beta-HCG to be done before planning type of surgery.

In the evaluation of testicular masses, USS can be very helpful and the presence of "*hypoechoic mass*" in the testis is suggestive of a malignancy. Presence of fluid in the tunica vaginalis (hydrocele) does not exclude testicular cancer. FNAC has no role to play in diagnosing testicular cancer and should not be done.

23. CANCERS OF THE URINARY TRACT

A chronic smoker above 60 years of age who presents with hematuria with or without pain in the pelvic region must be evaluated to rule out carcinoma of the urinary bladder. Urine for cytology (malignant cells) and cystoscopic biopsy are the cornerstones of the diagnosis. A CT scan is essential for disease staging. Superficial bladder cancers are supremely amenable to Transurethral Resection and topical chemotherapy and have an excellent survival. If diagnosed late with muscle invasive disease, treatment usually involves cystectomy and/or radiotherapy, yet results are not very good.

Renal cell carcinoma is less common but certainly compatible with long term survival if diagnosed while the disease is still confined to the Gerota's fascia. Metastatic disease has no consistently reliable therapy and results are poor.The usual presentation is painless total hematuria with or without an abdominal lump; USS is very useful to characterize the renal lump, and an abdominal CT scan is essential to stage disease.

24. BRAIN TUMOURS

Malignant brain tumours are rare. Their importance lies in their potential for producing marked derangement in mental and physical function. Headache, often in the morning, vomiting, personality change and drowsiness are the usual indicators of raised intracranial tension. Fundoscopic examination is helpful to diagnose this condition. These symptoms improve markedly with steroids and hypertonic glucose.

Seizures are a very common initial presentation and there may be focal neurological or speech defects. The investigation of choice in these lesions is a contrast enhanced MRI as a CT scan is known to miss the presence of brain tumours, especially those in the posterior fossa.

25. BONE TUMOURS

These are very rare tumours and they are very often diagnosed late simply because they are not thought of. Improved awareness of the possibility of bone cancer should lead to earlier diagnosis. While benign bone lesions like fibrous dysplasia, simple or aneurysmal bone cysts, non-ossifying fibromas are far more common than bone cancer, it bears emphasis that any atypical feature on X-rays should prompt a biopsy. While planning biopsy, site of biopsy should be such that it can be removed and does not compromise the subsequent definitive surgical procedures

26. SCREENING :

Screening for carcinomas of oral cavity, breast and cervix have an important role to play in the early diagnosis of these cancers. In military stations, SEMOs should organize such screening camps in conjunction with OC SHOs if present in the station and dental officers as well as specialist in surgery and gynaecology . Such camps will go a long way in early detection and better management.

27. NEWER TRENDS

There have been rapid gains in our knowledge about pathogenesis, diagnosis and treatment of cancer in the last two decades. Improved techniques of imaging like Spiral CT, PET and SPECT scans, Virtual endoscopy and the like have added newer perspectives to our understanding. Research and developments in immunohistochemistry, tumour markers, molecular biology, and cytogenetics have helped classify and prognosticate tumours better. Given the morbidity of various forms of treatment, it is now possible to apply therapy more selectively and specifically.

28 RECOMMENDATIONS

a) All MOs must develop a strong sense of suspicion as to the possibility of cancer.

b) Whenever a cancer is suspected, the MO should record a detailed history and conduct a thorough clinical examination.

c) If specific investigations are available locally, all attempts must be made to confirm the histological diagnosis, without undue delay.

d) All tissue blocks / slides must be sent alongwith the patient to the Oncology Centre when the patient is transferred.

e) While transferring the patient, the MO should explain regarding the possibility of prolonged treatment in the Oncology Centre and arrange necessary administrative support.

f) Constant efforts must be made to educate the troops and their families about cancer. Widely prevalent myths about this disease such as " Cancer is Incurable", " Cancer is Infectious" and "Operation spreads the cancer" must be removed.

29. CONCLUSION

Early diagnosis of cancer is a challenge as well as an opportunity. Detection of malignancies in early stages requires widespread use of simple techniques and co-ordination with the laboratory. Such concerted efforts can lead to identification of tumours when treatment is highly effective, leading to prolonged survival and cure.

The contents of this memorandum should act as a sensitizer to MOs throughout the services to the treatability of most cancers in early stages.