The Singapore Family Physician

The College of General Practitioners Singapore
Vol. XVII No. 3
July/Sept 1991

ISSN 0377-5305

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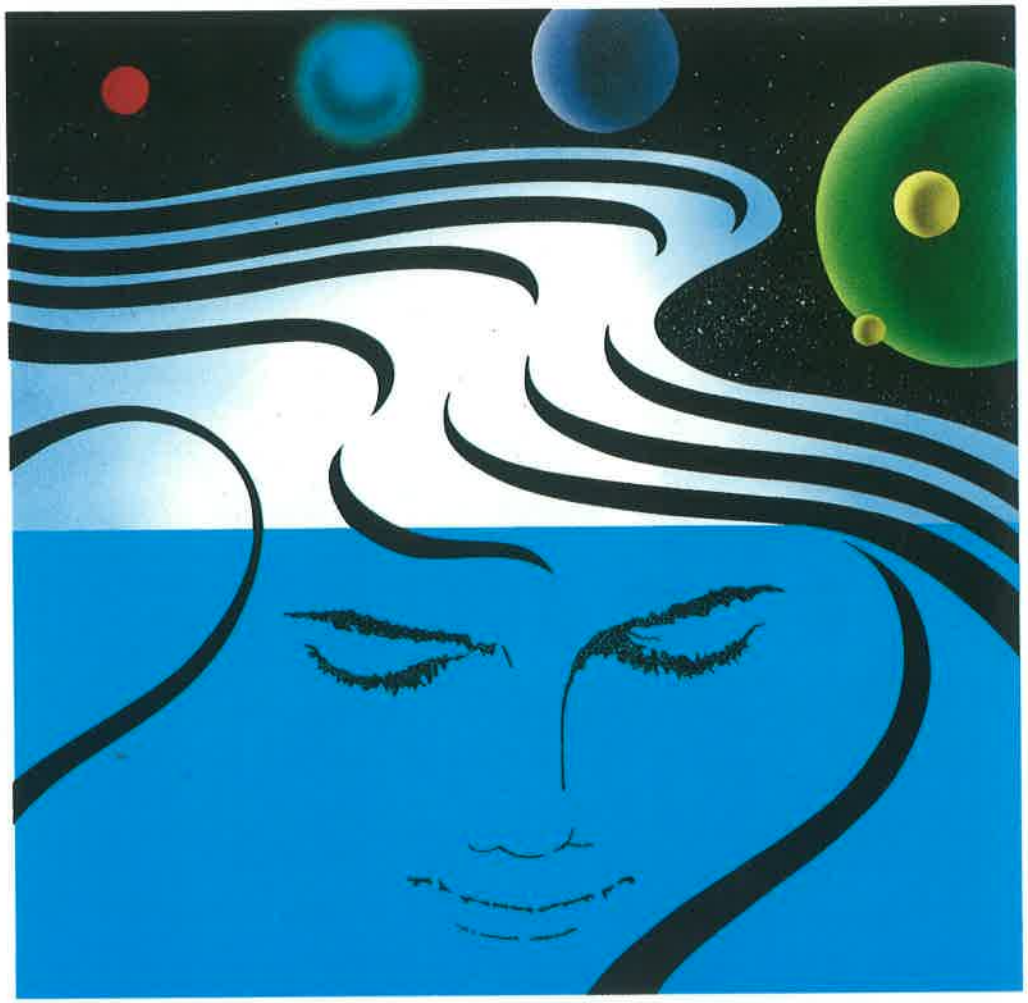

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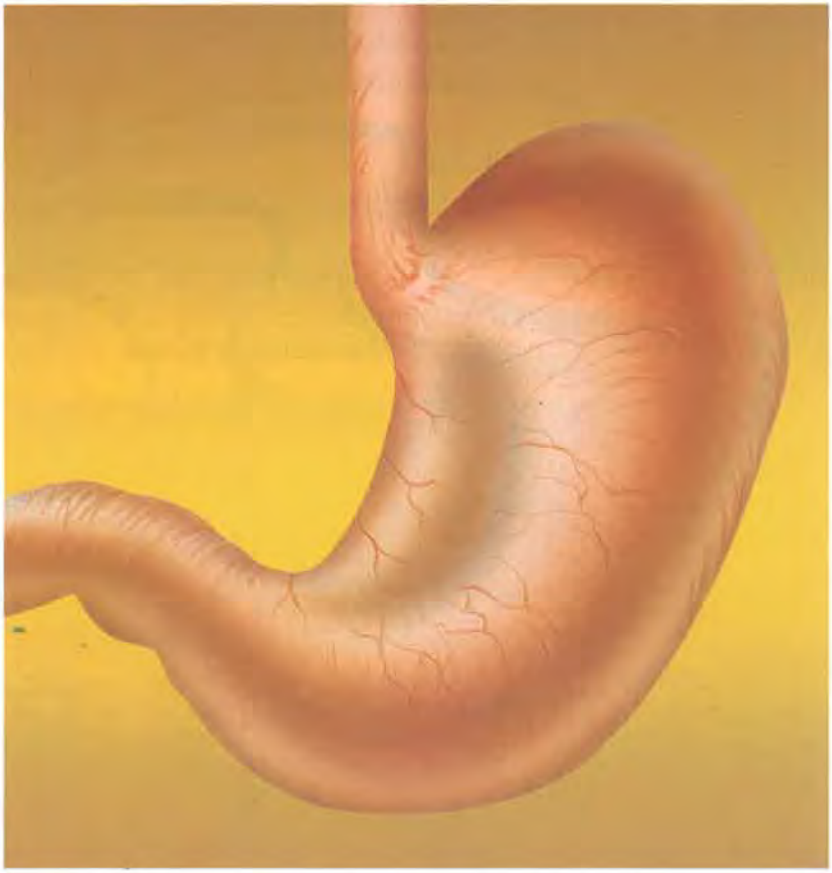

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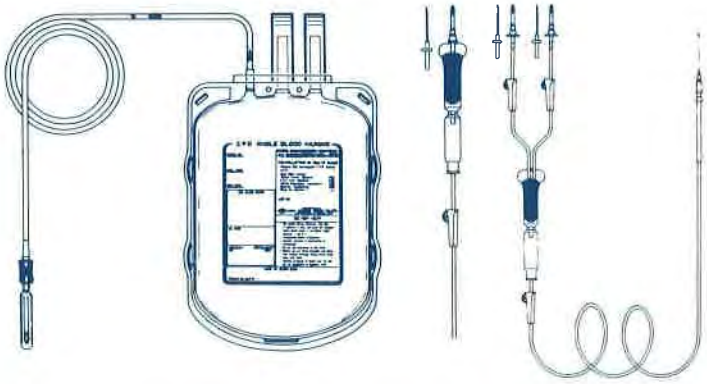

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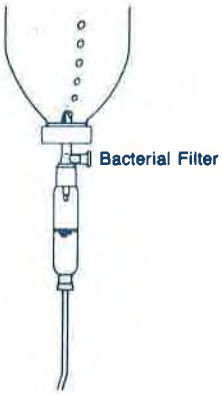

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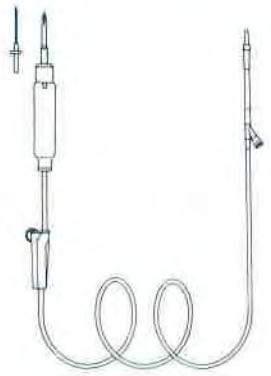

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EDITORIAL

HOUSE-CALLS AND FAMILY DOCTORS REVISITED

The controversy over house-calls by doctors rears its head every once in a while, and debate and furore is whipped up in the media by the public, doctors, the professional associations and even the Medical Council joining in the fray. The crux of the rather heated and emotive exchanges lay in inadequate differentiation being made between house-calls for emergency cases and those for non-emergencies, and what doctors and patients regards as an emergency.

In an emergency, a doctor has a moral and possibly ethical responsibility to come to the patient's help, provided of course that he is not treating another emergency. This applies to all doctors, both generalists and specialists. However, the complaints from the public are directed only at general practitioners, and the specialists have been spared their patients' chagrin, even though the specialists unilaterally decided a long time ago that they would not do house-calls.

The General Practitioner

For the general practitioner who receives a request for an urgent house-call, certain considerations are necessary. If it is clearly a case which should be handled in hospital e.g. chest pain, head injury, drug overdose or severe burns, it would suffice for him to advise the caller to send the patient straight to hospital by ambulance and give advice on any first aid necessary till the ambulance comes. Not withstanding this, if it is possible for him to get to the patient before the ambulance does, he should make every attempt to do so, even if he is ill-equipped to tackle the problem and can do no more than be with the sick person till the ambulance arrives.

If the request is made during his busy clinic hours, he has to exercise his judgement to decide where he is more needed, not forgetting his obligation to those patients in his clinic awaiting his attention, some of whom may be also seriously ill.

When the patient is known to the doctor, it will be easy for him to make the correct assessment and the appropriate response, which may vary from advice over the telephone to an urgent home visit. Herein lies the importance and value of each family appointing a Family Doctor, who can be called in an emergency or presumed emergency. The family builds up and develops a special relationship with the Family Doctor or Family Physician, who will know the patient and his family. He will thus know when he must make a house-call or when over-the-phone advice will suffice.

The Family Doctor

Visiting patients at home is one of the means by which bonds between the Family Doctor and the patient or his family are forged and strengthened. As the doctor-patient-family relationship develops over the years, the quality of health care improves. From the patient's point of view, home care can be crucial. Norman Cousins, in his book, *Anatomy of an Illness*, has movingly described the peace of mind that comes from being cared for at home, even in serious illness. For the doctor, home visits can enrich his own working life from caring for patients at their homes.

The Family Doctor will make house-calls to assess and manage his patients who are acutely ill if they are too ill, in severe pain or too old, or where there a danger of the problem being exacerbated by movement and its attendant anxiety. He will assess the need for admission to hospital, weighing the ever-increasing cost of

hospital care against his first-hand knowledge of the patient's home conditions, family function and support and other factors. Visiting his patients who have been discharged from hospital will help him assess the problems and difficulties in adapting and adjusting to the home environment.

With the increasing proportion of the elderly in the population, home visits will allow the Family Doctor to manage – treat, assess progress and monitor – his patients with chronic illnesses, advances in electronics having made it easier to bring medical technology into the home. Finally, in the case of the patient with terminal illness, regular visits by the Family Doctor are very important for the patient and his family even when apparently "nothing can be done". The doctor's visits are appreciated, not for technical reasons, but for the succour and support he provides at the family's time of crisis.

Thus, to be a good Family Doctor, a general practitioner must make a commitment to doing **necessary** house-calls as part of the contract with patients. Each doctor or practice must be responsible for his or its own patients' care, both *during* and *after* clinic hours.

How can the Family Doctor in solo practice who has to work morning, afternoon, evening and night sessions, sometimes seven days a week, do this? How does he meet his own physical, emotional, social and psychological needs, spend time with family, attend continual medical education sessions, and also be responsible for his patients' care day and night? He can take an assistant doctor or a partner or even a locum tenens to take over some of his work and duties to his patients and/or appoint a reliable after-hours service to deputise for him after his usual consultation hours. Further, several "solo" doctors in an area can arrange a roster for night calls for that district, so that the doctors can each have some free time.

What about the patients? How do they keep up their end of the contract with their Family Doctor? The Family Doctor-patient relationship is a two-way street based on mutual respect, trust and confidence. The patient must be loyal to his doctor and avoid "doctor-hopping". He must learn to differentiate between urgent and non-urgent problems, and must not abuse the contract by making frivolous requests for house-calls just for his own convenience. Patients must also trust their Family Doctor. If he, with his experience and wisdom, assesses the problem (for which the request for a house-call was made) as not being an emergency, or if he advises urgently sending for an ambulance, they must understand and must listen to and follow his advice and instructions. If the situation is a non-emergency, but the patient still has to be seen at home, they must allow the doctor to visit later, as soon as he is able to. They must also never forget that their Family Doctor is a human being and cannot be available to all his patients twenty-four hours a day, three hundred and sixty-five days a year. They must accept his assistant, partner or locum or his after-hours deputies at some times. As one doctor wrote to the local newspaper during the last debate in 1988, "an overworked and overstressed doctor is a danger to himself as well as his patients".

The Primary Health Care Doctor

Can the primary health care doctor at the government clinic be a Family Doctor? By the yardstick defined above, the answer is definitely no. If the Ministry of Health really wants to promote the concept of each family having its own Family Doctor, it must either arrange for its primary health care doctors to do house-calls for their patients, or give up the curative part of its role in the primary health care delivery system, so that Family Doctors in private practice are not burdened by requests for house-calls for members of the public who are not their patients.

MV

CASE REPORT

TRANSLOCATION OF A MULTILOAD 250 (IUCD) INTO THE RECTOSIGMOID JUNCTION IN A PATIENT WITH PELVIC INFLAMMATORY DISEASE

** S M Phua, MBBS, MRCOG*
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Abstract:

We present a 42 year old lady, who was operated for a left tubo-ovarian abscess and incidentally found to have translocation of a multiload 250 (IUCD) into the rectosigmoid junction. The translocation occurred as a result of expulsion of the device through the dilated right fallopian tube.

Keywords:

Translocation, Intrauterine contraceptive device, Pelvic inflammatory disease.

INTRODUCTION

Intrauterine contraceptive device (IUCD) is an acceptable and commonly used method of contraception. One of the rare complications of IUCD is that of translocation of the device. Translocation can occur as a result of perforation of the uterine wall or due to expulsion through the fallopian tube. Expulsion through the tube may occur through a dilated tube that has been damaged by pelvic inflammatory disease, as illustrated by the case presented.

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CASE REPORT

Madam KBK is a 42 year old lady, married with 2 children. She was referred to our hospital with a complaint of pain in the left iliac fossa. She had a pelvic ultra-sound scan by a radiologist in private practice. The scan showed multiple cysts in the left ovary. The largest cyst measured 4.0 x 3.5 x 2.5 cm. She had an IUCD inserted 5 years ago.

On examination, she was an average built, healthy lady. She was afebrile, her abdomen was soft but there was slight tenderness in the left iliac fossa. Speculum examination revealed a healthy parous cervix. However the IUCD string was missing. Vaginal examination revealed a normal size, anteverted uterus. There was a left adnexal mass which was slightly tender. There was no vaginal discharge. The ultra-sound scan was repeated and it revealed the same findings

as the previous scan. The IUCD was not detected. An abdominal X-ray was done and showed the coiled copper stem of an IUCD at the right sacro-iliac joint (see figure 1). Her haemoglobin level was 11 gm% and white cell count was 14,000. It was explained to her that she had a left ovarian mass and the nature of the mass could only be ascertained by a laparotomy. She was told that her IUCD had translocated.

At laparotomy she was found to have a left tubo-ovarian abscess measuring about 5 cm in diameter. The left tube was grossly distorted and densely adherent to the left ovary, forming an abscess. The right tube was found to be stuck to the rectosigmoid junction. The tube was also distorted and dilated to a diameter of about 1.5 cm. The right ovary was normal. The uterus was normal in size.

The fimbrial end of the right tube was dissected away from the rectosigmoid junction. A multiload 250 IUCD was found with the stem in the fimbrial end of the right tube and the horizontal arm penetrating into the rectosigmoid junction. The perforation in the rectosigmoid junction was repaired in layers. Right partial salpingectomy and left salpingo-oophorectomy was performed.

Post-operatively, the patient was on drip and suck. She was given a course of ampillicin, flagyl and gentamycin. Her recovery was uneventful.

DISCUSSION

Intrauterine contraceptive device is considered a safe and effective method of contraception (DATTA panelists 1989). However one of its most serious disadvantages is that of the risk of pelvic inflammatory disease. Pelvic inflammatory disease with the resultant salpingitis often gives rise to distorted and dilated tubes as in the case discussed. Even in asymptomatic patients, there is evidence of higher risk of salpingitis in women using IUCD (Ghosh 1989). Vanlancker et at (1987) found that inflammatory response was more common among women using copper devices than among those wearing non-copper IUCDs. Dilated and inflamed tubes serve as a route for translocation of IUCD, as illustrated in this case. The use of IUCD is contraindicated in women with pelvic infection. It is also contraindicated in women at high risk of pelvic inflammatory disease. IUCD should only be used in women who are in the middle to older reproductive years, in a stable monogamous relationship and not at risk for sexually transmitted disease (DATTA panelists 1989).

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FIGURE 1

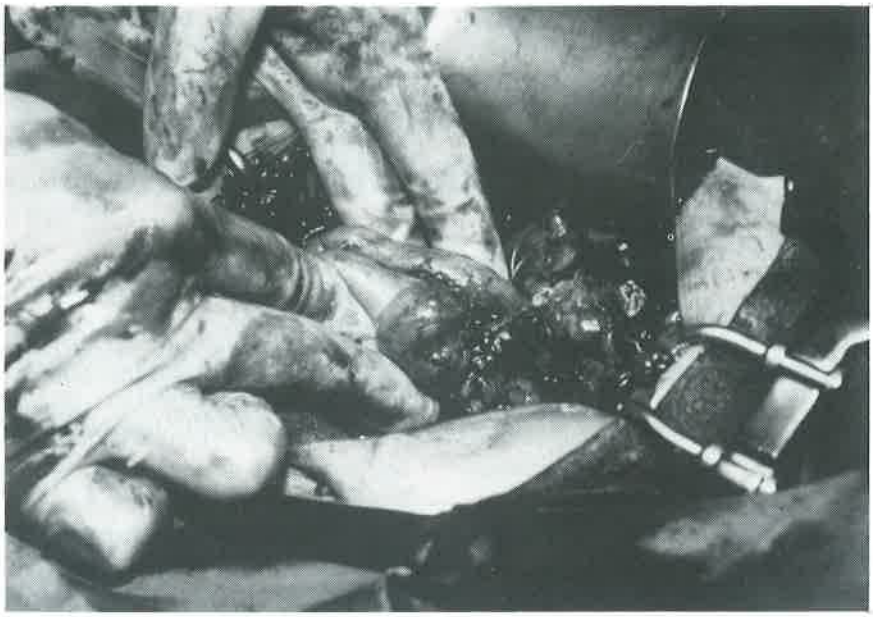
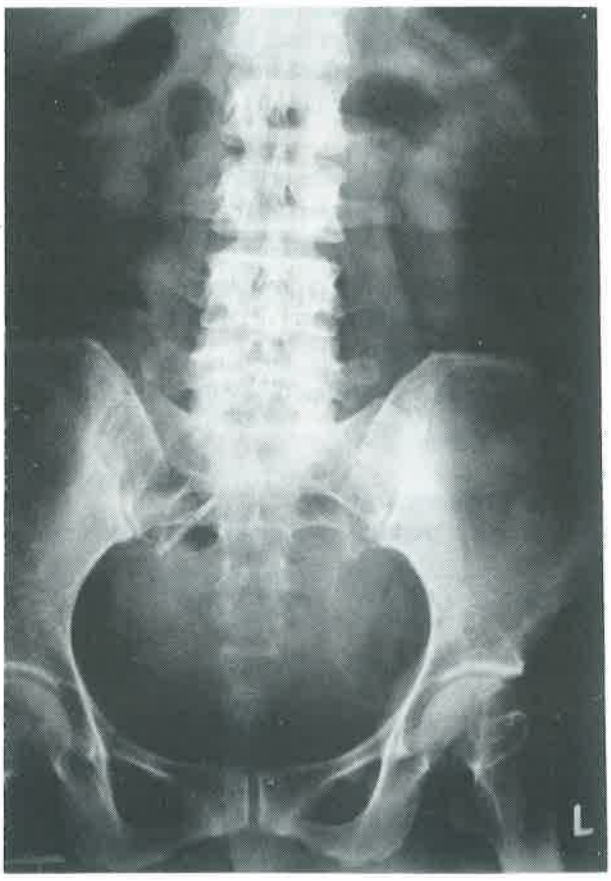


FIGURE 2



ORIGINAL

SURGICAL CONDITIONS OF THE ANTERIOR MEDIASTINUM

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Abstract:

Eighteen patients who underwent surgical procedures for anterior mediastinal pathology seen at the Division of Cardiothoracic Surgery, National University Hospital were retrospectively reviewed. The ratio of male to female patients was 2:1 with ages ranging from 19 to 64 with a mean of 42 years.

Seven patients were referred for thymectomies for generalised myasthenia gravis. Five patients were asymptomatic. The other patients had varied localized or systemic symptoms. Paraneoplastic syndromes seen in this series included myasthenia gravis, pure red cell aplasia, autoimmune haemolytic anaemia and dermatomyositis. Only twelve patients had a mediastinal mass seen on CXR.

Histological examination revealed that in the majority of cases (78%), the resected specimens were of thymic origin. The others were Germ Cell tumours (16.6%), and lymphomas (5.5%). There were 11 benign tumours and 7 malignant tumours.

Median sternotomy for total tumour resection was the main mode of therapy, with no hospital mortality and significant improvement or complete remission after thymectomy.

It is recommended that anterior mediastinal tumours should not be passively observed. Surgical procedures are recommended either for treatment or to obtain precise histological diagnosis for optimal medical therapy.

Keywords:

Anterior mediastinal tumour, myasthenia gravis, median sternotomy, thymus

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INTRODUCTION

Surgical pathology of the anterior mediastinum involves mainly the thymus gland.[1-3] Apart from a primary mediastinal mass, other lesions include those arising outside the mediastinum that are located so close they often

extend into the anterior mediastinum.[1] Surgical excision may result in the cure of several benign and malignant tumours, and with the increased success of treating unresectable malignant tumours; the establishment of a precise histologic diagnosis is important for the initiation of optimum therapy. Thus, the observation of anterior mediastinal pathology can rarely be justified.

MATERIALS & METHODS

Records of patients who underwent surgery for anterior mediastinal lesions from November 1986 to September 1990 at National University Hospital were retrospectively reviewed. Data was collected to determine the incidence and pattern of conditions seen locally with respect to epidemiology, presenting symptoms, extent of tumour at diagnosis, pathologic findings and subsequent follow-up.

A total of 18 cases were studied accounting for 10% of all non-cardiac-thoracic cases seen in the specified period. There were twelve males and six females, with the age ranged between 19 and 64 years (mean of 42). Seventeen were Chinese and one was Malay.

There were five asymptomatic patients. Seven patients presented with symptoms of generalised Myasthenia Gravis (MG) without symptoms directly related to the anterior mediastinal tumours. The other patients presented with varied symptoms as shown in Table I.

Chest roentgenograms (CXR) revealed anterior mediastinal masses in twelve patients. All six patients with normal CXR suffered from MG. Pre-operative computed tomographic (CT) scans showed positive result in twelve of seventeen cases, with evidence of local invasion by tumour in four cases. Only one patient had evidence of metastasis to the liver at the time of presentation.

Surgical resection was performed via median sternotomy in fourteen and posterolateral thoracotomy in two. Two patients had prior biopsies taken, one by mediastinotomy and the other by lateral thoracotomy. Complete resection was possible in eleven cases, of which seven were thymectomies for generalised MG. Structures involved by the invasive tumour seen at surgery are shown in Table II. Six patients required adjunctve radiotherapy and/or chemotherapy while two had chemotherapy as the main mode of therapy.

RESULTS

A summary of the histopathological findings is shown in Table III. The ratio of benign to malignant cases was 11:7. Of the seven patients with Myasthenia Gravis, 4 had normal thymuses, two had hyperplastic thymuses and 1 had an encapsulated thymoma with surrounding hyperplasia. Other paraneoplastic conditions associated with thymic pathology seen in this series included Pure Red Cell Aplasia in two patients and Autoimmune Haemolytic Anaemia with Dermatomyositis in one patient.

There was no hospital mortality and no significantly morbidity. Over an average follow-up period of 20 months, two of seven patients with malignant lesions have developed recurrences with one case of late death from advanced thymic carcinoma. All patients with benign lesions remain asymptomatic. Of the seven patients with MG, six obtained partial or complete remission after an average follow-up period of 20 months. One patient was lost to follow-up.

DISCUSSION

The differential diagnosis of anterior mediastinal masses is extensive. Most authors report thymic neoplasms (30 - 50%), lymphomas (25%) and germ cell tumours (15 - 20%)[1-3] as the commonest lesions in the anterior mediastinum. In our series, thymic neoplasms contributed to 77.7% of the anterior mediastinal tumours, with germ-cell tumours contributing to 16.6% and lymphomas, 5.6%. The apparent low incidence of lymphoma is due to its frequent wide involvement at the time of presentation,[5] thus rarely necessitating mediastinal biopsies for diagnosis. Histology of resected thymic neoplasms most frequently demonstrated thymomas, of which half were encapsulated and half were invasive. This is consistent with the results of Large and Davis.[4,5] The unusual

diagnosis of Non-Hodgkin's Lymphoma was made in one patient as fewer than 10%[6] of all Non-Hodgkin's Lymphoma are primary in the mediastinum.

Anterior mediastinal tumours were asymptomatic in 40% of the patients who were discovered to have them. These were detected incidentally on CXRs. That the presence or absence of symptoms has prognostic significance[1] is confirmed by our study with 33.3% of malignant cases being asymptomatic compared to 80% in benign cases.

Chest films are often the initial mode of diagnostic evaluation since history and physical examination often may not lead to the diagnosis. CT scans are useful for definition of morphology of the lesion and determination of invasion as shown in four of five cases with proven invasion at surgery.[7] Since precise histologic diagnosis is essential, cytology via fine needle aspiration under CT guidance was performed in two cases. This yielded inconclusive results in both cases.

Median sternotomy was the most common approach to the anterior mediastinum (77.7%). Lateral thoracotomies were done in patients with evidence of lateral masses seen on CXR and CT scans. Encapsulated, benign tumours were easily removed. However, malignant tumours were often densely adherent to intrathoracic structures making total excision impossible.

While thymectomy is an acceptable treatment for MG, disagreement exists as to its timing.[8,9] The 57.1% improvement rate and 28.6% remission rate are consistent with results available in literature.[8,9] The natural history of anterior mediastinal tumours varies from those with slow, benign growths to aggressive, invasive neoplasms that are often associated with widespread metastasis rapidly leading to death. Complete resection is the treatment of choice in thymomas, with encapsulated thymomas which are fully resected carrying the most favourable prognosis.[10] Unfortunately, only two out of four cases could be completely resected. Although one patient already had distant metastasis at diagnosis, debulking surgery was done as palliative treatment for symptomatic relief. Thymic carcinomas often cannot be completely resected due to the aggressive nature of the tumour and the extent of spread of the tumour at diagnosis as seen in our cases. Isolated mediastinal lymphomas are treated medically with chemotherapy and the appropriate therapy immediately started.[11] Thus it is important to obtain a positive histologic diagnosis via a surgical approach. This can be achieved via mediastinotomy, median sternotomy or thoracotomy.

Anterior mediastinal masses should not be passively observed because of the significant risks of malignancy and the low surgical complication rate.

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TABLE I: PRESENTING SYMPTOMS

SYMPTOMATOLOGY	No.	%
Asymptomatic	5	27.8
Symtoms related to Myasthenia Gravis	7	38.9
Cough	4	22.2
Chest pain	4	22.2
Dyspnoea	2	11.1
Haemoptysis	1	5.6
Weight loss	3	16.7
Fatigue	3	16.7
Fever	2	11.1

TABLE II: STRUCTURES INVOLVED IN INVASIVE TUMOUR

	No.	%
Pericardium	3	21.4
Lung	3	21.4
Great vessels	3	21.4
Hilum	3	21.4
Pleura	2	14.3
Phrenic nerve	2	14.3

TABLE III: HISTOLOGICAL FINDINGS

HISTOLOGY	No.	%
Normal Thymus	4	22.2
Thymic Hyperplasia	3	16.7
Thymoma	4	22.2
Thymic carcinoma	3	16.7
Teratoma (Benign)	2	11.1
Malignant Germ Cell Tumour	1	5.6
Non-Hodgkin's Lymphoma	1	5.6

ORIGINAL

THE MANAGEMENT OF ANAL FISTULA & ABSCESS

Seow-Choen, MBBS, FRCS (Ed), AM.

INTRODUCTION

Although recognised as a distinct surgical entity for several millenia, anal fistula continues to be very troublesome to both surgeons and patients.

EPIDEMIOLOGY OF ANAL FISTULA

The great majority of studies on anal fistula are on small groups of selected patients. Males predominate in most series with a male to female ratio varying from 2:1 to 7:1. Age distribution is spread throughout adult life with the maximal incidence between the third and fifth decades.

PATHOGENESIS OF ANAL FISTULA

The cryptoglandular hypothesis for the pathogenesis of anal fistula postulates that anal fistula and abscess begin in an infected anal intramuscular gland and spread to the rest of the perianorectal tissues.

CLASSIFICATION OF ANAL FISTULA

Accurate and meaningful description of complex fistulae can be very difficult. A good system of classification however should provide accurate and easily understood information that will permit wide understanding of what is being described, enable therapeutic options to be compared and therefore correct surgical procedures to be undertaken.

A very widely used system of classification relates the fistula to both the anal glands and the anal sphincters and levator ani. In this system anal fistulae are divided into five major groups. Intersphincteric fistulae which track in between the internal and external anal sphincters, transphincteric fistulae that penetrate the external sphincter at varying levels, suprasphincteric fistulae which pass upwards in the intersphincteric plane to loop over the top of the puborectails and emerge through the levator ani to reach the skin, and extrasphincteric fistulae which track outside the sphincter mechanism. The last group comprises fistulae that are found in the subcutaneous plane and which are thus called subcutaneous or superficial fistulae.

Fistulae are classified according to the course taken by the main or primary track which is the track linking the internal and external openings. Secondary tracks are defined by qualifying the primary tracks eg, transphincteric track with a supralevator extension. The term 'secondary tracks' or 'extensions' is usually used for important extensions from the main or primary track. An important type of secondary track is due to circumferential spread or horseshoeing and mainly takes place in the intersphincteric, ischiorectal or the supralevator planes.

Evaluation of anal fistula

Accurate preoperative delineation of the anatomy of anal fistula is important if post

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operative recurrence or incontinence is to be avoided. The five essential points to be obtained from a clinical examination of an anal fistula were enumerated as long ago as 1900. These are the location of the internal opening, the external opening, the primary track, the secondary track and the presence or absence of underlying disease. The external opening is usually obvious so that the patho-anatomy of most fistulae can be delineated clinically by locating the internal orifice and defining the presence and type of secondary extension that may be present. Digital examination has been shown to be up to 79%, 84% and 71% accurate in defining the internal opening, primary tract and secondary track of anal fistulae respectively. Poor preoperative resting tone or voluntary anal contraction indicate an already compromised internal and external anal sphincter function respectively and mean that conservative surgery may be necessary to avoid anal incontinence.

Systematic and careful examination is thus always important and will give the clinician important data about the patho-anatomy of the fistula. Intersphincteric tracks tend to open externally close to the anal verge whilst transphincteric and more complicated fistulae will tend to open further away. Goodsall's rule states that fistulae having their external opening, behind a plane passing transversely through the centre of the anus usually have their internal aperture in the midline posteriorly while those with external orifices anterior to this plane have internal openings immediately opposite. Internal openings may be felt as indurated nodules or pits leading to indurated tracks or they may be seen to exude pus when the tracks or abscesses are gently massaged. Fibrosis is a frequent pointer to the site of the internal opening. Gentle use of probes along the dentate line or through the external opening may be useful in locating internal openings.

Besides the use of probes, intra-operative injection of methylene blue, saline or other solutions has been used to help find the internal opening.

Sigmoidoscopy should be performed as part of the clinical routine to uncover associated underlying pathology. Barium enema or colonoscopy however need not be routine as their yield is low in anal fistulae and they should be performed only when indicated.

MANAGEMENT OF THE ACUTE ANORECTAL ABSCESS

The term fistulous abscess was introduced in 1954 to stress that anal abscesses and fistulae are a spectrum of the same disease process. Traditionally, anorectal abscess has been treated by drainage ether via a stab incision or saucerization. With the wide acceptance of the cryptoglandular aetiology for anal suppuration primary or delayed fistulotomy with excision of the offending anal gland has taken on great significance. Anorectal abscess is said to be cured permanently only when removal of crypts and ducts is performed in addition to adequate drainage. The high incidence (48%-62%) of recurrent abscesses of fistulae following simple incision and drainage is said to be reduced to 0% to 3.6% following the application of immediate fistulotomy. It has also been shown that where a fistula was not found during the initial drainage, a subsequent search for the fistula need be conducted only if culture of the pus obtained during the drainage procedure grew gut-specific organisms. Anorectal abscesses which grow skin-derived organisms only are not associated with a fistulae and therefore an abscess which grow these organisms only need not be subjected to a second procedure.

COMPLICATED FORMS OF ANORECTAL FISTULOUS ABSCESS

Three factors in complicated fistulae tend to perpetuate the disease process. Firstly, the presence of the disease focus within the anal intramuscular gland or elsewhere within the anal canal. Secondly, the constant contamination resulting from the high intra-rectal pressure forcing intraluminal content through the internal opening and lastly, repeated surgery itself may create complicated tracks if not carefully or correctly performed.

Women particularly are prone to sphincter damage during surgery for anal fistulae and extra care must be taken in female patients.

Although complicated fistulous abscess are viewed with fear by many non-specialist

surgeons, proper treatment should result in a low recurrence rate. Incision and drainage or primary fistulotomy may be used for the primary fistulous abscess. Setons can be used whenever laying open is considered dangerous in terms of subsequent anal continence. Secondary extensions may be drained by counter incisions, complete lay open, insertion of various types of surgical drains or by setons. Extensive laying open however is not necessary as healing will then be delayed and hospitalisation unduly prolonged as well as causing anal deformity and incontinence. Defunctioning colostomy may required occasionally either because adequate fistulotomy will cause severe anal incontinence or because of severe anal sepsis. Sometimes patients with very problematic fistulae after multiple surgery may prefer the construction of a permanent colostomy. Indeed some patients may require proctectomy because of chronic disability if all else fails.

MASSIVE ANORECTAL SUPPURATION

Anorectal abscess can precipitate extensive and severe infection which may lead to death, especially in the obese diabetic. Surgeons must be specially careful with diabetics presenting with anorectal suppuration. These patients may be septic or moribund on presentation or they may become rapidly so if not adequately treated. These patients can be recognised by perianal crepitation, erythematous indurated perianal skin, blistering or gangrene or abdominal wall induration, tenderness or a vague mass. Plain abdominal films may show soft tissue gas. Leucocytosis with a marked shift to the left may be present. These patients require radical debridement of infected or necrotic tissue.

MANAGEMENT OF CHRONIC ANAL FISTULA

Approximately 85-95% of all anal fistulae are easy to treat. Superficial, intersphincteric and low transphincteric fistulae are thus readily managed by either classical lay open (fistulotomy) or by excision (fistulectomy) with a low recurrence rate and with minimal risk of post operative incontinence. The 5-15% of anal fistulae that are difficult to manage will have to be dealt with by other methods.

Setons can be used in patients with complex fistula, or in high fistula, or in problematic or difficult fistula where the landmarks have been so distorted that continence cannot be guaranteed if fistulotomy is performed, or if the surgeon opts to be cautious. Setons can be used in several ways. Firstly, they can be applied loosely when used as drains, or secondly, to stimulate fibrosis around the track or thirdly, as markers to enable better post operative assessment by outlining the track, and thus enable better assessment of the fistula and the external sphincter and puborectalis. They can also be applied tightly if used to cut slowly through the track.

The mucosal advancement flap technique in the treatment of anal fistulae may also be used in selected cases of complicated anal fistulae and its advantages include a reduction in the duration of healing, no additional damage to the anal sphincter and no risks to deformity of the anal canal and finally that it is a one stage procedure if primary healing is achieved. The techniques involves a total fistulectomy or coring out of the primary and secondary tracks, excision of the internal opening and closure of the rectal defect with a rectal mucosal advancement flap.

MALIGNANT TRANSFORMATION IN CHRONIC ANAL FISTULA

Chronic anal fistulae can undergo malignant change, and granulation tissue or better multiple biopsies of fistula track or fistulectomy specimen must be examined histologically in patients with long standing fistulae, especially if mucinous discharge of mucin globules are seen during surgery. These tumours are slow growing, locally invasive and usually are of low grade differentiation. Metastases occur most frequently to the inguinal region. Radical resection of the anorectum offers the only hope of cure as local excision results in a high recurrence rate.

CONCLUSION

Anal fistula is a common cause of chronic irritation to both patients and surgeons. Treatment failure may be decreased by a good appreciation of normal anorectal anatomy and

fistula patho-anatomy as well as a wide and practical knowledge of the possible treatment regimes.

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ORIGINAL

THE GENERAL PRACTITIONER AND DRUG ABUSE

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Summary:

This article was written to give a brief but comprehensive review of the drug problem with special reference to the situation in Singapore. General practitioners are involved in the management of this problem at several levels and to varying extents. This article provides information to those who are interested in the work. It covers the definitions, classification, histological aspects and the present situation in Singapore. It also deals with factors associated with drug abuse, the medical aspects of the various substances abused, the legal aspects, treatment and rehabilitation of drug abusers, and the voluntary organisations available to help drug abusers in Singapore. Lastly it discusses briefly the role of the family physician in the management of drug abuse.

INTRODUCTION

In Singapore, the strict laws on trafficking of drugs has kept the nation relatively drug free. Nevertheless it remains a latent danger amongst the young and adventurous individuals. As the frontline doctor, the general practitioner has to be vigilant to the drug-abusing patient. Often he also has the challenging task of counselling the patient who is a drug abuser and his family. Up to date information on this subject will be a help. This paper reviews the predisposing factors, effects of drug abuse, the law on drug abuse, treatment and rehabilitation of drug abusers, the role of the Singapore Anti-Narcotics Association as well as the role of the family practitioner.

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DEFINITIONS

Defining drug abuse is not an easy task. The World Health Organisation Expert Committee, in its attempt at devising a system of nomenclature and classification, underwent several revisions to arrive at the present definitions, which are by no means perfect and without criticism. In 1957, a distinction was made between *drug addiction* and *drug habituation*. This led to some confusion and the term drug dependence was used to replace both in 1964. The 1964 definition of 'drug dependence' made no distinction between *dependence* and *abuse*, and was thus redefined in 1969. The following are the definitions currently accepted:

(a) A **Drug** is any substance that, when taken into the living organism, may modify one or more of its functions.

(b) **Drug Abuse** is persistent or sporadic excessive use of a drug inconsistent with, or unrelated to, accepted medical practice.

(c) **Drug Dependence** is a state-psychic and sometimes also physical – resulting from the interaction between a living organism and a drug. This is characterised by behavioural and other responses that always include a compulsion to take the drug, on a continuous or periodic basis, in order to experience its psychic effects, and sometimes to avoid the discomfort of its absence.

Tolerance may or may not be present. A person may be dependent on more than one drug.

(d) **Tolerance** is the phenomenon of dose increase to maintain the same drug effect.

(e) **Physical Dependence** is an adaptive state that manifests itself by intense physical disturbances when the administration of the drug is suspended.

(f) **Psychic or psychological dependence** is the intense craving and an urge to seek periodic or continuous administration of the drug to produce a pleasure or to avoid discomfort.

CLASSIFICATION

Dependence-producing drugs can be classified into the following categories:

(a) **Opiates**

These include opium, morphine, pethidine, heroin, methadone. Some, e.g. morphine and pethidine have important medical uses.

(b) **Sedatives & hypnotics**

Barbiturates and benzodiazepines are the common ones abused.

(c) **Cannabis (Marijuana)**

This is known by various names e.g. ganja, hashish, hemp, pot, weed and grass.

(d) **Stimulants**

Amphetamines and related substances, and cocaine.

(e) **Hallucinogens**

LSD (lysergic acid diethylamide) is the best known in this group.

(f) **Volatile Substances**

The volatile compounds commonly misused are:

(i) Adhesives – e.g. toluene, acetone

(ii) Aerosols – e.g. halons, methylene chloride

(iii) Solvents – e.g. trichloroethylene

(iv) Fuel gases – e.g. butane, propane

HISTORY OF DRUG USE IN SINGAPORE

Opium consumption in Singapore dated from the founding of modern Singapore in 1819, when the signing of the treaty establishing it was accompanied by gifts including opium. It was brought in by the British East India Company. Its use was legal and the Government had the monopoly in its trade. Opium users were registered and could purchase opium from Government Chandu (prepared opium) Retailing Shops. There were 16,552 registered addicts in 1941 – most of whom were Chinese – out of an estimated population of 770,000, which gives a minimum prevalence rate of 2.15%. The actual number of addicts were of course higher, as registration of addicts officially stopped in 1934. After the Second World War, the smoking of opium was made illegal by the implementation of the opium and Chandu Proclamation No. 43. It became an offence punishable by fine of imprisonment.

Morphine was introduced between 1890 and 1900. The parenteral mode of morphine use was noted as far back as in the early 1900s. It was used by some as an antidote to opium. In the 1950s, morphine dens sprouted in the poorer sections of Singapore; the majority of abusers were opium addicts who found opium too weak for their needs. The open sale of morphine was banned in 1960. The first death attributed to morphine injection in Singapore was in 1973. The victim was a 17 year old boy who started using cannabis and methaqualone pills when he was 15.

Heroin was first noticed to be a drug of abuse in the early 1970s. In 1977, Operation Ferret in Singapore brought the heroin abuse problem under control till the late 1980s, when there was a resurgence of the number of addicts

arrested. The Anti Drug Abuse Campaign was launched in 1989 to counteract this trend.

Marijuana was used by certain Indian and Pakistani labourers. It was reported variously as a 'medicinal' drug, an aphrodisiac and an 'energiser'. Its abuse reached an alarming proportion in the 1960s amongst the young people. It has since decreased.

Volatile substance abuse in Singapore was first noticed in the mid-seventies. The first death was reported in 1977.

PRESENT SITUATION IN SINGAPORE

Profile of Drug Abuse

Heroin is the main drug of abuse. 5,220 heroin addicts were arrested in 1988, comprising 91.3% of all drug offenders arrested. Current heroin addict population is estimated to be about 9,000, compared to 13,000 in 1977. New addicts accounted for 23% of all heroin addicts arrested in 1989 compared to 67% in 1977. Unlike the West, less than 2% of addicts undergoing detoxification in Singapore showed severe withdrawal symptoms, indicating that most of the abusers were not heavily addicted. This is related to the finding that the majority of the offenders arrested are smokers, consuming an average of one straw (0.05 gm) per day. There are very few intravenous heroin users in Singapore.

Cannabis ranks a distant second (5.5%) as a drug of abuse in Singapore, followed by opium (2.8%) and tranquilisers (0.4%), according 1988 arrest figures. Four hundred and twenty four volatile substance inhalers were arrested in 1990 (1,112 in 1987). Rohypnol (Flunitrazepam), and Mandrax (methaqualone), popular in the late 1970s, are no longer much abused.

Profile of Drug Offenders

This has not changed much over the years. The majority of drug offenders are from the lower socioeconomic background, with little formal education. As at March 1991, 3% of drug takers under supervision had no formal education, and 70% attended primary school only (more than half did not complete primary education). Only 5.5% completed secondary school. None had tertiary education. Most of the drug addicts were unemployed or held odd jobs. More than 90% of addicts are males.

The age and ethnic distribution of heroin addicts have changed slightly in the last 10 years. In 1977, 31.4% of drug offenders arrested were below 20 years old, compared to 10.4% in 1988. 46% of heroin addicts arrested in 1988 were in the 20-29 age group. An emerging trend noted is the increase in the proportion and number of Malay heroin addicts arrested. Between 1983 and 1985, Malay heroin addicts comprised 31.8% of the total number of addicts. In 1989, 49% of addicts arrested were of Malay origin. In absolute terms the number of Malay heroin addicts arrested rose from 480 (total number of addicts arrested: 2,986) in 1983 to 2,182 (total 4,449) in 1989. The proportion of new Malay addicts increased from 40% in 1983 to 60% in 1989.

Opium smokers are mainly Chinese. The majority are males over 50 years of age. Inhalant abusers are generally younger (15-19 years), and this has not changed over the last 10 years. Males comprised 88% of those detected as at April 1991. More than 80% were Chinese.

PREDISPOSING FACTORS

Many theories have been put forward to explain why some people take drugs. The WHO Expert Committee on Drug Abuse stated in its twentieth report that no single 'cause' of taking drugs has been demonstrated but that persons who take dependence-producing drugs apparently do so from a wide variety of stated and perhaps unconscious reasons at various times. The following are some of the factors associated with the nonmedical use of drugs:

Individual Factors

Peer group pressure, pleasure and curiosity are the main risk factors resulting in illicit drug use in the young. Becker, in his study on marijuana use in jazz musicians and young people, suggested the social learning process in drug abuse. A young person has to be introduced to the drug and taught its use and effects, usually by his friends. Other predisposing factors to drug

abuse include low self-esteem, poor academic achievement, lack of ambition and not practising any religion. There is no consistent personality type prone to drug dependence.

Family Factors

The extent of the role to which the family unit plays in causing an individual to take drugs remains unclear. Though there is little doubt that a disturbed upbringing increase a person's vulnerability, it is not inevitable that he will take drugs. In spite of a considerable amount of research, it has not been proven that the family is the root cause of drug misuse. It is observed that whilst family disruption may be a factor in individual cases, drug misuse often begins at an age when family influences decline and are superseded by other factors, such as peer group pressure.

Parental example, however, have been found to influence the development of drug use in their children. Studies performed at the New Jersey Medical School between 1969 and 1974 showed that parental use of mood-altering drugs was associated with a two to sevenfold greater likelihood of illicit drug use in the children. Similar tendency is noted in children whose parents are heavy tobacco smokers (Lavender & Scheffet, 1973), who are alcoholics (Rosenberg 1972), and who are liberal in their sue of medicines to treat both physical and psychological problems (Blum, 1969).

Community Factors

Social deprivation, adverse influences and the ready availability of a drug have been shown to be contributory factors. Drug use may lead to crime and vice versa. Longitudinal studies in America have shown that the amount of crime committed during periods of active drug use far exceeded that committed during drug-free periods. Du Pont et al reported that treatment of drug addiction can result in a decrease in crime rate. There is a known association between problem drug use and unemployment. Certain jobs carry a high risk of drug abuse.

EFFECTS OF DRUG ABUSE

Psychosocial Effects

For dependent drug takers, the taking of drugs and maintenance of their supply soon become the first priority in life. This results in family discord, decline in work performance, financial problems, trouble with the law, and isolation from normal supporting systems.

Psychological effects include lowered self-esteem from inability to stop taking drugs, the projection of self-hatred resulting in verbal and physical aggression towards others, including children. Drug abusers also exhibit aggressive behaviour towards themselves, overdoses being one such behaviour.

Pharmacological Effects

These are varied, and depend on the individual classes abused.

OPIATES

Opium is the sun-dried milky white exudate from the poppy. *Papaver somniferum.* **Morphine**, a constituent of opium, is 20 times stronger than opium. **Heroin** (diacetylmorphine) is a semi-synthetic derivative of morphine. It was originally produced in the search for a 'safer' drug than morphine, but turned out to be 10 times more potent and more addictive to its greater lipid-solubility. Common street names of heroin include *peh hoon, ubat aboh, asam* and *barang*. Methods of administration include spiked cigarettes, where heroin is inserted into the end of the cigarette and smoked; 'chasing the dragon', when heroin is placed on a piece of tin foil, heated over a flame and the smoke inhaled via a straw; 'playing the mouth organ', which is similar to 'chasing the dragon', with the straw replaced by a match box cover. Mainlining, that is, intravenous injection, of heroin is not popular in Singapore.

General Effects on the Body

Opiates act mainly on the central nervous system and the muscles. Effects produced are mainly depressant and include analgesia, euphoria, sedation, drowsiness and lethargy. Other effects include pupillary constriction, bradycardia, vomiting, constipation and flushing of the skin. Heroin has a powerful analgesic property, but its capacity to produce euphoria leads to greater tendency for abuse.

Problems of Dependence

Physical dependence manifests as withdrawal symptoms when there is abrupt cessation of regular use. These include restlessness, insomnia, pain in the muscles and joints, running nose and eyes, sweating, abdominal cramps, vomiting, diarrhoea. Accompanying signs include mydriasis and tachycardia. The effects begin about 6-12 hours after the last dose, and reach a peak after 36-48 hours. **Psychological dependence** manifests as a subjective craving to experience the effects of the drug, to provide a feeling of well-being and to escape from reality. Dependence leads to **tolerance**, which in turn leads to overdose and death.

Detection of an Opiate Abuser

There is no single discriminatory symptom or sign. A high index of suspicion is needed. Signs include rawness around the nostrils in those who inhale the drug, and needle tracks and thickened veins in the mainliners. Behavioural changes in work or school may be noticed.

SEDATIVES AND HYPNOTICS

These drugs are commonly taken for anxiety and insomnia. A sedative produces calmness by reducing the level of wakefulness. When given in a big dose, it has a hypnotic effect.

Barbiturates

These were the main hypnotics abused in the 1960s and 1970s, and are uncommon in present-day Singapore. They produce sedation by depressing unselectively all areas of the brain. They also produce an euphoric effect. Prolonged intake suppresses sleep, and causes tolerance. It also results in dependence. Sudden stopping of the drug may cause convulsions and death.

Benzodiazepines

These are currently the most commonly prescribed drugs for anxiety and insomnia in Singapore as well as the rest of the world. They are rapidly absorbed and metabolised in the liver. A small dose produces an anti-anxiety effect and a larger dose a hypnotic effect. Unlike barbiturates, that act by selectively depressing the areas of the brain connected with anxiety. Flunitrazepam (Rohypnol) was abused for its euphoric effects. Tolerance and mild dependence can develop. Withdrawal effects include rebound anxiety and insomnia.

Other Drugs known to be abused include paraldehyde, chloral hydrate and methaqualone (MX pills).

CANNABIS (MARIJUANA)

Marijuana is obtained from the flowering tops and the leaves of the plant *Cannabis sativa*. The resin of the plant contains the active ingredient, tetrahydrocannabinol. Preparations of the drugs are in 3 grades, viz (a) **Bhang**, the least potent, from uncultivated plants, and has a low resin content; (b) **Ganja**, second grade , from carefully selected cultivated plants, with a higher quality and quantity of resin; and (c) **Hashish**, the most potent, obtained from the tops of matured plant.

Effects of Marijuana

The drug is more potent when smoked than when taken orally. Effects are felt within a few minutes and peak at 30 minutes. The drug is concentrated in fatty tissues of the body, including the brain, and excreted in the urine. There is initial euphoria followed by calmness or drowsiness. Characteristic features are altered perception of time and enhancement of various sensations. There is also impairment of short term memory, muddled thinking and poor concentration. Sometimes the abuser may experience unpleasant or nightmarish sensations ('bad trip'). Physical effects include tachydardia, hypertension, conjunctival injection, muscle weakness and dry mouth. Behavioural abnormalities schizophrenic-like illness can occur. **Physical dependence** is rare, but sudden stopping of the drug in chronic users may result in withdrawal symptoms e.g. sweating, tremors, restlessness, nausea and disturbed sleep. **Psychological dependence** is more common, and is usually mild, manifested as a compulsion to smoke the drug. **Tolerance** can occur. "Reversed tolerance', whereby the individual needs less and less of the drug, has also been noted to occur.

STIMULANTS

Amphetamines and cocaine are central nervous systems stimulants and have almost identical central excitatory and peripheral effects, except that the effects of amphetamines last longer and cocaine has local anaesthetic action. Pure stimulant abusers are uncommon in Singapore.

Amphetamines

Amphetamines are abused because of their ability to combat fatigue and enhance the activities that require physical exertion. First synthesised in 1887, amphetamines are actually a family of compounds including methamphetamine and dextroamphetamine. They were first marketed in 1931 as nasal decongestants, when the ability to produce sleeplessness was noted. Oral and intravenous forms are available. Current Therapeutic indications are: (a) narcolepsy, and (b) hyperkinetic behaviour in brain-damaged children (paradoxical effect).

Effects of amphetamine are apparent about 30 minutes after oral ingestion. The drug remains in the body for 24 hours or longer. It is concentrated in the brain, and is excreted both unchanged and as its metabolite. Amphetamine raises the blood pressure and causes arrhythmia, slowing of intestinal movement and constipation. It also increases metabolic rate, and so users sometimes have a slightly raised body temperature. Effects on the brain include increased wakefulness, alertness and a decreased sense of fatigue. Toxic side effects include generalised fits and stroke. **Amphetamine psychosis** may occur, characterised by paranoid delusion, auditory and visual hallucinations. Such patients may become suicidal or violent.

Psychological dependence is very common, because abusers find the stimulant effects pleasant. **Tolerance** and overdose occur. **Physical dependence** and withdrawal states are not seen with amphetamine abuse, but acute termination of the drug may lead to a 'crash', with accompanying lethargy, social withdrawal and depression.

Cocaine

Cocaine is not commonly abused in Singapore. It is derived from the leaves of the shrub, *Erythroxylus coca* or *E. Novgranatense*. It was chewed by the South American Indians since about 2500 B.C., for the anti-fatigue and anti-hunger effects. A tea made from coca leaves can be used to treat mountain sickness. Coca contains 0.5-1.5% cocaine.

There are 3 main types of cocaine preparations, namely :

(1) **Coca paste** (pasta, basuko) – the first extraction product during the manufacture of cocaine, containing 40 - 90% cocaine sulphate. It is usually smoked with marijuana or tobacco;

(2) **Cocaine** (coke, snow) – derived from the treatment of coca paste with hydrochloric acid, containing more than 98% cocaine hydrochloride. It is a white powder which may be sniffed, taken orally or injected;

(3) **Free base** – alkaloid of cocaine HCI. It has a lower vapourising point than cocaine hydrochloride, and thus less is lost when it is heated and inhaled.

Cocaine produces stimulant effects resembling those of amphetamine. It induces a sense of euphoria, together with feelings of increased confidence and energy. There is tachycardia, mydriasis and raised body temperature. One small dose lasts for about an hour, followed by a phase of depression, lethargy and irritability. The abuser has insomnia, paranoid ideation, and may be aggressive. Tactile hallucination is sometimes experienced. 'Formication' is quite characteristic of the long-term abuser. It is described as the sensation, sometimes visual, of small animals e.g. worms, ants, lice, crawling all over the body, the so-called 'cocaine bugs'. **Psychological dependence** occurs but there is no physical dependence. Mild anxiety and depressive symptoms are present on withdrawal.

HALLUCINOGENS

These are sometimes called 'psychedelic drugs'. They produce mainly visual hallucinations. The group comprises: (1) **Synthetic drugs** – LSD, mescaline, phencyclidine and analogues, and (2) **Naturally**

occurring drugs – magic mushrooms, fly agaric, morning glory seeds, grated nutmeg and mace, and ergot. Naturally occurring psychedelics have been taken for their effects for centuries.

D-lyseergic Acid Diethylamide (LSD)

The discovery of LSD in 1938 by Albert Hoffman marked the introduction of the first synthetic psychedelic. LSD is the 25th analogue of ergot, hence the name LSD25. It was marketed by Sandoz in the 1950s for treatment of drug and alcohol dependence. The misuse by young people in the 1960s led to higher legislation and control. Its use is almost non-existent in Singapore.

Sympathomimetic effects of LSD occur after 15-20 minutes of taking the drug, viz. mydriasis, raised blood pressure and tachycardia. There may be tremors, piloerection, weakness, nausea and a raised body temperature. Psychological effects occur in about 40-60 minutes. There is much individual variation. These include euphoria followed by depression and anxiety, unmotivated laughing sometimes accompanied by tears, a feeling of well-being or ecstasy, and a sense of oppressive malaise and despair, to name a few. Effects of the drug last 8-12 hours. The feeling of profound depression may lead to suicide. 'Bad trips' may occur. These usually happen in individuals with an unstable personality. The most common effect is an acute panic reaction. 'Flashbacks' are characteristic of LSD use, and refer to spontaneous recurrences of the original LSD experience long after the acute effects have worn off. They may occur after a single dose and may be as frequent as several times a day. Flashbacks have been observed to accompany periods of stress and anxiety. They are usually self-limiting and tend to diminish in frequency, intensity and duration with time. Usage of other substances e.g. marijuana may precipitate flashbacks.

Tolerance develops rapidly and is lost as rapidly after discontinuation of the drug. There is no LSD withdrawal syndrome.

VOLATILE SUBSTANCES

Volatile substances most abused are solvents. Glue sniffing is the most common. Other substances sniffed include Tipp-Ex thinners (trichloroethylene), lighter fuel (butane, propane), nail polish remover (acetone), aerosols (a mixture of volatile compounds).

The commonest pattern is adolescents and school children using glue meant for repairing puncture bicycle tyres. Typically, they gather in small groups, pour a can of glue into a plastic bag, and inhale directly through the mouth. The bag is passed from person to person. One small can of glue, which contains 99% toluene, costs $2 – $3.

Effects of Volatile Solvents

Volatile solvents are rapidly absorbed and easily reach the brain. They are excreted through the liver and kidney in 2-3 hours, mainly as hippuric acid. Initially, they produce an excitatory effect. The abuser may appear drunk. This followed by auditory or visual hallucination. Later cerebral depressant effects appear, with disorientation, blurred vision, dizziness, slurred speech, ataxia and drowsiness. Loss of consciousness, fits and deaths occur in overdose. **Psychological** and later **physical dependence** develop. **Tolerance** occurs.

THE LAW AND SUBSTANCE ABUSE

Narcotics: Misuse of Drugs Act 1973 (Amendments 1975 & 1990)

In Singapore, it is an offence for a person to prepare, posses, consume, or sell controlled drugs. Drug abusers and drug traffickers are dealt with differently.

Punishment of Drug Traffickers/Possessors

The death penalty is mandatory for trafficking, manufacturing, importing or exporting of more than: (a) 30 gm of morphine, (b) 15 gm of heroin, (c) 30 gm of cocaine, (d) 500 gm of cannabis, (e) 200 gm of cannabis resin and (f) 1.2 kg of opium. For possession of less than the above, the punishment is jail sentence of 20 - 30 years and 15 strokes of the cane. For other situations not mentioned above, the punishment is minimum of 2 years imprisonment and 2 strokes.

There is also a presumption clause which states that a person caught in possession of 2 gm

of heroin, 3 gm of morphine, 3 gm of cocaine, 15 gm of cannabis, 10 gm of cannabis resin, or 100 gm of opium would be deemed to have the drugs in his possession for trafficking.

Penalty for Drug Abusers

Penalty includes imprisonment of up to 10 years, a fine of $ 20,000, or both. This is usually not carried out, as drug abusers are regarded as victims and not criminals. The Misuse of Drugs (Approved Institutions and Treatment and Rehabilitation) Regulations, 1976, allows for compulsory rehabilitative treatment of drug abusers arrested.

Enforcement Agencies

The **Central Narcotics Bureau** coordinates and plans for the disruption of drug supplies. They also supervise the compulsory rehabilitation of drug abusers. The **Police** arrest the drug abusers and traffickers. The **Customs and Excise Department** prevents and detects the smuggling of illicit drugs into the country at the various entry points. The **Prisons Department** is responsible for the running of the Drug Rehabilitation Centres.

Treatment of Drug Abusers

Identification of Drug Abusers

All drug abusers arrested are sent for compulsory rehabilitation in one of the Drug Rehabilitation Centres (DRC). Medical evidence of drug use must be present before this decision can be made. These are:

(a) Evidence of being caught red-handed using drugs or possessing equipment required in the consumption of drugs.

(b) Medical evidence given by 2 medical practitioners who examine the suspect separately.

(c) A positive urine test. (This can now be done on the spot using the instant urine testing machines. The urine specimens are sent to the Department of Scientific Services for confirmatory tests).

The final decision to send a suspect to the DRCs rests with the Director of the Central Narcotics Bureau.

Treatment at the Drug Rehabilitation Centre

At the DRC, the drug abuser, now called an inmate, is examined by a medical practitioner. If found to be medically fit, and under 55 years of age, he is then to undergo a period of **detoxification** (Stage 1) popularly known as the 'cold turkey'. This usually last 7 days, during which no medication is given to ease the withdrawal symptoms.

Stage 2 of the treatment programme involves **recuperation and orientation**. This usually last one week, during which the inmate recuperates from his detoxification experience and acquaints himself with various aspects of the rehabilitation programme.

Stage 3 consists of one week of **education or indoctrination**, during which the harmful effects of drugs and the useful role the inmate can play in society are explained to him.

Stage 4 lasts about 2 months, and involves **physical training** of the military type to inculcate discipline and to improve the general health of the inmates. Counselling sessions are also introduced at this time.

The **work programme** (Stage 5) constitutes the last period of the inmate's stay in the DRC, and is aimed to prepare him for productive employment once he leaves the centre.

The length of stay at a DRC is determined by the inmate's progress, and response to rehabilitation. Each case is reviewed once every 6 months by a Review Committee, who will determine the inmate's suitability for discharge. The detention could be extended to a maximum period of $2^1/_2$ years followed by 6 months in the Day Release Scheme. Inmates in the Day Release Scheme go out to work during the day and return to the DRC at night.

Treatment for First Timers

Not all who are arrested for drugs abuse for the first time will undergo treatment at the DRCs. Those who are young, without criminal or drug antecedents, will be placed on an early release scheme called the **Exit Counselling Programme** (ECP). This last 2 weeks and consists mainly of intensive counselling. The

first-timers are interned separately from the repeated offenders. Those found to be unsuitable for the ECP will be sent for rehabilitation in the DRCs for a duration of 3-6 months.

Rehabilitation – Supervision

The Supervision Scheme

Upon discharge from the DRCs, the inmates are placed in the Compulsory Supervision Scheme for 2 years, during which they have to fulfil a list of requirements including reporting every 5 days to designated Police Stations for urine tests.

Supervision is done by CNB officers, who monitor the progress through interviews, and who conduct surprise checks on the supervises at their homes and at the places of work.

Half-way Houses

Those who do not have supportive families or who have difficulty adjusting to life in society are placed temporarily in 'half-way houses'. Job placement can be arranged by SCORE (Singapore Co-operative of Rehabilitative Enterprise).

Volatile Substances: The Intoxicating Substances Act 1987

Punishment of Abusers and Suppliers

The penalty for inhalant abusers is a fine not exceeding $ 2,000 or imprisonment not exceeding 6 months or both. The penalty for suppliers/sellers of intoxicating substances is a fine not exceeding $ 5,000 or an imprisonment not exceeding 2 years or both.

The CNB is empowered to require retailers to furnish information or keep a sales record of intoxicating substances. Failure to comply is an offence punishable by fine or imprisonment or both.

Suspected inhalant abusers are required to undergo a blood test for toluene. A blood toluene concentration 1 microgram/ml or more constitutes a positive result, and the suspect is considered an inhalant abuser unless proven otherwise.

Abusers detained for the first time are required to undergo supervision for 6 - 12 months. An abuser who relapses during the supervision period may be admitted to an approved centre for treatment and rehabilitation. Those guilty of repeatedly breaching the Supervision Order may be liable for prosecution and fine.

Treatment & Rehabilitation

Institutionalised treatment and rehabilitation is the last resort for repeated offenders. This last 6 - 12 months, and counselling is provided.

Ex-abusers undergo supervision for 6 - 12 months upon discharge. Supervisees are required to report to designated Police stations regularly. Only those who exhibit signs and symptoms of inhalant abuse would be required to do a blood test. Parents of abusers are encouraged to be involved in the rehabilitation process.

THE ROLE OF THE SINGAPORE ANTI-NARCOTICS ASSOCIATION

SANA, or the Singapore Anti-Narcotics Association, is an independent voluntary organisation established under the Societies Act in 1972. It receives an annual grant of $ 154,000 from the Singapore Government, and obtains the rest of the funds from donations and fund-raising projects. Its main areas of work are: (a) the aftercare of drug releases from the DRCs, and (b) the prevention of the drug menace by public education and information dissemination.

Rehabilitation – Aftercare

Volunteer Aftercare (Counselling) Services

There are 6 religious and 4 secular Aftercare Counselling Services affiliated to SANA. These organise activities aimed at helping ex-drug abusers return to life in society with the help of Voluntary Aftercare Officers (VAOs). They also provide counselling for inmates in DRCs and those under the Exit Counselling Programme.

Neighbourhood Scheme

Grassroot organisations such as the Residents' Committee and Citizen Consultative Committees are recruited to help in the

implementation of anti-drug campaigns, to organise healthy activities for the young, to monitor the drug abuse situation in their particular constituencies and to recruit volunteers for the aftercare programme.

Half-Way Houses

In 1990 there were 6 Christian Half-way Houses affiliated to the Christian Aftercare (Counselling) Services, with a total of 148 residents, 123 of whom had drug or inhalant abuse problems.

Prevention

The objective of preventive education are to systematically reach out to as many sectors of the population as possible, and to involve the community and concerned citizens in the fight against drug abuse.

The publicity strategy to achieve these are set at 2 levels, namely: (1) to create general awareness, and (2) to turn the awareness into a positive recognition of the danger of drug abuse.

Some of the activities organised by SANA to achieve the above include exhibitions and talks held at schools and public places, the Drug Abuse Resistance Education (DARE) Programme, and the Drug and Inhalant Abuse Awareness Programmes. It also publishes a bimonthly newsletter to keep the public informed. At the request of the Ministry of Home Affairs, SANA is now operating a 24-hour hotline service. This service aims to provide support and immediate help to those involved in drug-related crises.

THE ROLE OF THE FAMILY PHYSICIAN

On the part of the family physician, 4 levels of involvement are identified. On the **Personal** level, the family physician has to be careful when prescribing drugs with addictive potential, such as the sedatives and hypnotics. Even phensedyl, a popular cough mixture containing codeine, has been known to be abused by some drug addicts. The family physician should be well versed in the medical aspects of the common drugs abused, their toxic side effects and methods of treating an emergency resulting from suspected drug misuse. He should also have a sound knowledge of the local drug problem and the law, so as to be able to advise his patient and the family members, to act as liaison with the various Government agencies and voluntary organisations involved in the care of drug abusers.

The management of the **patient** who is a drug abuser involves not only physical but also social and psychological care. Continuity of care is important. This implies providing general medical care for any incidental illness or injury, counselling and advice, and referral when the need arises. The doctor has to be firm yet supportive. He must take care that he is not manipulated by the patient. It is important to know his limitations in treating the patient's drug problem and he should not attempt to rehabilitate the patient without the help of established rehabilitative agencies.

The family physician should be a source of support and help for the whole **family**. On discovering a drug problem in a member of the family, especially in one of the children, the initial reaction of family members is one of shock and disbelief. The family physician is well placed to help them deal with their feelings of guilt, bewilderment, denial and sense of stigma. He can also act as a source of information on where and how to get help, as well as provide support in one form or another during the various stages of the abuser's treatment and rehabilitation.

Finally, the family physician can offer his services to the **Community** by helping in the voluntary organisations to disseminate information. This can be done in the practice premises by using posters, or talking to patients; as well as on a broader scale e.g. taking part in public talks and forums. He can also help in counselling if that is his area of interest and expertise.

CONCLUSION

The drug abuse problem in Singapore, though contained, is nevertheless ever-present. One must not be complacent, as is seen in the increase of cases of heroin addicts arrested in the years since 1988, after many years of relative

'calm' following the big swoop (Operation Ferret) in 1977. The family physician can help in many ways in efforts to stamp out drug abuse.

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Acknowledgement

The author wishes to thank the Singapore Anti-Narcotics Association and the Central Narcotics Bureau for providing up-to-date information on the drug problem in Singapore and the role of SANA against drug abuse. The author also wishes to thank Dr Goh Lee Gan, Head, Division of Family Medicine, Department of Community Occupational and Family Medicine, for encouragement and invaluable help rendered.

ORIGINAL

UPDATE ON NEUROLOGICAL IMAGING – A CLINICAL RADIOLOGICAL APPROACH –

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HEADACHE

The appropriate initial imaging modality to use depends on whether the headache is chronic in nature or acute and severe.

A. Chronic Headache

Commonest type of chronic headache is tension headache. Migraine and sinusitis account for most of the others. Chronic headache without neurological signs is infrequently a sign on intracranial tumour.

1. If the history is typical of tension headache or classical migraine and there are no EEG or neurologic abnormalities, no imaging procedures are usually indicated.

2. If the headache is cough or laughter induced, associated with papilloedema or the migraine is atypical or if uncomplicated headache is unduly persistent or progressive, then MRI of the brain is the imaging procedure of choice.

3. If mastoid disease or sinusitis is suspected as the cause of headache, plain radiographs of the appropriate areas should be requested for initially.

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B. Acute onset severe headache (Suspected Subarachnoid Haemorrhage)

In patients with acute headaches, with or without neurological signs and in whom clinically a subarachnoid bleed is suspected:

1. *SXR*

   Not needed unless suspicion of associated trauma.

2. *CT Scan of the Brain*

   Plain non-contrast CT scan is the examination of choice to detect a subarachnoid haemorrhage. If possible it should be done before lumbar puncture. In the uncooperative or combative patient, the advantage of the faster scan time with CT is an important advantage.

3. *MRI of the Brain*

   This is not the preferred imaging procedure in patients with acute headache as CT is more sensitive than MRI in detecting subarachnoid haemorrhage.

4. *Cerebral Angiography*

   Patients with subarachnoid haemorrhage usually require further evaluation to demonstrate the underlying cause such as aneurysm or AV malformation. A high quality high resolution carotid angiogram should be performed. The timing of the angiogram is often debated but generally should only be performed when the patient is fully conscious and is a candidate for neurosurgery.

SUDDEN FOCAL NEUROLOGIC DEFICIT (STROKE)

Ischaemia in a focal area of the brain may result in a sudden focal neurologic deficit. Cerebral ischaemia usually manifests clinically in the form of a stroke syndrome.

Stroke syndromes are episodes of focal neurological deterioration which occur suddenly and in which the deficits become maximal within minutes or several hours. There are four types of stroke syndrome.

1. Transient Ischameic Attacks (TIA) lasting less than 24 hours.
2. Reversible Ischaemic Neurological Deficit (RIND), lasting longer than 24 hours but less than a week with complete or almost complete recovery.
3. Stroke in evolution, where following acute onset of neurologic deficit the clinical condition worsens over minutes to several hours before reaching maximal severity.
4. Completed stroke, an acutely developing neurological deficit that rapidly stabilizes without subsequent worsening.

Most stroke syndromes are the result of thrombosis or embolic obstruction of an intracranial artery or due to cerebral haemorrhage from cerebro-vascular disease. Episodes of rapid neurological deterioration may be caused also by tumour, infection, subdural haematoma or hypoxia.

Imaging of stroke syndromes is directed at demonstrating the cause of the syndrome and to aid appropriate treatment of the syndrome.

A. Transient Ischaemic Attacks

At the initial presentation, non-contrast CT scan of the brain can be performed. The scan is usually normal and done to exclude pseudostroke syndrome (neurological conditions simulating TIAs such as chronic subdural tumour).

MRI is currently however the preferred imaging modality. MR is more sensitive than CT in the detection of infarcts and white matter disease, as well as in assessing lesions of the posterior fossa and brain stem. Using special software on the latest scanners, MR angiography can also be done to demonstrate the patency of the carotid arteries and the large intracerebral vessels around the Circle of Willis.

Principle cause of TIAs are emboli and haemodynamic insufficiency. If a cardiac cause is suspected for the emboli 2D echocardiography is indicated. Otherwise non-invasive neurovascular tests such as duplex Doppler ultrasound of the neck should be performed to exclude a lesion of the carotid or vertebrobasilar circulation. If there is evidence either clinically or on ultrasound of significant vascular stenosis and the patient is a potential candidate for carotid endarterectomy, carotid angiography is indicated. This can be performed by an intraarterial digital subtraction method (DSA) or by conventional angiography.

B. Stroke

Non-contrast CT is currently the initial examination of choice in acute stroke. CT is more specific for diagnosis of the presence of haemorrhage or haemorrhagic infarction in the acute situation than MRI. Faster scan time also means it is easier to perform in uncooperative or ill patients.

Once an intracranial haemorrhage is demonstrated and its CT appearances are typical for a hypersensitive bleed, then follow-up CT or MRI scans are usually done to document resolution of the haematoma. If the appearances are atypical or suggestive of a presence of a tumour or other underlying pathology such as aneurysm, then follow-up CT with contrast, MRI and/or cerebral angiography may be indicated.

C. Progressive Neurologic Deficits

Chronic progressive neurologic abnormalities such as hemiparesis, aphasia, personality change and other deficits may be due to cerebral tumour or chronic subdural haematoma or other space-occupying lesion. As MR is much more

sensitive in the detection of intracranial abnormalities than CT is should be the initial imaging study performed.

IMAGING OF THE CRANIAL NERVES

Cranial Nerve II (Optic Nerve)

General indications for imaging may be divided into those primarily aimed at the globe, the orbit and the visual pathways. The visual pathways are comprised of three parts: the optic nerve, the optic chiasm and the retrochiasmal structures (optic tract, lateral geniculate bodies, optic radiations and visual cortex).

For problems of the globe, ultrasound may be done initially. Occasionally CT or MRI may be indicated, for example in the assessment of benign or malignant tumours, such as retinoblastoma or in trauma, to localize foreign bodies. For problems of the orbit such as proptosis, inflammatory disease or tumour, CT or MRI can be used. CT however is preferred in the assessment of trauma for bone detail and foreign body localization.

Imaging of the optic nerves is indicated for a variety of problems. The most common is that of partial or complete monocular visual loss (scotoma). This indicates a lesion in the prechiasmal visual pathway. A lesion at the optic chiasm classically produces bitemporal or heteronymous field defects while retrochiasmal lesions in the visual pathway usually create homonymous hemianopia. Sudden loss of vision, which may be associated with retroorbital pain suggests optic neuritis while slow progressive visual loss suggests a tumour of the optic nerve or compression by an extrinsic mass, especially if proptosis is present. If optic atrophy or papilloedema, especially unilateral, is present, this is often an indication for imaging of the optic nerves. Bilateral papilloedema suggests intracranial disease while unilateral papilloedema suggests optic nerve pathology. MRI is the imaging procedure of choice for assessment of the visual pathways as it displays the whole visual pathway including the optic chiasm, optic radiation, visual cortex, cavernous sinus and brain stem much better than CT.

Unilateral temporary visual loss may also be caused by emboli or thrombosis of the opthalmic artery (amaurosis fugax) that is often due to extracranial vascular occlusive disease. Duplex colour doppler ultrasound of the carotid arteries should be the first investigation to look for atherosclerotic plaques in the carotid arteries. If ischemic changes are to be detected intracranially, then MRI is the next investigation.

Cranial Nerves III, IV and VI

Cranial nerves III (oculomotor nerve), IV (trochlear nerve) and VI (abducens nerve) innervate the extraocular muscles. Dysfunction of one or more of these nerves results in ocular misalignment and diplopia such as lateral, vertical or medial diplopia depending on the nerve involved. Diplopia can also be due to other causes such as refractive abnormalities.

These nerves have shared orbital functions and similar courses from the brain stem, through the cisterns, cavernous sinuses and superior orbital fissures. Neuropathies of these nerves are most easily approached by determining whether the deficit is isolated or complex and associated with other neurologic findings.

1. *Complex III, IV, VI Cranial Neuropathy*

   Non-isolated III, VI, VI cranial neuropathy is localized to the brain stem, when one or more of these nerves dysfunction and there are associated brain stem symptoms or signs then. When no associated brain stem symptoms are present the lesion is present in the cerbellopontine angle cistern or petrous apex, cavernous sinus, superior orbital fissure or orbital apex. Causes include neoplasm, aneurysm or infarction. MRI is the imaging investigation of choice.

2. *Isolated Oculomotor Nerve*

   If the patient is over 40 years of age and there is associated pupillary involvement, immediate angiogram is indicated to search for a posterior communicating artery aneurysm. If there is pupillary sparing, the lesion is probably due to microvascular infarction especially if patient is hypersensitive or diabetic. Close clinical observation is indicated and imaging

procedures are not essential initially unless loss of pupil function develops.

If the patient is under 40 years of age, regardless of pupil size, MRI and angiography are indicated to exclude presence of aneurysm.

3. *Isolated Trochlear Nerve Palsy*

Usually due to trauma. Otherwise usually due to microvascular infarction or tumour. If patient is diabetic or hypertensive, no radiological imaging is usually required. Otherwise MRI should be done. If due to neoplasm, most are not isolated nerve palsies.

4. *Isolated Abducens Nerve Palsy*

In young patients (age 15 to 40) multiple sclerosis, hypertension and collagen vascular disease must be ruled out as potential causes. MRI is indicated to exclude MS.

In older patient, it is usually due to microvascular infarction and no imaging is usually required; otherwise MRI is recommended.

Note that myasthenia gravis can stimulate any pattern of oculomotor disturbance and its diagnosis is made by a positive Tensilon test.

Cranial Nerve V

The trigemial nerve is the largest of the cranial nerves and has both sensory and motor functions. It mediates sensation to the scalp, face and nervous membranes of the nose and mouth. Motor innervation is seen in the mandibular division only with the muscles of mastication supplied. Symptoms include facial pain, burning, itching or numbness or tic douloureux.

Excellent imaging can be achieved with MRI. Use of gadolinum contrast is often useful in diagnosis of trigeminal neuritis.

If the facial pain is atypical or there is a progressive history of multiple cranial nerve involvement or additional symptoms such as trismus or otalgia are present or prior history of cancer, then patient should have MRI. Typical trigeminal neuralgia or tic douloureux need not be evaluated by MRI unless surgery is planned.

Cranial Nerve VII

First decide if the facial area nerve palsy is a central or peripheral paralysis. All of the unilateral muscles of facial expression are paralysed in a peripheral injury while central paralysis results in paralysis of the contralateral muscles of facial expression with sparing of the muscles of the forehead.

For a peripheral facial nerve palsy if cranial nerve VI is also involved, the lesion can be localized to the brain stem. If cranial nerve VIII is also involved, the cerebellopontine angle – internal auditory canal area is the level of the lesion. If the three special functions of lacrimation, sound damping and taste are absent, the lesion can be localized to the temporal bone. If there is VII nerve palsy with preservation of the three special functions, extracranial disease (intraparotid) of the nerve is present.

If a central lesion (pons) or lesion at the cerebellopontine angle is suspected, MRI is the imaging procedure of choice. If a temporal bone lesion is suspected, CT or MRI can be performed. CT is better for demonstrating fine bone detail. For the parotid segment of the facial nerve, CT or MRI are suitable imaging studies.

In Bell's palsy no imaging procedure in the initial phase is indicated. If there is atypical Bell's palsy, that is persistent (longer than four months), progressive or recurrent peripheral facial nerve paralysis, then MRI should be performed to look for a clinically occult cause.

Cranial Nerve VIII

Hearing loss and tinnitus are the main symptoms of acoustic pathway pathology. If unilateral sensorineural hearing loss is present, the injury can be localized to between the cochlea and the cochlea nuclei in the brain stem. Involvement of the auditory pathway above the cochlea nuclei usually causes bilateral sensorineural hearing loss.

Sophisticated audiometric testing can often localize the lesion causing sensorineural hearing loss to either the sensory or neural component of

the acoustic pathway. When the lesion is suspected to be in the cochlea (sensory), CT is preferred as the structures of the bony labyrinth can be better demonstrated. When the lesion is suspected to be in the retrochochlear (neural) region of the acoustic pathway, MRI, which may require use of gadolinium contrast, to detect acoustic neuroma is the procedure of choice.

Cranial Nerves IX, X, XI & XII

These nerves originate in the brain stem, and pass through the skull base onto the head and neck region. MRI is ideally suited to evaluate patients with symptoms referable to these cranial nerves. Isolated palsies of these cranial nerves are uncommon and usually complex neuropathies are present. If there is more than one cranial nerve involved, progressive history, past history of treated malignancies progressive otalgia with other symptoms (eg. dysphagia) or smoking, alcoholism, or vocal cord paresis with other findings such as brachial plexopathy or other cranial nerve involvement, then MRI of the posterior fossa, skull base and upper parapharyngeal area is indicated.

In vocal cord paresis if there are associated signs in the lower neck, brachial plexus or chest, then CXR and MRI or CT to study the larynx, thyroid and course of recurrent laryngeal nerves is indicated. In isolated vocal cord paresis, MRI of posterior fossa, skull base and parapharyngeal area as well as the neck and thorax may be indicated but often will be negative.

HEARING LOSS

A thorough ENT examination and audiometric testing are mandatory. Once the type of deficit has been elicited, this determines the need, if any, for imaging studies.

1. If there is evidence of a conductive hearing loss, fine 1 mm section high resolution of CT scan of the temporal bones should be performed as fine bone detail images can be obtained. This will demonstrate temporal bone lesions such as mastoiditis or cholesteatoma or a middle ear congenital deformity which may be associated with external auditory canal dysplasia.
2. If there is evidence of a sensorineural hearing loss than MRI should be performed initially to exclude a tumour such as small acoustic neuroma or meningioma in the posterior fossa, before a diagnosis of viral disease, Meniere's disease or vestibular neuritis is made, as the cause of the symptoms.
3. If a metabolic cause, drug toxicity or a degenerative conduction defect is suspected as the cause of the hearing loss, no imaging studies are usually indicated.

ATAXIA / VERTIGO / PERSISTENT DIZZINESS

If symptoms only occur with postural change, this suggests orthostatic dizziness. Orthostatic hypotension may be due to certain drugs, intravascular volume depletion or autonomic dysfunction and no imaging is usually required.

If symptoms are not postural but associated with a spinning sensation, nausea and ataxia then a vestibular of CNS (posterior fossa) cause is likely. ENT and a neurologic examination should be done and audiometric and vestibular function tests can be performed. Following this patients should have a MRI as the initial screening modality to detect a lesion in the posterior fossa brain stem or cerebello-pontine angle (eg acoustic neuroma).

If otoscopic examination reveals a vascular or pulsatile mass in the middle ear, then CT scan of the temporal bone should be performed. Intra-arterial digital subtraction angiography may also be required to evaluate pulsatile tinnitus or vascular tympanic membrane. Idiopathic diseases such as Meniere's disease or vestibular neuritis usually do not require any radiological investigations but symptomatic treatment. If vertebrobasilar disease or TIA is clinically suspected as the cause of symptoms and MRI is normal, then antiplatelet therapy could be started.

ACUTE HEAD TRAUMA

1. Plain Skull Radiographs (SXR)

SXR are the simplest method of assessing skull fractures and are indicated when there

is clinical evidence of a skull fracture, including those which are depressed or compound in nature, those which involve the facial bones or base of skull clinically, or in cases of penetrating injury or suspected foreign bodies.

However, are SXR indicated in all head injuries? This is a controversial subject as some believe that all patients with a history of head injury, even if not associated with loss of consciousness or cerebral symptoms need SXRs. This is partly for medicolegal reasons or to detect fractures that are not clinically evident. Other authorities feel that SXR should not be requested for indiscriminately but only if there are definite cerebral symptoms and signs such as loss of consciousness, drowsiness, penetrating injury, deterioration in consciousness, focal neurological signs or evidence of fracture (as mentioned earlier).

2. *Computed Tomography (CT) of the Brain*

CT scans of the brain are indicated in all patients who are unconscious following head injury or whose level of consciousness deteriorates or fluctuates after initial assessment or those with unexplained focal neurological signs. CT is also indicated in patients with evidence of depressed or compound fractures, fractures of the base of skull, presence of a fracture on plain films, possible intracranial foreign body from penetrating injury, and in those with previous craniotomy or shunt placement

3. *Magnetic Resonance Imaging (MRI) of the Brain*

MRI is not the preferred method of imaging most acutely ill or badly injured patients because of long procedure time and difficulty of scanning and monitoring uncooperative patients especially those on life support systems. CT is preferable as well as being more sensitive at detecting fractures and bone injury than MRI.

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NON-STEROIDAL ANTI-INFLAMMATORY DRUGS

Omar B S T, MBBS (S'pore), MCGP (S'pore), FRACGP

INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDS) are among the most widely used in medicine today and undoubtedly produce symptomatic benefit for many patients. Unfortunately their potential for harm is also high and, in order to gain maximum benefit with minimum risk, certain principles must be followed when prescribing them. Aspirin is the prototype, having been used in one form or another for hundred of years. NSAIDs exhibit analgesic, antipyretic and antiplatelet effects in addition to anti-inflammatory effects.

MECHANISM OF ACTION

The exact mechanism of action NSAIDs is unknown. Many effects have been found in vitro, but their correlation with clinical efficacy is poor. All are inhibitors of prostaglandin synthesis, either cyclooxygenase or lipooxygenase inhibitors (Figure 1). Other properties possibly contributing to their clinical effects include inhibition of neutrophil function, lymphocyte activation, oxygen radical generation and cytokine production.

INDICATIONS

Their main use has been directed towards inflammatory rheumatic conditions but there are an increasing number of indications for these drugs (Figure 2). There is growing use of NSAIDs in the treatment and prophylaxis of several cardiovascular, cerbrovascular and gynaecological conditions. Their role in pain relief has expanded far beyond rheumatological conditions.

CLASSIFICATION

The most commonly used classification for NSAIDs is that based on the parent structure from which the drug is derived (Figure 3). However, this classification seems to be of little value in the clinical aspects of prescribing.

Although we know that some patients will respond to one drug more favourably than another, there is little to suggest that this response is group-related. Thus the responsiveness is termed 'idiosyncratic', and when a doctor is forced to alter to a second agent, a response from a drug within the same group is as likely as from a drug in another group. Similarly, there is little convincing evidence that any of the groups have a better side-effect profile than other groups.

PHARMACOKINETICS

The various NSAIDs differ considerably in their pharmacokinetic properties although some similarities exist. They are well absorbed by mouth. All are extensively bound to plasma albumin. Elimination is by hepatic metabolism and their elimination half-lives vary considerably (Figure 3).

General Practitioner
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Singapore 1646

FIGURE 1. NSAIDS act by inhibiting prostaglandin synthesis but probably have additional modes of action.

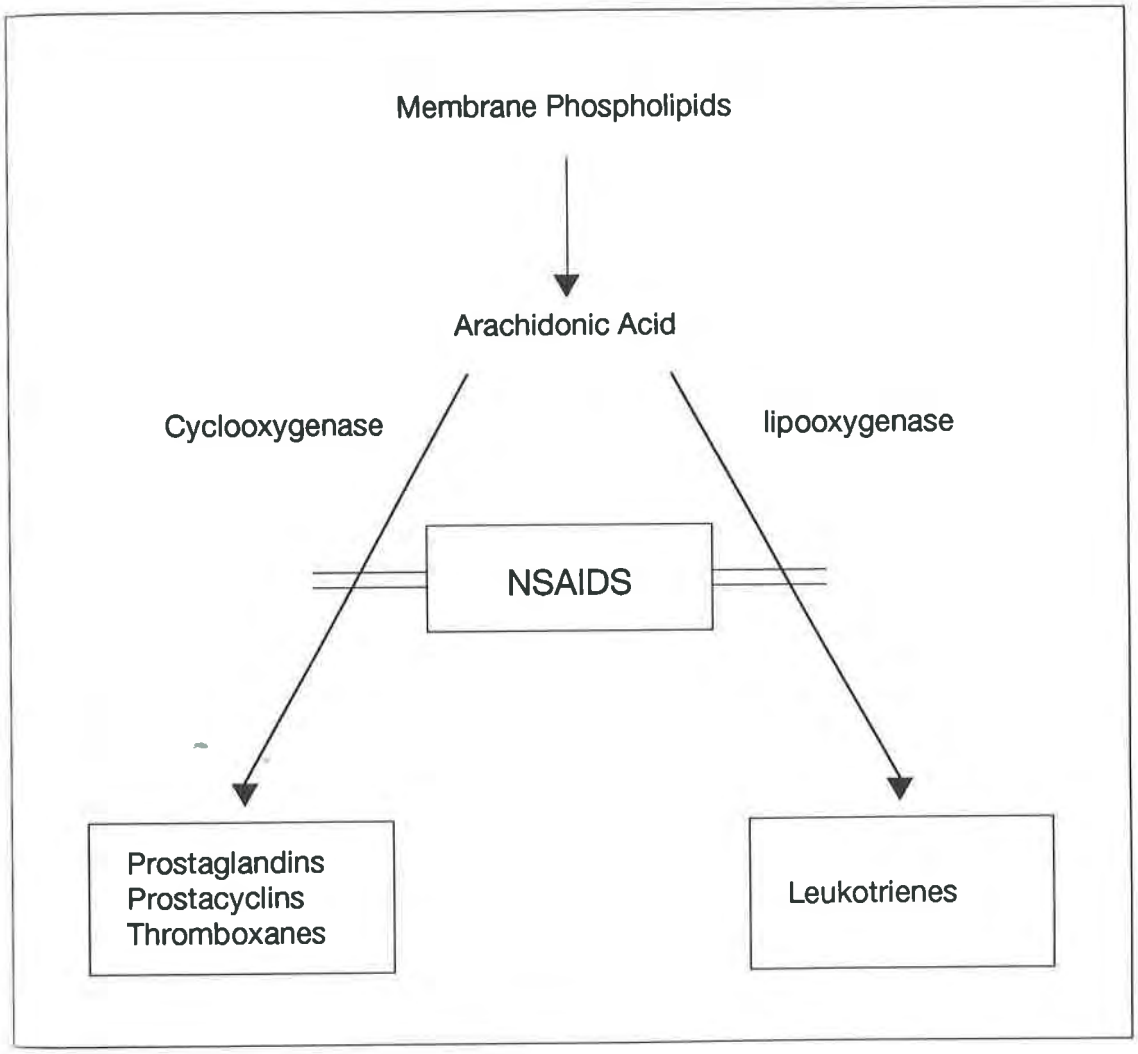

FIGURE 2. Some indications for NSAIDS

Category	Specific Indication
Analgesia	Post-surgical including dental Biliary and ureteric colic (parenteral route most effective) Cancer-absorbed pain Post-herpetic neuralgia
Antipyresis	
Anti-inflammatory	Inflammatory rheumatic conditions Trauma, including sports injuries Thrombophlebitis Anterior uveitis and other inflammatory eye reactions
Antithrombotic (aspirin)	Cerebrovascular accident prevention Prevention of infarction in unstable angina and post myocardial infarction Prevention of occlusion of coronary artery bypass grafts and arteriovenous shunts Prevention of embolism from prosthetic heart valves
Vascular disease	Closure of patent ductus arteriosus Treatment and prophylaxis of migraine
Gynaecology	Dysmenorrhoea, and premenstrual tension Menorrhagia Delay preterm labour (but the possibility of premature closure of the fetal ductus arteriorus precludes this use, certainly beyond brief periods)

FIGURE 3. NSAIDS : classification, half-lives and dosing schedules

Drug	Half-life (hrs)	Dosing interval (hrs)	Daily dose (mg)
Aspirin and derivatives:			
Aspirin *	2 – 15	6 – 8	1200 – 3600
Diflunisal (Dolobid®)	10 – 20	12 – 24	500 – 1500
Salsalate (Disalcid®)		8 – 12	1500 – 3000
Propionic acids:			
Fenbufen (Cinopal®) **	7 – 15	12	600 – 900
Flurbiprofen (Froben®)	3 – 6	6 – 8	100 – 200
Ibuprofen (Brufen®)	2 – 5	6 – 8	400 – 2400
Ketoprofen (Oruvail®) **	2 – 4	6 – 12	100 – 200
Naproxen (Synflex®)	10 – 20	12	550 – 1375
Tiaprofenic acid (Surgam®)	2 – 5	8 – 12	300 – 600
Fenamates:			
Mefenamic acid (Ponstan®)	2 – 5	6 – 8	500 – 1500
Acetic acids:			
Diclofenac (Voltaren®)	2 – 3	8 – 12	50 – 150
Indomethacin (Indocid®)	4 – 8	6 – 8	20 – 200
Sulindac (Clinoril®)	6 – 10	12	200 – 400
Enolic acids:			
Phenylbutazone ***	40 – 80	12 – 24	100 – 300
Oxicams:			
Piroxicam (Feldene®)	40 – 80	24	10 – 40
Tenoxicam (Tilcotil®)	30 – 50	24	20

* Half-life increases with increasing doses; for antithrombotic purposes 100 mg daily is sufficient.

** Pro-drug; half-life shown is that of metabolite.

*** For ankylosing spondylitis only.

Studies on synovial fluid kinetics have demonstrated that these concentrations are more sustained and show less variability than plasma concentrations. Practically, this means that many of the short half-life NSAIDs such as ibuprofen, diclofenac or ketoprofen can be reasonably effective in a twice-daily dosing regimen. There has been a continuing trend in the last few years to produce NSAIDs which are effective in once-daily doses. This can be done by developing slow-release preparations of short half-life NSAIDs or by using long half-life drugs such as piroxicam or tenoxicam.

Clearance of some NSAIDs can be affected by renal disease and age. This is important to remember because many patients taking these medications are elderly and have underlying renal disease. The clearance of indomethacin, ketoprofen, naproxen and diflunisal is decreased in patients with renal insufficiency; The clearance of ketoprofen, naproxen and salicylate is reduced in the elderly. These data emphasize the care that should be taken when prescribing NSAIDs to these patients.

ADVERSE EFFECTS

The side-effect profile of NSAIDs is well known (Figure 4). The main adverse effect of NSAIDs is gastro-intestinal ulceration, which most commonly occurs in the stomach. All can cause gastro-intestinal haemorrhage, not only by a direct irritant effect, but also due to the systemic action of the drug. The elderly patient is at particular risk. The use of suppositories, slow-release preparations or pro-drugs such as sulindac or fenbufen has only partly solved this problem. Ibuprofen is lease likely to cause ulceration but there is little to choose between the remaining NSAIDs.

Dyspepsia can be reduced by using the lowest effective dose of NSAID, administering the drug with food or immediately after meals and finally co-administering the drug with antacids. In general, the total amount of NSAIDs absorbed is not greatly affected by concurrent administration of food or antacids. H2-antagonists such as cimetidine or ranitidine have not been completely effective in preventing gastric ulcer formation. The increasingly common practice of combining H2-receptor antagonists with NSAIDs is not recommended without adequate gastrointestinal investigation. There is some evidence that prophylactic use of prostaglandin analogues such as misoprostol might reduce the incidence of peptic ulceration. Although these drugs are potentially very exciting, their use should probably be confined to patients at high risk, such as the elderly or those with a past history of peptic ulceration.

All NSAIDs have the potential to cause renal side-effects. Factors predisposing to renal side-effects include: underlying renal dysfunction, volume depletion, congestive cardiac failure, diabetes mellitus and hepatocellular dysfunction. Sulindac has been claimed to be less likely to cause further renal impairment when compared with other NSAIDs. This is controversial and caution should still be employed when using this drug in patients at risk.

Transient rise in liver enzymes levels is seen with many NSAIDs and in particular with salicylates. This does not usually cause a serious problem, though hepatic reactions are slightly more common with sulindac and diclofenac.

Most skin reactions to NSAIDs are relatively mild, but fatal reactions, including erythema multiforme, have been described. Skin reactions particularly occur with the long half-life drugs.

Some NSAIDs, particularly indomethacin, can produce central nervous system side-effects such as headache and dizziness, and hallucinations have been reported. Tinnitus commonly accompanies salicylate therapy.

Blood dyscrasias such as agranulocytosis are rare. These were a particular problem with phenylbutazone, which is now restricted to use in ankylosing spondylitis. Asthma may be precipitated by aspirin and occasionally other NSAIDs. Mefenamic acid can produce diarrhoea.

CONTRAINDICATIONS

There are few absolute contraindications to the use of NSAIDs. Aspirin should not be given to young children (under the age of 12 years) because of the risk of Reye's syndrome. A few

FIGURE 4. Main side-effects of NSAIDs

Gastrointestinal
dyspepsia, ulceration, haemorrhage, perforation, stomatitis

Renal
acute renal failure, hypertension, fluid retention, hyperkalaemia, interstitial nephritis

Hepatic
hepatocellular damage, Reye's syndrome

Dermatological
erythema multiforme or variants, bullous eruptions, photosensitivity, fixed drug eruptions, urticaria

CNS
headache, dizziness, confusion, nausea

Haematological
aplastic anaemia, red cell aplasia, thrombocytopenia, neutropenia, haemolytic anaemia

Pulmonary
bronchospasm, pulmonary oedema

Systemic
anaphylactoid reactions

FIGURE 5. Interactions of NSAID

Drug affected	*Effect*
Oral anticoagulants	Potentiation of anticoagulant effect especially with phenylbutazone; in addition all NSAIDs reduce platelet function.
Antihypertensives	Attenuation of hypotensive effect with all NSAIDs (especially indomethacin) with possible exception of sulindac. Hyperkalaemia and increased risk of renal failure on administation of ACE inhibitors with indomethacin and possibly other NSAIDs.
Diuretics	Risk of nephrotoxicity of NSAIDs increased; reduced diuretic effect with all NSAIDs (especially indomethacin) with possible exception of sulindac; and increased risk of hyperkalaemia with potassium-sparing diuretics.
Cardiac glycosides	NSAIDs may exacerbate heart failure, reduce GFR and increase plasma digoxin level.
Sulphonylureas	Some NSAIDs (especially salicylate, phenylbutazone) may increase plasma concentrations of sulphonylureas and thereby cause hypoglycaemia.
Antiepileptics	Effect of phenytoin enhanced by aspirin and phenylbutazone, metabolism of sodium valproate inhibited by aspirin.
Cytotoxics	Reduced renal clearance of methotrexate possibly by all NSAIDs.
Lithium	Excretion reduced with all NSAIDs with possible exception of sulindac and aspirin

patients will be genuinely hypersensitive to a NSAID although this is very unusual. NSAIDs should not be given to patients with active peptic ulceration. Special care is needed if there is serious liver disease and in patients with a bleeding diathesis as NSAIDs prolong the bleeding time. They can produce fluid retention and increase the blood pressure, and so worsen hypertension and cardiac failure. The safety of many of these drugs in pregnancy and in nursing mothers has not been fully established.

DRUG INTERACTIONS

Concern over possible drug interactions involving NSAIDs might be anticipated since these widely prescribed drugs are frequently taken by the elderly and groups of patients already on other drugs. Major interactions of NSAIDs which the clinician needs to remember are shown in Figure 5.

PRACTICAL PRESCRIBING

There is no ideal NSAID. All may cause adverse effects. The following points should be noted when prescribing a NSAID:

- Make a small selection of NSAIDs from different chemical groups and get to know them. Initially family practitioners should prescribe the NSAIDs with which they are familiar, and not necessarily the newest drug. It is better to use long established drugs. More is known about them and they will be cheaper.
- Use only one NSAID at a time and ensure adequate dosage. If the patient has not responded to an adequate dose within 2-3 weeks, an alternative NSAID should be given.
- Be flexible in dosage schedules. Symptoms may vary according to the time of the day e.g. early morning stiffness. Optimum response to a NSAID may depend on time of administration.
- Long half-life drugs such as piroxicam or tenoxicam should be avoided in the elderly.
- It is important to justify the use of the NSAID in the short term and in the long term.
- Other methods of pain relief should always be considered, such as the use of pure analgesic agents (e.g. paracetamol) or physical treatments (e.g. heat, cold, exercise and hydrotherapy).

CONCLUSION

There is now a bewildering array of strongly promoted agents. Despite this, no one drug has been shown to be clearly superior to the remainder in terms of symptomatic relief, disease suppression or toxic effects. It is important that constant vigilance is maintained for side effects and drug interactions, particularly in elderly patients. It is advisable to become familiar with a few drugs and restrict use to these. Unfortunately, individual response to a particular NSAID is somewhat unpredictable and the choice of drug is inescapably empirical.

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MULTIPLE CHOICE QUESTIONS

1. The following considerations should govern the choice of anti-inflammatory drugs in rheumatic disorders:
   A. short half-life NSAIDs must be given at least three times daily
   B. if the patient has not responded to an adequate dose within one week, an alternative NSAIDs should be given
   C. a patient who has not responded to an NSAID from a particular group is most unlikely to respond to an alternative NSAID from the same group
   D. long half-life NSAIDs should be avoided in the elderly
   E. therapy should be planned so as to exploit the synergistic action of drugs from different chemical groups.

2. Known side effects of NSAIDs include:
   A. stomatitis
   B. fluid retention
   C. bronchospasm
   D. headaches
   E. hepatocellular damage.

3. The following statements about NSAIDs are true:
   A. Aspirin should not be given to children under the age of 12 years
   B. Gastric symptoms occur only with oral administration
   C. Ibuprofen is least likely to cause ulceration
   D. Indomethacin may cause dizziness and headache
   E. Sulindac does not cause renal side effects.

4. NSAIDs potentiate the therapeutic action of the following:
   A. propranolol
   B. frusemide
   C. nifedipine
   D. warfarin
   E. digoxin

Answers

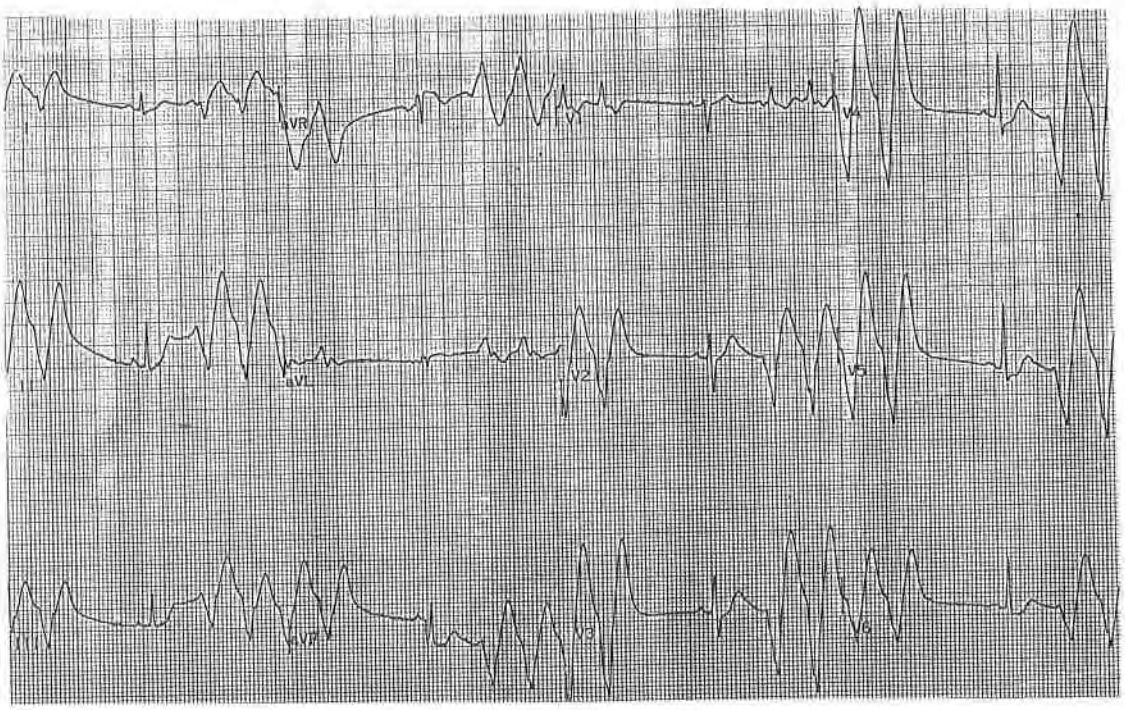
1. D
2. A, B, C, D, E
3. A, C, D
4. D, E

ECG QUIZ

Contributed by Dr Baldev Singh
MBBS (S'pore) M Med (Int Med) MRCP (UK)

The ECG was recorded from a 36 year old Caucasian male during the recovery period following an exercise treadmill test.

What are the abnormalities?

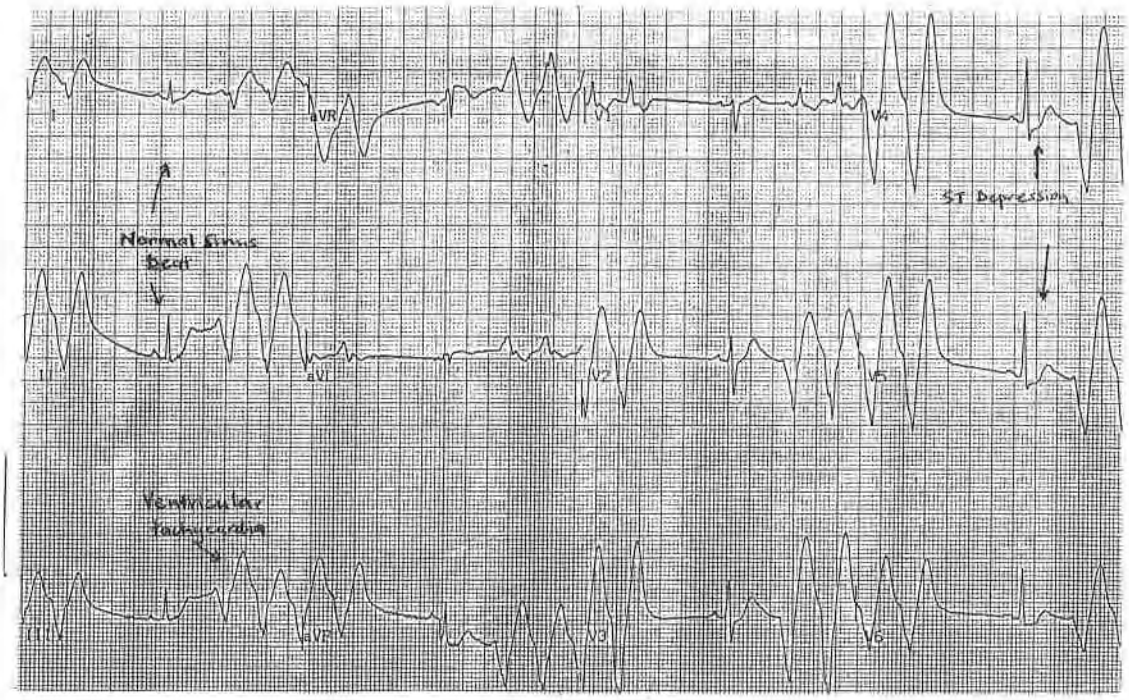


Turn to page 156 for answers.

ANSWERS TO ECG QUIZ

The ECG shows only one normal sinus complex in each lead. This is preceded by a P wave and the QRS complex is narrow. The other complexes are wide bizarre and rapid. These are runs of ventricular tachycardia. The sinus complexes in V4, V5, V6 show horizontal ST depression indicating ischaemia.

Coronary angiography confirmed the presence of 3 vessel coronary artery disease in this patient.



WORLD HEALTH ORGANIZATION PUBLICATIONS

NEW BOOK ANNOUNCEMENTS

The Use of Essential Drugs – Model List of Essential Drugs (Sixth List)

Fourth Report of the WHO Expert Committee *Technical Report Series*, No. 796 1990, 57 pages ISBN 92 4 120796 5

This book presents and explain the sixth model list of essential drugs issued by WHO as part of its efforts to extend the benefits of modern drugs to the world's population. Intended to guide the selection of drugs in countries where the need is great and the resources are small, the list identifies a core group of prophylactic and therapeutic substances judged capable of meeting the vast majority of health needs and thus deserving priority in purchasing decisions and procurement schemes.

The first half of the report provides updated information on several components of national drug policy necessary to assure that essential drugs, corresponding to essential health needs, are available at all times in adequate amounts and in the proper dosage. Readers are given advice on the adaptation of the model list to local needs and disease patterns, on the choice between equivalent drugs, and on the selection of an appropriate dosage form. New in this edition is a section devoted to the need for reserve antimicrobials third-generation cefalosporins, the quinolones, and vancomycin in those cases where information is available on the sensitivity of important bacterial pathogens. Other topics include methods of quality assurance and the use of drug utilization surveys to quantify drug inventory or to evaluate patterns of drug utilization.

The sixth WHO model list of essential drugs is then presented, together with an explanation of changes made when revising the list. Organized according to the therapeutic group, the list includes information on route of administration, dosage forms, and strengths for each of 275 drugs.

The list has been expanded to include an additional 16 drugs; new subsections cover antithrombotic drugs, sun-blocking agents, and insect repellents. Revision in the list also alert readers to cases where advances in pharmacology have made certain drugs obsolete. In total six substances have been withdrawn from the list.

In view of the large number of countries that have adopted the essential drugs concept, the publication of this revised list will be welcomed as a source of guidance that can help ensure that a country's investment in essential drugs is also in line with the latest knowledge about the efficacy and safety of drugs.

Health Education in the Control of Schistosomiasis

1990, 61 pages ISBN 92 4 154407 4

This manual gives health workers and educators a collection of model stories, illustrations, case studies, and questions for discussion that can be used to help people understand their role in the cause and prevention of schstosomiasis. Intended to form the basis of training and planning sessions in the field, the manual draws its authority from the recent development of simple, safe, and inexpensive technologies that lend themselves to community participation in the control of schistosomiasis. Although emphasis is placed on the consequences of water use practices and indiscriminate urination and defecation, the manual also offers advice on ways to persuade people to take advantage of screening services and to comply with medical treatment.

Readers are first introduced to several basic concepts of health education, including reasons why people do not generally recognize schistosomiasis as a priority problem, approaches to the "diagnosis" of behaviours that put people at risk, and general strategies for helping communities to adjust their traditional beliefs in line with modern concepts of disease. In keeping with the importance of planning and evaluation, the chapter also outlines and explains ten essential components of a written plan for health education.

The main part of the manual presents model training material organized to complement the three main strategies for control: improved water and sanitation facilities, screening and treatment programmes, and snail control measures. A final chapter assembles basic facts and practical information about the disease itself, the parasite, modern diagnostic tests and their cost, and the three new drugs that have made treatment safe and effective.

Any health worker familiar with the contents of this manual will be in a good position to explore community attitudes, find ways to communicate messages, and develop locally acceptable lines of action that can contribute greatly to the control of schistosomiasis.

Cancer Pain Relief and Palliative Care

Report of a WHO Expert Committee *Technical Report Series* No. 804 1990, 75 pages ISBN 92 4 120804 X

This report considers what can – and should – be done to comfort patients suffering from the distressing symptoms of advanced cancer. Prepared by nine renowned experts in oncology, neurology, pain management and nursing care, the book draws together the evidence and arguments needed to define clear lines of action, whether on the part of the medical and nursing professions or in the form of national legislation.

This report opens with a review of global trends in the incidence of cancer and prospects for cure that show why, for many years to come, palliative care will remain the only realistic, humane treatment for many cancer patients. The concept of palliative care is explained in terms of its concern with quality of life and comfort before death, emphasis on the family as the unit of care, dependence on a teamwork approach, organizational components and relationship to curative interventions.

The relief of cancer pain is considered in two sections. The first reviews the types of cancer pain and factors influencing its severity, and explains the simple, yet highly effective method of pain relief developed by WHO.

Subsequent sections concentrate on measures for the relief of other physical symptoms, the psychosocial needs of the patient and family, and the need for spiritual comfort.

A section devoted to ethics provides a number of important statements concerning the legal and ethical distinction between killing the pain and killing the patient, the need to recognize the limits of both medicine and the patient's physical and moral resources, and the ethical responsibility of the society that encourages home care to look after the family care-givers as well as the patient. The report takes a firm stand against the legalization of euthanasia. A final section addresses the importance of public and professional education as a measure for coping with the growing number of patients for whom palliative care will be the only realistic treatment option.

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  Headings and subheadings may be used in the text. Indicate the former by capitals, the latter in upper and lower case underlined.

  Arrange the manuscript in this order: (1) title page, (2) summary, (3) text, (4) references (5) tables, and (6) illustrations.
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* Include name, address and telephone number of the author to whom correspondence should be sent.
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* The summary should describe why the article was written and give the main argument or findings.
* Limit words as follows: 100 words for major articles; 50 words for case reports.
* Add at end of summary: an alphabet listing of up to 8 keywords which are useful for article indexing and retrieval.

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The text should have the following sequence:

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  Laboratory values should be in SI units with traditional units in parentheses.

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* Results: Present results in logical sequence in the text, tables and illustrations.
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Illustrations

* Diagrams, line drawings, photographs or flow charts are valuable but their use will be subject to editorial policy. Transparencies or prints are acceptable for colour reproduction at the authors' expense.
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Further reading

1. INTERNATIONAL COMMITTEE OF MEDICAL JOURNAL EDITORS. Uniform requirements for manuscripts submitted to biomedical journals. Ann Intern Med 1988; 108: 258-265.
2. Bailar III JC and Mosteller F. Guidelines for Statistical Reporting in Articles for Medical Journals. Ann Intern Med 1988; 108: 266-273.

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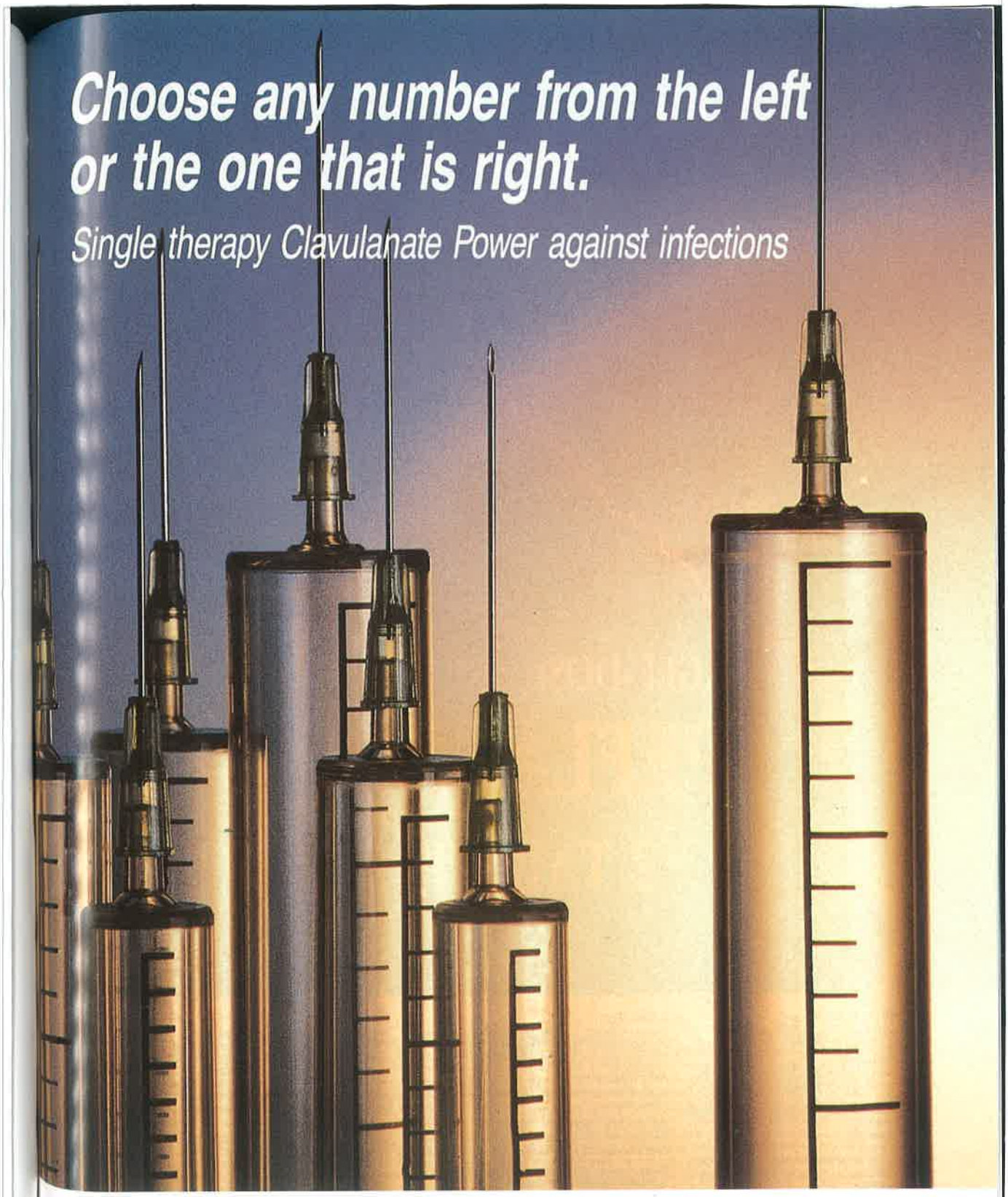

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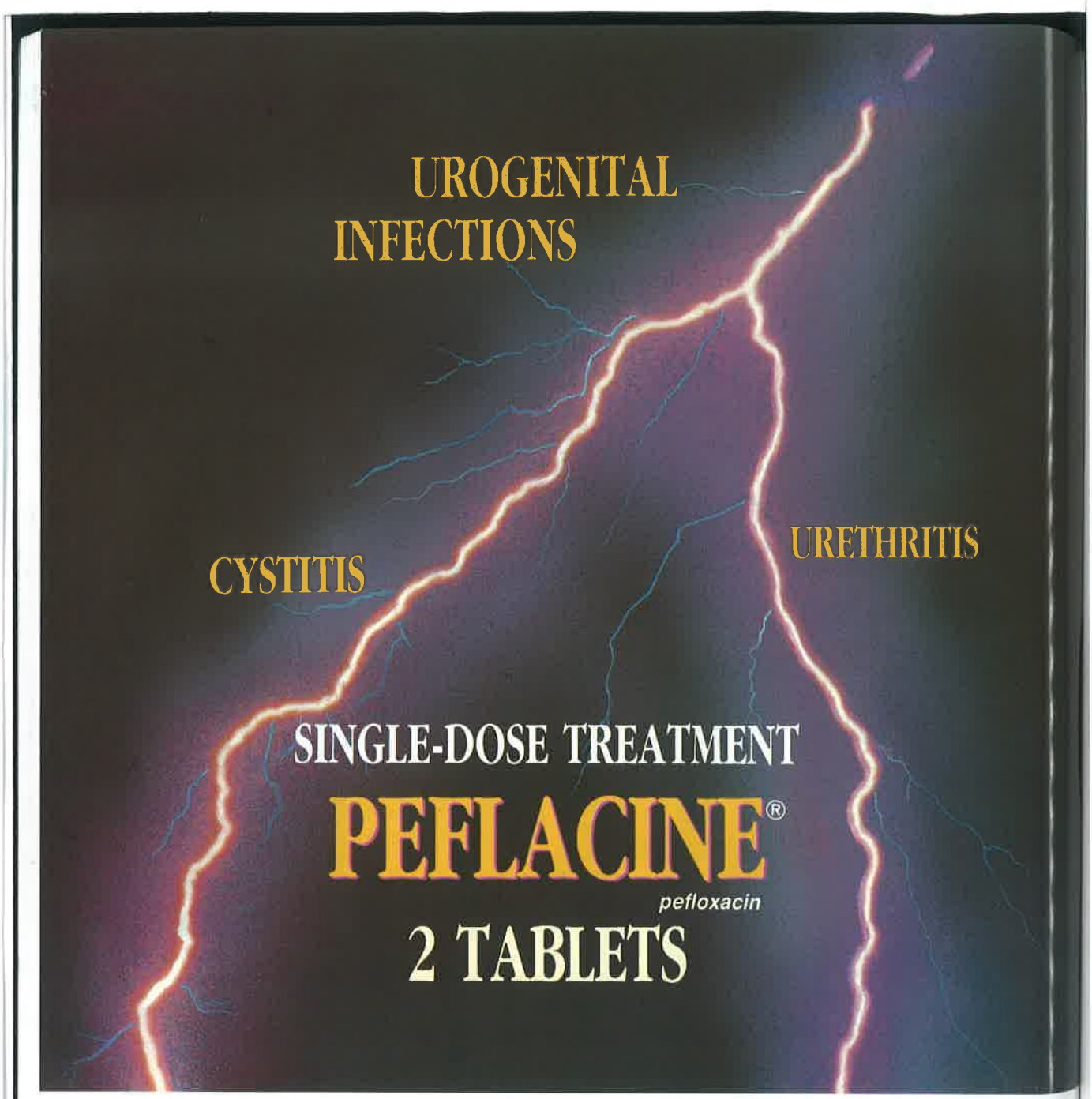

Prescribing information
Peflacine (Pefloxacin) is a synthetic antibiotic which belongs to the quinolone family.

MICROBIOLOGY
In-vitro tests on PEFLACINE demonstrate that the quinolones are bactericidal against the following organisms:-
Staphylococci, including S.epidermidis and methicillin resistant strains
Acineto bacter spp.
Enterobacter spp.
Pseudomonas aeruginosa
Proteus mirabilis
Providencia spp.
Escherichia coli
Klebsiella spp.

Other strains of Gram-negative organisms sensitive to PEFLACINE include Neisseria meningitidis and gonorrhoeae, Salmonella and Shigella species.

Most strains of Streptococcus and anaerobes are resistant to PEFLACINE.

Further information is available on request from

Indications
Severe infections, in adults caused by sensitive micro-organisms (gram-negative organisms and staphylococci), including cystitis and gonorrhoea

Administration
PEFLACINE is available in both intravenous and oral formulations.

By the oral route
PEFLACINE tablets (400mg) should be taken twice daily with meals to avoid gastrointestinal disturbances.

The recommended dosage for cystitis and gonorrhoea is 2 tablets (400mg each) stat.

By the **intravenous** route
Peflacine injection should be administered by slow intravenous injection (one hour) at the dosage of one ampoule of 400mg, diluted in 250ml. of isotonic glucose solution, twice daily. A chloride solution should not be used to prepare the dilution as Pefloxacin precipitates in the presence of chloride ions.

Dosage
Adults with normal liver function
On average, 800mg daily (either 2 tablets or 2 ampoules, each containing 400mg). An initial loading dose of 800mg may be given in order to produce effective blood concentrations more rapidly. Dosage need not be reduced in case of renal insufficiency. However, dosage should be adjusted in hepatic insufficiency.

Side-Effects
Digestive disorders: gastric pain, nausea, vomiting
Allergic skin reactions and photosensitivity
Muscular and/or articular pain
Thrombocytopenia at high doses (1600mg daily)
Neurological disorders: headache, disorders of vigilance

Contra-indications
Allergy to drugs of the quinolone family
Children under 15 years of age
Pregnancy
Nursing mothers

Packing
Tablets containing 400mg of Pefloxacin in box of 50.
Ampoules of 5ml, containing 400mg of Pefloxacin in box of 10.

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1 tablet daily

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Reverses the structural changes in hypertensive arteries...

- Reverses medial hypertrophy, improves the elastin/collagen ratio, and restores the elastic properties of hypertensive arteries (1,2,3)

... and ensures excellent antihypertensive control

- Effective round-the-clock BP control maintained long-term (4,5)
- Excellent patient acceptability (6)
- Meticulously determined, highly practical, single-tablet daily dosage (7)

Coversyl is a long-acting ACE inhibitor. **International non proprietary name:** Perindopril. **Indication:** Essential hypertension and Congestive Heart Failure. **Dosage and Administration:** *Hypertension:* 4 mg once a day in the morning. If necessary, the dose may be increased to 8 mg after one month of treatment. *Elderly patients:* start treatment at 2 mg daily. *Congestive Heart Failure:* 2 mg once a day in the morning and this may be increased to 4 mg after 15 days. **Contra-Indications:** Children. Pregnancy. Lactation. Patients with a history of hypersensitivity to Coversyl. **Precautions:** Assess renal function before and during treatment where appropriate. Renovascular hypertension. Surgery / Anaesthesia. Renal insufficiency: the dose should be cautiously adjusted in accordance with the creatinine clearance *(refer to complete data sheet).* Symptomatic hypotension is rarely seen, but is more likely in volume-depleted patients, those receiving diuretics, or with the first two doses. In diuretic-treated patients, stop the diuretic 3 days before starting Coversyl. A diuretic may later be given in association if necessary; potassium-sparing diuretics are not recommended. Commbination with neuroleptics or imipramine-type drugs may increase the hypotensive effect. Serum lithium concentrations may rise during lithium therapy. **Side Effects:** Rare and mild, usually at the start of treatment. Cough, fatigue, asthenia, headache, disturbances of mood and / or sleep have been reported. Less often taste impairment, epigastric discomfort, nausea, abdominal pain and rash. Reversible increases in blood urea and creatinine may be observed. Proteinuria has occurred in some patients. Rarely, angioneurotic oedema and decreases in haemoglobin, red cells and platelets have been reported. **Composition:** Each tablet contains 4 mg of the tert-butylamine salt of perindopril. **Presentation:** Boxes of 30 and 300 tablets of COVERSYL 4 mg (scored) and COVERSYL 2 mg. Refer to data sheet for complete prescribing information.

1. Levy et al., J. Hypertension, 1988, 6: S23-25. **2.** Christensen et al., J. Hypertension, 1989, 7: 83-90. **3.** Safar et al., Circulation, 1988, 78: 941-950. **4.** Safar et al., Arch. Mal. Cœur, 1989, 82: 51-56. **5.** Boissel et al., Data on file. **6.** Santoni et al., Clin. Exper. Hypertension, 1989, A11: 605-619. **7.** Lucconi et al., Eur. Heart J., 1988, 9: 1131-1136.

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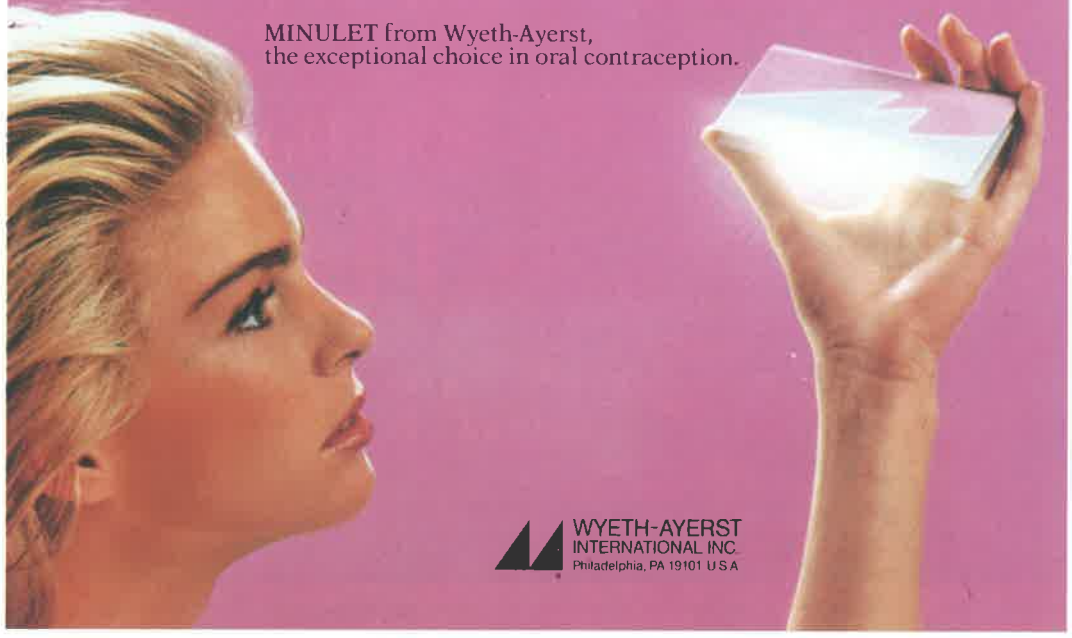

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References

1. Düsterberg B, Brill K, Clinical experience with a low-dose oral contraceptive containing gestodene. *Adv Contracept 6* (Suppl): 37–50, 1990.
2. Hoppe G, Gestodene, an innovative progestogen. *Contraception 37*(5): 493–501, 1988.
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4. Bonnar J, Daly L, Carroll E, Blood coagulation with a combination pill containing gestodene and ethinyl estradiol. *Int J Fertil 32* (Suppl): 21–28, 1987.

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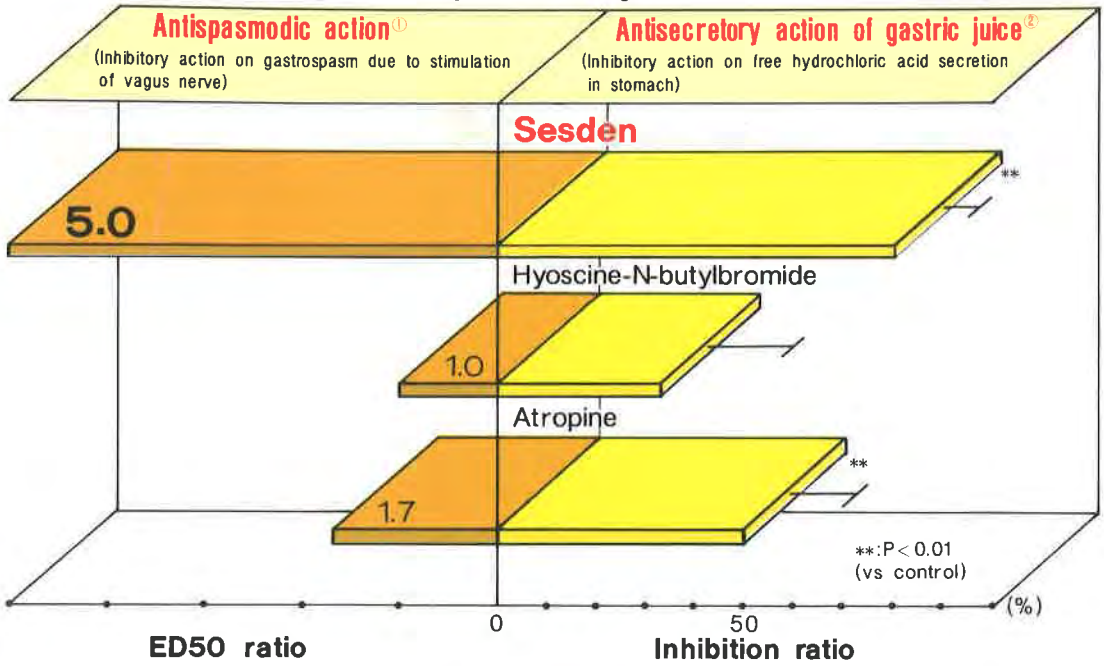

① H. Tamaki : Jpn. J. Pharmacol. 22 685(1972)
② S. Harigaya : Folia Pharmacol. Japon. 78 71(1981)

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SESDEN® (timepidium bromide)

[Composition] Capsule : Timepidium bromide 30 mg per capsule
Injection: Timepidium bromide 7.5 mg per ampoule(1ml)

[Indications] Capsule & Injection:
1. Pain due to spasm of smooth muscle caused by the following diseases: Gastritis, gastric and duodenal ulcer, intestinitis, gallbladder and bile-duct diseases and lithangiuria
2. Pain caused by pancreatitis

Injection:
1. Premedication for examination of gastrointestinal tract: Endoscopic and roentgenographic examination of gastrointestinal tract
2. Premedication for examination of urinary system

[Administration & Dosage]
Capsule : For adults, usually one capsule(30mg as timepidium bromide) is administered three times daily by oral administration
Injection: For adults, usually one ampoule(7.5mg as timepidium bromide) is administered at a time subcutaneously, intramuscularly or intravenously
The dosage may be increased or decreased according to the age and symptom of patients

[Precautions]
1. SESDEN capsule and injection should not be given to the patients with the following diseases:
   1) Glaucoma, 2) Dysuria, 3) Severe cardiac diseases, 4) Paralytic ileus, 5) Patients who had experience of hypersensitivity to this drug
2. SESDEN capsule and injection should be carefully given to patients with the following diseases:
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Prescribing Information

Indications:

Dosage:
Adult – one tablet of 7.5mg zopiclone at bedtime
Elderly – start with ½ tablet; increase dose if necessary

Side-effects and contra-indications

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