The Singapore Family Physician

The College of General Practitioners Singapore
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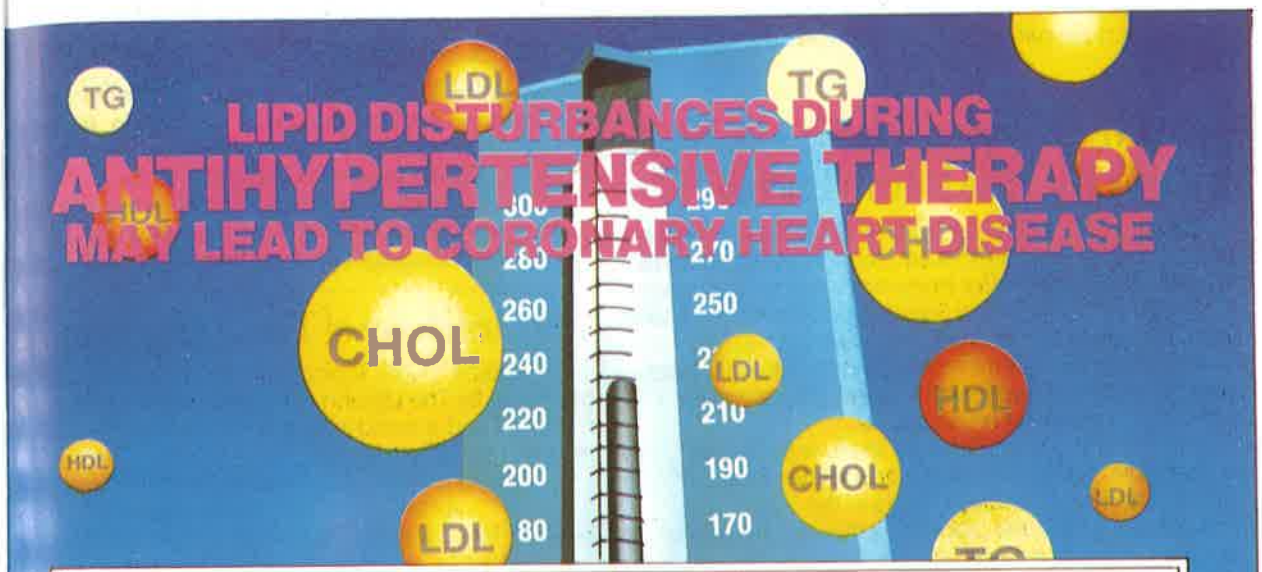

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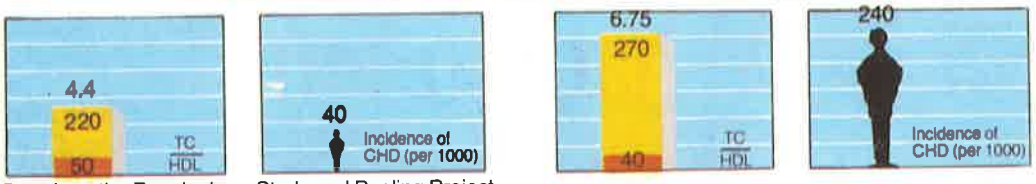

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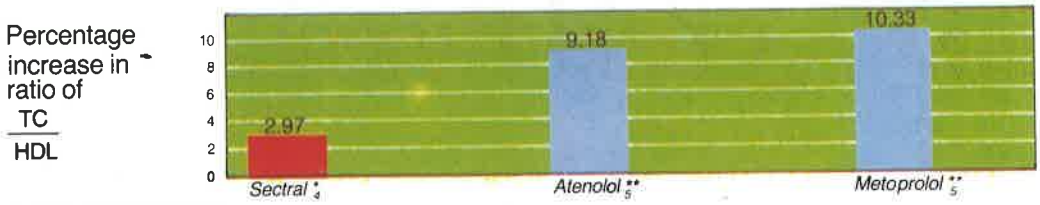

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❶ Safety an Efficacy of Topica Minoxidil in the Management of Androgenetic Alop – Robert L. Rietsche M.D. and Susan H. Duncan B.S. J. AM AC DERMATOL 1987; 16:677-85.

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EDITORIAL

RESEARCH IN GENERAL PRACTICE

"An active area of research" is one of the four criteria mentioned by McWhinney of a medical discipline; the other three are: a unique field of action, a defined body of knowledge and a training which is intellectually vigorous.

Active research builds on the body of knowledge, further clarifies the field of action and adds to the content of training programmes. Being thus far a relatively undocumented discipline, there is a need for more research in Family Medicine to strengthen its theoretical framework and body of knowledge.

WHAT RESEARCH?

Research need not be randomised controlled trials (RCT) of new drugs or the study of esoteric subjects to gain respectability. There are many everyday happenings that could be studied that will usefully add to our understanding of epidemiology of illness, response to illness, outcome of intervention and even doctor behaviour in the context of ambulatory care.

Early manifestations

As doctors of first contact, general practitioners encounter early manifestations of illness. Early appendicitis may not present with rebound tenderness. The patient may have only central abdominal pain and it may be difficult to differentiate it from intestinal colic, mesenteric adenitis or even food indiscretion at this stage of the disease.

In our medical training, exposure has largely been to clues of established disease. Thus, when we come face to face with early disease we encounter difficulties. We must be able to separate the early clues of serious from not so serious disease. There is a place for research to determine these systematically.

Longitudinal effects

We can also look at longitudinal effects of disease. General practitioners are more likely than specialists to look after patients over a long period of time. We are therefore well placed to look at long term effects of common chronic conditions like hypertension, diabetes mellitus, coronary artery disease and cerebral insufficiency.

The effects need not only be limited to physical ones. One could study the impact of illness on the patient and how he copes or fails to cope over time with the disease. One could also study the care giver. For instance, do we become mechanistic in our follow-up of the long term patient?

Outcomes

Third, we can look at outcomes. What is the outcome of our intervention in the patient's lifestyle and disease. How many patients became better? The actual number may be quite different from our mental perception: we may remember only our failures or only our successes. What has contributed to or what has prevented the good outcome? Look at it this way, we could in fact audit our own work through research. The answers may well be enlightening.

Conditions not usually seen by the specialist

Fourth, we could look at epidemiology of common problems that do not reach the specialists. We see many TIAs that refuse to go to hospital, many dyspepsias, many influenza-like ailments as well as viral exanthems. What became of them as a group could be another set of topics of useful research.

The case study

Finally, research need not be on numerate things. The humble case study, well documented, discussed and compared with what we already know is a good way of reiterating some principles and adding to the fund of knowledge.

WHAT GETS IN THE WAY?

The stumbling blocks to research in general practice are lack of research knowhow, attitude, time and money. Many of us remember research as a lot of mathematics that we did not clearly comprehend or the many things that must be recorded for multi-centre drug trials.

Many of us who were brave enough to venture into research in general practice may have met with bad experience. After days of hard work collecting data, we suddenly discover the study to be flawed because our definitions and criteria have not been clearly sorted out or we have not collected some important parameters. Others found that they could not complete the work because they have not estimated the time and resources required. They may have taken on too large a project or they may not have sorted out the bias or confounding factors of their research design before they started out. The reassuring point however, is that many of these difficulties are surmountable given some comprehension the nuts and bolts of research methodology which must indicate research design, protocol writing and project planning.

COPING WITH RESEARCH

Before we jump into the thick of research some strategy has to be worked out.

Reading: The literature search

A literature search is useful before one embarks on a research project for several reasons. The research one has in mind may have been done elsewhere. This finding need not be alarming because one may find some aspects of the results that one may like to verify or proceed from; one may find some useful information of the difficulties encountered and how these were resolved. One may discover a methodology and approach that has addressed the difficulties mentioned. Knowledge of what research has been done in one's topic has an orientation effect besides providing material for discussion and comparison of one's results.

Writing: The research protocol

There is much to be said for a research protocol being written up even if it is not a funding requirement. Such an activity helps to clarify what is to be done, to what purpose, how to do it and the expected benefits. Through putting pen on paper, we become more exact in what we are looking for.

Conference: Moving ideas around

Much benefit can come from discussing and seeking comments on one's proposed research project from helpful colleagues. Flaws in methodology may be uncovered. Better ideas may surface.

FROM DATA COLLECTION TO WRITING

Managing as a Project

The research effort is made up of many discrete activities that may have interrelated consequences. As such, it is useful to make use of techniques of project management like marking out milestones, tracing the critical path in time and identifying resources with respect to data collection, data entry and data processing. Unless activities are planned and adhered to, the research may drift into failure of completion.

Computer help

The microcomputer and the large number of available database software packages have made data capture both more accurate and less tedious. Packages like dBase PLUS and its clone FOX PLUS are useful database packages that are powerful and relatively easy to master.

For statistical computations one can write programmes in dBASE or make use of statistical packages like STATPAK or EPISTAT. The latter is a delightful public domain software that can generate results from random numbers to Chi squared tests and more. For the more serious researcher there are statistical packages like SPSS (Statistical Package for Social Sciences) or SAS (Statistical Analysis System) which are very powerful. One note of caution though. With powerful statistical packages one tends to be mesmerised by the statiscal indices that may be churned out. It is ever more important to know the basis for choosing one statistical test over another.

Write-up

Writing up a research project involves more than the text. Tables and illustrations

help the reader understand what we are trying to communicate. Here again, the computer has made work light.

There are standard word-processing software packages to choose from, like WORDSTAR, WORD and more recently WORDPERFECT version 5. For graphics there are packages like HARVARD PRESENTATION GRAPHICS and PC-STORYBOARD PLUS. Spreadsheet packages like LOTUS 1-2-3, SYMPHONY or FRAMEWORK II also provides graphics capability.

UNIFORM REQUIREMENTS FOR MANUSCRIPTS

The work of the International Committee of Medical Journal Editors since 1978 has helped to standardise and make uniform technical requirements for manuscripts to be submitted to journals. The 1988 edition of the Uniform Requirements for Manuscripts Submitted to Biomedical Journals can be found in the Annals of Internal Medicine (Ann Intern Med 1988; 108: 258-265) or the British Medical Journal. There is also published an accompanying set of guidelines for statistical reporting in articles for medical journals (Ann Intern Med 1988: 266-273).

GP RESEARCH CLUB AND ORGANISATIONS

Finally, there is the General Practice research club and related organisations. Such organisations help to promote and assist doctors in research by providing a forum where research ideas can be examined, pushed around and in the process be refined, enlarged and improved. Presentation of research works at these meetings provides opportunities for sharing and learning the technical aspects of research including evaluating one's work. Examples are the GP Research Club in UK, the EGPRW (European General Practice Research Workshop) in Europe and the NAPCRG (North American Primary Care Research Group in North America).

The Department of Community, Occupational and Family Medicine of the National University of Singapore is in the process of forming a research club for General Practice research as part of the activities of the Department's health care research interest group. It will initially run quarterly meetings and will provide a forum for discussion of research ideas, journal discussions of published research as well as organise talks and seminars on research methodology.

Research need not be a sterile academic pursuit. It should eventually be a normal activity of any medical practice where one uses it as a tool for continuing medical education and for self-help in quality assurance through self-audit.

GLG

EDITORIAL

PROSTATIC DISEASES AND THE GENERAL PRACTITIONER

In patients after age 50 years, bladder outlet obstruction due to prostatic diseases is the commonest urological problem in Singapore.[1]

This issue of the Singapore Family Physician features three topics on the prostate: benign prostatomegaly, carcinoma and prostatitis. These were papers first presented at a session jointly organised by the Urological Society of Singapore and the College of General Practitioners, Singapore. The role of the general practitioner in the management of such conditions in consultation with his specialist colleagues is highlighted.

A careful history and digital rectal examination remain the most practical means of detection of benign prostatic hypertrophy (BPH) and prostatic cancer. Outlet obstruction due to prostatic disease should always be considered in elderly males with urinary tract infections and renal failure. Acute or chronic retention of urine are more obvious pointers to the diagnosis.

With BPH the general practitioner needs to assess the severity and design a therapeutic approach that will provide symptomatic relief, preserve renal function and prevent infection. In conservative treatment, the use of alpha adrenergic blockers appear promising for mild cases of BPH. Present day endoscopic surgery for BPH (transurethral resection of prostate) in the hands of skilled urologists provides highly effective results with minimal morbidity and mortality. In the after care of patients recovering from prostatectomy, the general practitioner may be involved in explaining the expected pattern of recovering and the effects on sexual function, giving general advice on fluid intake and bladder retraining and managing urinary infections, post-operative haematuria and recurrent obstructive symptoms.

With prostatic cancer, although the natural history is highly variable and hence curative results of intervention still unclear, careful digital rectal examination is a simple practical screening test which can be recommended for all males above 50 years of age. Therapeutic intervention appropriate to the stage of disease, or a comprehensive palliative care plan can provide much relief to elderly patients, while early intervention in younger patients may increase the chances of survival.

Many questions about persistent prostatitis and prostatodynia remain unanswered for both the patient and the doctor. Nevertheless, the general practitioner can formulate a clear plan of action, which may involve referrals to a urologist or venerologist. In particular, the GP will have to attend to the psychological impact on the patient of a possibly chronic, frustrating condition.

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ORIGINAL ARTICLE

OVARIAN MASS – A REVIEW OF 102 CASES

Dr Chua Siok Meng* *MBBS Med (O & G) MRCOG AM*
Dr Phua Soo Mear** *MBBS*
Dr Chew Sek Yuen*** *MBBS FRCOG AM*

ABSTRACT

This report reviewed 102 consecutive cases of ovarian mass operated upon in A Unit, Kandang Kerbau Hospital, Singapore, in 1986. There were 43 tumor-like conditions, 43 benign, and 17 malignant tumours of the ovary. Endometriotic cysts were the commonest lesion found in the series. Mucinous tumours, both benign and malignant, were found to be more common than serious tumours. Abdominal pain was the most common presenting symptom. The majority of the neoplastic tumours were more than 5 cm in diameter, and malignant tumours were significantly more often bilateral than benign tumours.

86 of the patients had ultrasonography pre-operatively by members of the staff of A Unit, and it detected the ovarian mass in 77 (89.5%) of them. Ultrasonography also accurately predicted the nature of the tumour in 64 (83.1%) of the patients and was accurate in the assessment of the size of the tumour to a margin of 3 cm in 61 (79.2%) of the patients.

INTRODUCTION

One of the frequent indications for laparatomy in gynaecology is an ovarian mass. The silent nature, inaccessability for early detection and its wide variety of histology and clinical presentations makes ovarian masses one of the most challenging tasks for the attending gynaecologist. Often the true nature of the mass is not known until laparatomy is performed. The treacherous nature of ovarian tumours lies in the dismal prognosis of its malignant variety which, although less common than cervical or uterine cancer, cause more deaths than both combined (1).

* *Registrar*
** *Trainee*
*** *Head*
A Unit Kandang Kerbau Hospital

In an attempt to obtain a better perspective of this condition in the local context, a retrospective review of 102 consecutive laparatomies for ovarian mass performed at A Unit, Kandang Kerbau Hospital, Singapore, was made. The pattern of the condition with regards to its histology, epidemiology, and clinical presentations was analysed. In Singapore ultrasonography in obstetric and gynaecology is more commonly performed by general obstetricians and gynaecologists than by specialist ultrasonists. Under such a context the usefulness of ultrasonography in the management of ovarian mass was evaluated too.

PATIENTS AND METHODS

The case-records of 102 consecutive patients who had laparatomies for ovarian mass performed at A Unit, Kandang Kerbau Hospital, Singapore, in 1986 were analysed. The age and parity of the patients, the clinical presentations, the size and site of the masses, and their histology were studied. 86 of the patients had ultrasound scans pre-operatively by any one of the six registrars in the department and the results were analysed with regards to its sensitivity in detection of the ovarian mass and its accuracy in the assessment of the size and nature of the mass.

RESULTS

There were 102 consecutive laparatomies for ovarian mass. The histology of the lesions were classified into three broad categories. (Table 1). There were 43 (42%) non-neoplastic ovarian mass, 42(41.3%) benign neoplastic tumours, and 17 (16.7%) malignant neoplastic tumours.

Of the non-neoplastic ovarian masses, the commonest was endometriotic cysts of the ovaries which constituted 76.7%. 18.6% were functional cysts which include 5 corpus luteal cysts, 1 follicular cyst and 1 polycystic ovary. The remaining 2 (4.7%) were inflammatory cysts.

There were 42 benign neoplastic tumours, comprising 41.2% of all the patients studied. The commonest was 13 cases of mucinous cystadenoma comprising 33.3% of the benign tumours found. There were 12 (28.6%) benign ovarian teratoma, 10 (23.9%) serious cystadenoma, and 5 (11.9%) ovarian fibroma. One patient presented with acute abdomen and was found to have a twisted right ovarian cyst measuring 15 cm in diameter. The histology was reported as having features consistent with a benign cyst that had undergone severe haemorrhagic infarction and therefore not possible to classify.

TABLE 1: HISTORY OF THE OVARIAN MASS

NON-NEOPLASTIC MASS	**43/102 (42.2%)**
– Endometriotic cysts	33/43 (76.7%)
– Functional cysts	8/43 (18.6%)
– Inflammatory cysts	2/43 (4.7%)
BENIGN NEOPLASTIC TUMOUR	**42/102 (41.2%)**
– Mucinous cystadenoma	14/42 (33.3%)
– Teratoma	12/42 (28.6%)
– Serous cystadenoma	10/42 (23.8%)
– Fibroma	5/42 (11.9%)
– Unclassified	1/42 (2.4%)
MALIGNANT NEOPLASTIC TUMOUR	**17/102 (16.7%)**
– Mucinous Ca	10/17 (58.8%)
– Serous Ca	2/17 (11.8%)
– Brenner Cell Ca	1/17 (5.9%)
– Endometrioid Ca	1/17 (5.9%)
– Granulosa Cell Ca	1/17 (5.9%)
– Secondaries	2/17 (11.8%)

There were 17 malignant neoplastic tumours, comprising 16.7% of all the cases studied. 10 (58.8%) of these were mucinous cystadenocarcinoma. There were 2 cases of serious cystadenocarcinoma, 1 case each of malignant Brenner Cell carcinoma, endometriod carcinoma, granulosa cell carcinoma, and 2 cases of secondary malignancies of the ovaries. Of the latter, one had the primary malignancy in the colon while the origin of the other case was not known.

28.8% of the ovarian neoplasms were malignant. The ratio of primary malignant ovarian tumours to benign ovarian tumours was 1:2.8. 14 (93.3%) of the 15 primary malignant ovarian tumours were of epithelial origin.

Tables 2 and 3 summarised the age and parity distribution of the patients. Those with malignant tumours were older and more were nulliparous. However the differences among the three groups were not statistically significant.

TABLE 3: DISTRIBUTION OF NULLIPARITY

	No.	%
Non-neoplastic mass	16/43	37.2%
Benign neoplastic tumour	13/42	31.0%
Malignant neoplastic tumour	8/17	47.1%

($p > 0.05$)

The main presenting symptom of the patients is shown in Table 4. The commonest presenting symptom was abdominal pain or discomfort of duration ranging from 1 week to 10 years, which affected 42.2% of the patients. 5.9% of the patients presented with acute abdomen due to either torsion, rupture or haemorrhage into the ovarian cyst. 15.7% of the patients had disturbances of their menstruation such as menorrhagia, epimenorrhea, intermenstrual bleeding or post-menopausal bleeding as the main presenting symptom. 21.6% of the patients presented with an abdominal mass. 9.8% of

TABLE 2: AGE DISTRIBUTION

	MEAN AGE (YRS)	SD	RANGE (YRS)
Non-neoplastic mass	35.4	7.74	19 – 49
Benign neoplastic tumour	37.7	12.19	18 – 65
Malignant neoplastic tumour	40.3	13.60	15 – 66

($P < 0.05$)

TABLE 4.: CLINICAL PRESENTATIONS

MAIN SYMPTOM	NON-NEOPLASTIC No. %	BENIGN No. %	MALIGNANT No. %	TOTAL No. %
Abdominal Pain	22 (51.2)	12 (28.6)	9 (52.9)	43 (42.2)
Acute Abdomen	2 (4.7)	3 (7.1)	1 (5.9)	6 (5.9)
Menstrual Disorders	8 (18.4)	6 (14.3)	2 (11.8)	16 (15.7)
Abdominal Mass	6 (14.0)	12 (28.6)	4 (23.5)	22 (21.6)
Others	2 (4.7)*	3 (7.1)**	0 (0.0)	5 (4.9)
Asymptomatic	3 (7.0)	6 (14.3)	1 (5.9)	10 (9.8)
	43 (100)	42 (100)	17 (100)	102 (100)

* 1 urinary retention
1 subfertility

** 2 difficulty in micturition
1 subfertility

TABLE 5: SIZE OF OVARIAN MASS AT LAPARATOMY

	< 5 CM No. %	> 5 CM No. %
Non-neoplastic mass	10 23.3%	33 76.7%
Benign neoplastic tumour	2 4.8%	40 95.2%
Malignant neoplastic tumour	0 0.0%	17 100.0%
Total	12	90
	($P < 0.05$)	

TABLE 6: UNILATERAL VS BILATERAL OVARIAN MASS

	UNLATERAL No. %	BILATERAL No. %	TOTAL No.
Non-neoplastic mass	27 62.8	16 37.2	43
Benign neoplastic tumour	40 95.2	2 4.8	42
Malignant neoplastic tumour	10 58.8	7 41.2	17
Total	77	25	102
	($p < 0.01$)		

the patients were assymptomatic and had their ovarian mass found during routine physical examinations. The remaining 4.9% had other symptoms which included 2 cases with subfertility, and 3 cases with urinary symptoms.

The size of the ovarian mass at laparatomy is shown in Table 5. 11.8% of the ovarian masses were less than 5 cm in diameter and the majority of these were non-neoplastic. Of the neoplastic ovarian tumours, 95.2% of the benign and all of the malignant tumours were more than 5 cm in diameter.

The distribution of unilateral and bilateral ovarian masses is shown in Table 6. 41.2% of the malignant tumours were bilateral as compared to 4.8% of the benign tumours. For the non-neoplastic ovarian mass, 37.2% were bilateral and majority of these were endometriotic cysts.

The rôle of ultrasonography was analysed next (Tables 7-9). Ultrasonography had sensitivity of 89.5% while the sensitivity for pelvic examination was 84/9%. The difference between the two was not significant. Ultrasonography correctly predicted the cystic or solid nature of the ovarian mass in 83.1% of the cases. It also accurately assessed the size of the ovarian mass to 3 cm margin in 79.3% of the cases.

TABLE 7: ULTRASONIC DETECTION OF OVARIAN MASS

No. patients	Pelvic Examination	Ultrasound
66	+	+
7	+	–
11	–	+
2	–	–
86		
Pelvic Examination sensitivity= 73/86 (84.9%) Ultrasound sensitivity = 77/86 (89.5%) ($P < 0.05$)		

TABLE 8: ULTRASONIC ASSESSMENT OF NATURE OVARIAN MASS

No. patients	Ultrasound Findings	Laparatomy
61	Cystic	Cystic
7	Cystic	Solid
3	Solid	Solid
6	Solid	Cystic
77		
Same – 64/77 (83.1%) Different – 13/77 (16.9%)		

TABLE 9: ULTRASONIC ASSESSMENT OF SIZE OF OVARIAN MASS

Difference with laparatomy finding	Ultrasound
≤ 3 cm	61 (79.3%)
> 3 cm	16 (20.8%)

DISCUSSION

In the International Histological Typing of Ovarian Tumours by the World Health Organisation, non-neoplastic tumours of the ovary was classified under "Tumour-like Conditions" (2). In this study 42% of the patients had non-neoplastic ovarian mass, of which 76.7% were endometriotic, making it not only the commonest tumour-like condition of the ovary but also the overall commonest lesion. This is not surprising as endometriosis is one of the most commonly encountered diseases in gynaecology. Its incidence reportedly ranges from 7-50% (3.4), and it involves the ovaries in 60% of the cases (5). 42% of the endometriomas in this study were bilateral, making it the commonest bilateral ovarian lesion as well.

There has been much debate as to whether some endometriotic lesions of the ovary should be considered as benign neoplasm. There is no strong argument against the possible neoplastic nature of some. though clearly not all, cases of ovarian endometriosis (6). Malignant transformation in ovarian endometriosis had been documented and the frequency of malignant tranformation estimated to be less than 1% (7.8).

18.6% of the tumour-like condition of the ovary in this study were functional cysts. Generally these lesions may be managed conservatively but these 8 patients were symptomatic and more sinister pathology could not be excluded pre-operatively. 4.7 of the tumour-like conditions were inflammatory lesions. They comprise of a case of

bilateral ovarian abscesses following a septic abortion and a case of a 16 cm diameter tuberculous abscess of the left ovary. Although the local incidence of tuberculosis had decreased over the past decades, we are yet to eradicate it.

57.9% of the lesions were neoplastic tumours of the ovary. The distribution of the various types of tumours was comparable to that found in other major studies (6). However it is interesting to note that while most studies showed a slight preponderance of serous over mucinous tumours, this study showed the reverse. For benign neoplasm, 33.3% were mucinous compared to 23.8% of serous systadenoma. In the malignant group the difference was even greater with 58.8% being mucinous and only 11.8% being serous cystadenocarcinoma. Due to the small number of patients studied the significance of this finding cannot be ascertained but similiar finding had been reported by another study from this region (9).

In the analysis of the age distribution of the patients, those with malignant lesions were older in age, while the range of ages were equally broad for all three groups. Thus although malignant ovarian tumours are more common in the peri- and post-menopausal women, youth does not preclude malignancy. In the analysis of parity distribution, there was a greater proportion of nulliparous women in the malignant group. Although this was not significantly so in this study, other major studies have demonstrated association between nulliparity and ovarian malignancy (10,11).

Abdominal pain or discomfort of varying duration was the overall commonest clinical pressentation. In the non-neoplastic group, pain was common because of the preponderance of endometriotic lesions. Benign tumours tend to grow quietly and present as abdominal mass. Indeed 28.6% of patients with benign tumours in this study presented with an abdominal mass, an equal proportion presented with pain. while 14.3% were assymptomatic. For the malignant tumours the commonest presentation was pain which affected 10 (58/8%) of the 17 patients while 4 (23.5%) presented with abdominal mass. 2 (11.8%) patients had menstrual disorder, one having a granulosa cell carcinoma while the other had a mucinous cystadenocarcinoma, both tumours are known to be capable of hormonal secretions. Only 1 patient was asymptomatic. Malignant tumours are generally more symptomatic, a fact attributable to their rapid growth. Our findings concur with that found by other (12).

In this study the significance of the size of the ovarian tumour was shown by the finding that the majority of the ovarian mass more than 5 cm in diameter were neoplastic. In fact 95.2% of the benign neoplastic tumours and all of the malignant tumours were more than 5 cm in diameter. The corollary is all masses less than 5 cm in diameter were found to be non-malignant.

For the non-neoplastic ovarian masses, 37.2% were bilateral and most of these were endometriotic. For the neoplastic tumours, it is significant that most of the bilateral tumours were malignant. However as it is difficult to differentiate between the non-neoplastic and the neoplastic tumours preoperatively, the finding of bilateral tumours alone is insufficient to suggest malignancy.

It is over three decades since Ian Donald pioneered the use of ultrasound in obstetrics and gynaecology. Its role in obstetrics is now well established (15) and its role in gynaecology had been increasing (16-18). Undoubtedly in the hands of these experts ultrasonography has tremendous value. However as more and more obstetricians and gynaecologists are performing ultrasound scans it would be interesting to study its value in the hands of general obstetricians and gynaecologists instead of specialist ultrasonists.

In this study the ultrasound scans were performed by any one of the six registrars in the department who are all general obstetricians and gynaecologists. In their hands the sensitively of ultrasonography in detection of ovarian mass was 89.5%. This is comparable with the results of experts (13,14). However as shown in this study too, the sensitivity of physical examination in the detection of ovarian mass is comparable to that achieved with ultrasonography, thus negating the advantage of the latter in this respect.

The main value of ultrasonography in the management of ovarian mass lies not in the

detection of the mass but in its ability to assess the size and nature of the mass (14). Such findings may alter the management as a mass over 5 cm in diameter or solid in nature would warrant exploration, while a smaller or cystic mass may be observed and managed conservatively. In this study, ultrasonography accurately estimated the size of the ovarian mass to 3 cm difference from the laparatomy finding in almost 80% of the cases, and its ability to assess the solid or cystic nature of the ovarian mass was 83.1%. Other studies with scans by experts had reported over 90% accuracy in this respect (13,14).

Recently criticisms had been made on the performance of ultrasound scans by operators who are not certified as competent ultrasonists (19). Such certification is lacking locally. Although our results are encouraging, efforts must still be made to provide formal training for budding gynaecologists in the technique of ultrasonography so as to ensure quality and to improve the accuracy of our scans.

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ORIGINAL ARTICLE

CELLULAR COOPERATION AND INTERACTION IN THE IMMUNE RESPONSE

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Humoral & Cell-mediated Immunity

The mounting of the host immune response exemplifies a highly sophisticated and intricate 'information flow' system in biology in which the participating cellular elements and their products interact with one another closely and in a complex manner to achieve a common goal, that is, to inactivate the antigen which elicited it.

Humoral immunity (HI) is mediated through the action of a repertoire of specific antibodies or immunoglobulins synthesized by B lymphocytes. The other major group of lymphocytes, T cells, which comprise several sub-population, are the principal effectors in cell-mediated immunity (CMI). Considering viral immunity as an example, these two arms of the immune system complement each other in a general sense – HI prevents reinfection and haematogenous dissemination of free virions whilst CMI limits viral replication and restricts cell-to-cell spread (Borysiewicz & Sissons, 1986). Such a conventional division is purely an artificial and arbitrary one, for in reality these responses are generated simultaneously, and cooperate with each other and indeed with other leucocytes.

Lessons learnt from immunodificiency diseases have taught us a great deal about the effector mechanisms of the immune system and their interactions. With the advent of monoclonal antibodies, markers developed for the identification of lymphocyte subcategories have added significantly to our understanding of their roles and interrelationships (Kung et al. 1979).

Helper T Cells and immunoregulatory substances.

Lance, Medawar & Simpson (1977) have appropriately used the terms "synergy" and "antergy" to describe positive and negative immune cell interactions respectively.

Although some antigens (designated "thymus-independent") are capable of triggering clonal selection, proliferation and maturation of B cells, the vast majority of antigens (designated "thymus-dependent") rely on assistance from helper T cells.

However, before this T-B collaboration can occur, these antigens (including viruses) must be internalized, processed and presented to helper T cells by "professional" antigen-presenting cells (APCs) in order to evoke a T cell response. These APCs, which include macrophages and dendritic cells, process and express on their surfaces, the antigens in conjunction with major histocompatibility complex (MHC)-coded class II molecules, corecognized by helper T cells. In addition, the APC secretes a soluble monokine factor called interleukin 1 (IL1) or endogenous pyrogen, which non-specifically activates the helper T cell.

Under such influences, the stimulated helper T cell then elaborates immunoregulatory hormones which include B cell growth factor (BCGF), interleukin 2(IL2) and interferon (IFN). BCGF induces proliferation and differentiation of, and antibody production by the corresponding specific B cells. IL 2 or T cell growth factor, a mitogen, is necessary for the continued growth and clonal expansion of both specific T helper and T cytotoxic subsets, thus augmenting T cell responses (T-T synergy). Furthermore, in view of its involvement in the activation of spontaneous natural killer (NK) cells as well as its ability to promote tumour rejection in experimental animals, IL 2 has aroused considerable interest as a potential immunotherapeutic agent

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in oncology. Recent advances in molecular biology have enabled cloning and characterization of the human IL 2 gene (Degrave et al. 1983), and sufficient quantities of IL 2 are now available to explore further the exciting possible benefits of this potent factor. In this context, interferon is certainly no exception, and it too has been manufactured in quantity to recombinant DNA technology employing yeast or bacterial hosts. Stimulated T cells release type II IFN which performs a variety of immunomodulatory functions, including increasing NK cell and monocyte cytotoxicity, enhancing macrophage actvity and upregulating the expression of MHC antigens. The antiviral and antitumour properties of IFN hold much promise for its future clinical use (Gresser, 1983), and indeed a commercially prepared IFN, Wellferon, is currently one of the drugs of choice for the induction of remission in hairy cell leukaemia.

The importance of the intermediary role of the helper T cell in immune defence is reflected by the development of the extremely lethal disease of AIDS (acquired immune deficiency syndrome) when the human immunodeficiency virus (HIV) attacks and decimates the victim's helper T cells (which express CD4 markers), rendering the patient susceptible to a whole range of opportunistic infections, and even certain malignancies (Wong-Staal & Gallo, 1985). Ongoing fundamental research on T helper and other accessory cells may throw more light on their functions, and contribute to the untiring efforts to conquer this dreaded scourge.

A number of other lymphokines synthesized and secreted by activated T cells further illustrate the task of these chemical mediators in influencing cellular interaction, notably with the macrophage, which some immunologists have applauded as the "best supporting player" in the dramatic saga of the immune response. Thus, acting in the scenario are lymphokines which recruit macrophages to the site of the reaction (macrophage chemotactic factor); discourage their mobility from that site (migration-inhibition factor); and heighten their intracellular killing ability (macrophage-activating factor). Besides their antigen processing-presentation role in the afferent limb of the immunological response, these ubiquitous effector cells are also actively involved in the efferent phase, by phagocytosis of microorganisms and immune complexes, and destruction of tumour and graft cells (Nathan, Murrey & Cohn, 1980).

Cytotoxic T Cells.

Cytotoxic T cells represent yet another subpopulation of T lymphocytes, and operate as effectors especially against virally-infected cells and cancer cells. Interestingly, an obligate requirement for the recognition and destruction of virus-infected target cells is their surface expression of MHC class I self antigens together with new virus-encoded antigens (Zinkernagel et al. 1978).

Suppressor T cells.

T-B and T-T antergy define the phenomena whereby regulatory T cells belonging to the T suppressor subset (which express CD 8 receptors) exert inhibitory effects on B cells and other T cell subsets respectively. The down-regulation of B cell responses to thymus-dependent antigens is probably attributed to suppression of T helper and/or B lymphocytes. Suppressor T cells play a key role in immune tolerance, and autoimmune disorders have been suggested to be associated with defective suppressor activity – indeed, reductions in these cells have been correlated with clinical exacerbations in several of these disease.

Another striking illustration of how a failure in cellular cooperation in immunology can wreak havoc in the host is the finding that the growth of transplanted tumours in animals is increased in the presence of a large proportion of suppressor T cells. It is thought that these cells suppress the corresponding clone of cytotoxic T cells which are therefore restrained from destroying the tumour cells. This observation lends greater credence to the concept of immunological surveillance of cancer as expounded by Sir Macfarlane Burnet (1970).

B cells and Immunoglobulins.

B cells coordinate with one another through antibodies synthesized by different clones and directed against specific epitopes or antigenic determinants on the target cell surface (B-B synergy). Another feature of teamwork between plasma cells is their pro-

duction of several classes of immunoglobulins each with its own unique purpose. For example, the well-armed pentameric IgM molecule is aptly suited for its role in the primary antibody response when antigen is confronted for the first time; while its smaller counterpart, IgG, participates in the secondary response and confers protection on the foetus via placental transfer; and secretory IgA patrols the mucosal membranes, guarding these likely portals of entry from harmful invaders.

Notwithstanding the undesirable effects of homocytotropic IgE antibodies in type I immediate hypersensitivity reactions,these immunoglobulins interact with other leucocytes to counter helminthic infestations, widely endemic in many developing countries. IgE- coated mast cells degranulate in the vicinity of the worms, culminating in the discharge of vasoactive amines and eosinophils chemotactic factor of anaphylaxis (ECF-A) which attracts eosinophils to the area. In vitro cytotoxicity of antibody-bound schistosomula has been demostrated, and is probably related to the release of major basic protein from eosinophil granules (Butterworth, Vadas & David, 1980).

Fixation of complement to IgG or IgM antibody-antigen complexes triggers the classical pathway leading to the formation of activated components, ultimately causing target cell lysis. Amongst these activated proteins, C3a and C5a are strongly chemotatic for phagocytes, namely neutrophils and macrophages, which are attracted to the site of inflammation and take part in the removal of debris. C3b behaves as an opsonin by binding to a C3b surface receptor present on neutrophils and macrophages, thereby facilitating phagocyte-target cell contact and phagocytosis. This phenomenon of immune adherence and opsonization is also exhibited by antibodies whereby Fc receptors on the plasma membrane of neutrophils and macrophages bring about their close proximity to antibody-coated microorganisms, thus promoting phagocytosis.

An additional way in which B cells collaborate with effector cells via the mediation of immunoglobulins is through antibody-dependent cell-mediated cytotoxicity (ADCC). This process of ADCC involves killer (K) cells which are "null" lymphocytes (so called since they express neither B nor T markers) and possess surface Fc receptors hence fulfilling their cytotoxic function by binding to antibody-coated target cells. Tumour and virus-infected cells coated with immunoglobulins are believed to be among the "casualties" of ADCC.

Antibody production is under homeostatic control and is regulated by a "negative feedback" mechanism. This B-B antergy is accomplished by antibody eliminating antigen, or by competition between preformed antibody and B lymphocyte surface immunoglobulin receptors for antigen.

B and T Memory Cells.

Finally, B and T memory cells serve to recognize and provoke responses against specific antigens during subsequent encounters with them, and thus symbolize the cornerstone of the phenomenology of active immunization.

Hidden Mysteries and its implications.

Even though our current knowledge of cellular interactions in immunology is still far from complete, research continues to unravel more hidden mysteries. A better understanding and manipulation of this fascinating network would clearly have far-reaching implications and wide-ranging applications in medicine. Progress could be made in novel immunotherapeutic approaches to combat cancer; the prevention of graft rejection could be improved in this day and age of organ transplantation; sufferers of autoimmune, allergic and hypersensitivity disorders could expect more effective therapy; AIDS patients and other immunocompromised individuals could anticipate more hopeful treatment modalities.

But perhaps the tale of this remarkable equilibrium and fine- tuning mechanism at a cellular and molecular level should serve as a valuable sociology lesson in mutual cooperation for our modern superspecialized world. Humankind could also do well to ponder that, like in immunology, a breakdown in communication between its members can have rather disastrous consequences.

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UPDATE

UPDATE ON OCCUPATIONAL MEDICINE– OCCUPATIONAL DERMATOLOGY

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Introduction

Occupational skin disease has been defined as any "pathological condition of the skin for which job exposure can be shown to be a direct or contributory factor" by the Committee on Occupational Dermatoses of American Medical Association.

In the U.S.A., occupational skin disease is the most pervasive occupational health problem. It comprises more than 45% of reported work related diseases, but this reported incidence is estimated to be about 10 to 15 times less than the true incidence of occupational skin disease [1]. In Sweden, where registration of occupational disease is comprehensive, occupational dermatoses forms about 50% of all registered occupational diseases. In fact the W.H.O. had once described it as the most frequent occupational disease.

In Singapore, occupational skin disease is a leading notifiable occupational disease, and it has consistently been the second most frequently notified industrial disease in recent years.

However, as there is also a fair degree of under-reporting in Singapore, the magnitude of the problem is considerably larger.

Impact on Industry

The impact of this common occupational disease to industry is tremendous. A conservative estimate has been made that about one worker per thousand is affected annually, and the cost of occupational skin disease to the United States has been calculated to be possibly as high as US$400 million per year (for worker replacement, medical consultation, and legal and rehabilitative costs)[3].

In Singapore, for the years 1985 and 1986, more than $46,000 was paid in compensation fund. The average award per case was about $150[2].

Some functions of the skin at the workplace

The skin serves as an efficient protective layer of the body. Its high tensile strength and resiliency provides defense against physical injury, especially shearing stress, and the keratin layer acts as a barrier against irritating and sensitising chemicals, systemic poisons, and micro-organisms.

Melanin is believed to protect against the damaging effects of ultraviolet light, and the continual renewal of the cellular epidermis discourages bacterial and fungal colonisation. In addition, the skin function of thermoregulation is achieved by perspiration.

Occupational skin disease – important features to look for

The following features often give a good indicator of a possible occupational aetiology of skin disease, and should be elicited and noted in any worker presenting with skin disease.

The exact nature of work, exposures to possible dermatotoxic agents, work practices and habits should be noted. Whether protective equipment is worn and whether other workers are similarly affected should also be enquired.

The location of rash, its morphology, and its improvement (if any) during rest days and holidays from work are also important clues to the diagnosis. Finally, a search for other possible exposures such as domestic exposures e.g. laundry and dishwashing at

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home, hobbies and concurrent second occupations, should also be done.

Individual susceptibility plays an important role in the development of occupational skin disease. In particular, a history of atopy is important, as atopics have been found to be 13.5 times more likely to contract occupational dermatoses[4].

A suggested approach to diagnosis

Rycroft [5] has proposed that the following questions be asked in an approach to the diagnosis of occupational disease.

(1) Is it eczema or not?

Eczema and dermatitis, which are often used synonymously, is an inflammatory skin condition characterised by redness, swelling, small fluid filled blisters, oozing of this fluid, in the acute state. In the chronic stage, it appears as a scaling, cracking or thickening of the skin.

Most occupational dermatoses are eczematous reactions to contact factors in the workplace.

(2) Is it contact (exogenous) dermatitis or not?

Endogenous or constitutional eczemas such as atopic, seborrhoeic, varicose and discoid eczemas, are unlikely to be occupational in origin.

However, these endogenous eczemas can be aggravated by occupational factors, and may be a predisposing factor for a person to contract occupational skin disease.

Contact dermatitis is the most common occupational skin disease, comprising approximately 95% of all occupational dermatoses[3].

(3) If it is contact eczema, is it irritant or allergic in origin?

Irritants are substances which directly damage skin at the site of application through a non-immune mechanism. Irritant contact dermatitis comprises more than 75% of all occupational skin diseases. It can be broadly classified as an acute irritant dermatitis which is caused by contact with a strong irritating substance, or a chronic irritant dermatitis, which is a cumulative insult dermatitis caused by marginal irritants. In the cases of marginal irritants, individual susceptibility is an important consideration as to whether a person develops occupational skin disease.

Allergens may produce no direct damage during the initial contact, but may sensitise the person to the allergen, and evoke an allergic response in the body on subsequent contact. An allergic reaction occurs in the sensitised individual who subsequently contacts the allergic, and produces the dermatitis 36-48 hours later.

Patch testing is the definitive test for allergens. A series of suspected allergens are placed against the skin for 48 hours and subsequently read. False positive tests may be due to the irritancy of test substance, or the presence of active eczema elsewhere. A false negative patch test may be due to a missed allergen, which had been included in the test battery.

Table 1 lists the common occupational irritants and allergens in Singapore, based on patients with occupational skin disease seen in Middle Road Hospital.
Source: Goh C L, 1987[6]

(4) Are additional factors involved (e.g. sunlight)?

A phototoxic substance is a substance which depends upon the additional factor of sunlight for its irritants or toxic effect to be manifested. It is an exogenous chemical which can absorb ultraviolet radiation and initiate photochemical events in the tissues. Examples of such phototoxic agents include drugs such as phenothiazines, sulphonamides, and tetracyclines. However, certain workplace chemicals e.g. polycyclic aromatic hydrocarbons, are also known to cause such reactions.

Phototoxicity refers to chemically induced photosensitivity which does not have an immunologic basis and therefore exhibits a direct dose response relationship; while photoallergic reactions have an immunologic basis[7]. These are analogous to irritant and allergic contact dermatitis.

TABLE 1: COMMON OCCUPATIONAL IRRITANTS AND ALLERGENS IN SINGAPORE

COMMON OCCUPATIONAL IRRITANTS AND ALLERGENS IN SINGAPORE

Occupational Irritants (n = 310)		Occupational Allergens (n = 215)	
Coolants/soluble oils	20.0%	Chromate	49.3%
Cement	17.4%	Rubber chemicals	16.3%
Solvents	17.1%	Nickel	12.6%
Oil/grease	16.2%	Cobalt	13.0%
Soap/Detergents/water	11.9%	Resins	6.0%
Soldering flux	7.8%	Food	2.3%
Resins	4.8%	Soldering flux	1.4%
Others	4.8%		

Source: Goh C L, 1987 [6]

In such instances, standard patch tests would be negative, and positive reactions are seen only if the skin is exposed to these chemicals as well as ultraviolet radiation (photopatch testing).

Other causes of occupational skin disease

Other causes of occupational skin disease are relatively less common. Biological agents such as fungi, parasites; physical agents such as ionising radiation, mechanical factors, ultraviolet light, heat, and cold, can cause work related skin disease.Certain chemical agents, for example, the dioxins, can cause systemic toxicity and chloracne, while others, such as paratertiary butyl phenol and its homologues, can cause leucoderma[8].

Contact urticaria is a wheal and flare response on the application of materials to intact skin. It is now believed to be commoner than previously thought. Some exposures which can cause contact urticaria are: certain animals (e.g. caterpillars and other arthropods) and plants (e.g. seaweed), foods such as thyme and cayenne pepper, fragrances and flavouring such as Balsam of Peru and cinnamon oil, several types of medicaments, metals e.g. cobalt, and some preservatives (e.g. formaldehyde and sodium benzoate)[9].

Occupational skin cancers can occur with excessive exposure to ultraviolet radiation, polycyclic aromatic hydrocarbons, and arsenic. Certain statutory medical examinations (with special emphasis on clinical examination of the skin) are required for workers exposed to some of these cutaneous carcinogens – arsenic, tar, pitch, bitumen and creosote[10].

Some predisposing and aggravating factors

Several factors are known to predispose to the development of occupational skin disease or to aggravate existing skin conditions. As mentioned earlier, constitutional factors, for example, a history of atopy, is an important determinant. The presence of a breach in the intact skin, which may occur as lacerations or abrasions, is another risk factor for both irritant as well as allergic contact dermatitis.

In addition, an ill informed workman who is ignorant of work hazards, proper working practice, and who does not practise good personal hygiene, is at higher risk of occupational skin disease.The use of clean workclothes is also advisable. Skin contact with clothing contaminated by irritant solutions is akin to applying a poultice to the affected parts.

A poorly ventilated and excessively hot working environment induces perspiration, and can aggravate heat rashes and intertriginous skin lesions. Additionally, the sweat may act as a medium to dissolve irritant substances e.g. cement, into solutions.

Preventive Measures

Occupational skin diseases are eminently

preventive [11]. Well established principles of prevention such as the substitution of removal of the offending agent; isolation of the worker or enclosure of the process can be implemented to prevent occupational dermatoses. A well ventilated workplace is desirable, especially for work involving volatile solvents and irritant dusts and fibres.

Pre-placement and periodic medical examinations, health education and training of the workers for hazard awareness in proper handling techniques, and the importance of good personal hygiene also have a role to play in prevention.

The provision of adequate washing and drying facilities, and personal protective equipment (e.g. gloves, sleeves, aprons) which are properly maintained would also help prevent skin disease due to work.

Finally, continual surveillance of the occupational health situation and prompt investigation and management of any outbreak of occupational skin disease should be encouraged. It should also not be forgotten that notification of all cases of occupational skin disease to the Ministry of Labour is a statutory requirement in Singapore.

Conclusion

Occupational skin disease is a commonly encouraged work related illness. It is hoped that this paper has served as as update on this important subject in occupational medicine.

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UPDATE ON PROSTATIC DISEASES

ANATOMY AND MEDICAL TREATMENT OF BENIGN PROSTATIC HYPERPLASIA

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ANATOMY

The prostate is an accessory sexual organ of the male. It develops from epithelial outpouchings from the urethra during the 12th week of fetal life under the influence of androgenic hormone from the testes. The size of the prostate remains small after birth until puberty when it rapidly increases in size and continues to grow up to the third decades. It is classically described as a compressed inverted cone, situated in the true pelvis behind the symphysis pubis and in front of the ampulla of the rectum. The prostate has an anterior, a posterior and two infero-lateral surfaces. Anteriorly, it is attached to the pubic bone by pubi- prostatic ligament and posteriorly separated from the rectum by the strong Denovilliers' fascia. Superiorly it continues with the neck of the bladder. The urethra transverses the substance of the prostate and emerges at the apex at the level of urogenital diaphragm. The verumontanum which is situated at the distal end of the prostatic urethra is an important landmark during transurethral resection of the prostate. At this level, the ejaculatory ducts also enter into the prostatic urethra. A normal prostate measures 3 x 2 x 2 cm and weighs about 10gms.

Histologically, the prostate comprises 70% of glandular epithelium and 30% of fibromuscular stroma.

In the primate, the prostate consists of a cranial and a caudal lobes; however, no such distinction can be observed in men. The prostate was formerly classified by Lowsley into five lobes, that is the anterior, median, posterior and two lateral lobes. This arises from his belief that the prostate originates from five separate groups of glandular elements that later fused as one uniform gland. It is now replaced by the classification proposed by McNeal who identified four distinct zones within the prostate having morphologic, functional and pathologic significance. These four zones are:

1. the anterior fibromuscular stroma,
2. the central zone,
3. the peripheral zone and
4. the preprostatic zone.

The prostate gland derives its blood supply from the inferior vesical artery and it also has rich lymphatic communication which drains to the obturator lymph nodes, then into the internal iliac and the common iliac lymph nodes. The nerve supply is via the sympathetic and parasympathetic nerve plexuses. Recently, both alpha one and alpha two receptors have been found to be abundantly distributed within the capsule and tissue of the prostate. Stimulation of these receptors resulted in contraction of the smooth muscle of the prostate and increase in tone of the prostatic urethra.

The prostate is closely related to the urinary sphincter mechanisms and two distinct urethral sphincter mechanisms are seen in the male.

1. Proximal urethral sphincter mechanisms, or the internal sphincter which is situated around the bladder neck and consists of smooth muscle fibres under the involuntary control by visceral nerve. Damage of this sphincter will result in retrograde

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ejaculation of the semen.

2. Distal urethral sphincter mechanisms, or the external sphincter which is situated just distal to the verumontanum and consists of three components, the internal smooth muscle, intrinsic striated and extrinsic striated muscles. The most important muscle that is responsible for continence is the intrinsic striated which is a slow twitch muscle under the autonomic nervous control. Together with the internal smooth muscle, both are situated within the musculature of the urethra. The extrinsic striated muscle only attaches to the urethra at the posterior aspect and is a fast twitch fibres under the control of pundendal nerves. Following prostatectomy with removal of the internal sphincter, it is this distal urethral sphincter that is responsible for continence.

PATHOLOGY

Benign prostatic hyperplasia (BPH) is probably the most common neoplastic growth that occurs in men. In most instances, it starts to undergo hyperplasia after the age of 50 years. Benign prostatic hyperplasia originates from the proliferation of glandular epithelium and stroma from the preprostatic tissue around the urethra.

Nodule formation and its enlargement with increasing age is an important feature of benign prostatic hyperplasia which later results in bladder outlet obstruction. Hypertrophy of the detrusor muscle occurs in order to maintain flow. Changes like trabeculation, saccules and diverticuli formation are seen at this stage, As the obstruction progresses, hydronephrosis also occurs with impairment of renal function.

Though the presence of the testes and aging are two important features leading to the development of benign prostatic hyperplasia, the exact aetiological mechanism is still not clear. The theories proposed consist of:-

1 BPH reflecting merely a reaction of normal prostate cells to an abnormal endocrine environment.

2 BPH reflecting a stimulated growth of substantially altered prostate cells by a minimally altered hormomal environment and

3 BPH reflecting a variable mixture of these factors.

SYMPTOMATOLOGY

In the early stage of benign prostatic hyperplasia, the symptom is usually minimal due to compensatory hypertrophy of the detrusor muscle. As the adenoma enlarges further and causing more obstruction of the urethra, the obstructive symptoms become obvious and they consist of:–

1. poor stream of micturition,
2 hesitancy of micturition,
3 post micturition dribbling,
4 incomplete emptying and
5 retention of urine.

Although urinary retention is a late manifestation of benign prostatic hyperplasia, about 75% of our local patients presented to the doctors in this manner. Haematuria is not a common symptom by itself and is only seen in 5% of our patients. It tends to occur in those patients with large and congested prostate.

About 50 to 80% of patients with benign prostatic hyperplasia also develop unstable bladder and is associated with symptoms of frequency, urgency and urge incontinence. It is important to recognize these secondary irritative symptoms and distinguish them from patients with primary irritative symptoms caused by diseases affecting the bladder such as cystitis, bladder stone, neurogenic bladder and tuberculosis of the bladder. In patients with secondary irritative symptoms caused by benign prostatic hyperplasia, 75% of these patients showed improvement following prostatectomy; whereas in those primary irritative symptoms, surgery will only make the symptoms worse. The distinction between these two types of patients is best evaluated by urodynamic study.

MEDICAL TREATMENT

Up till now, there is no effective medical treatment to cure patients with benign prostatic hyperplasia and surgery remains the best and the most definite method to relieve the

obstruction.

Review of literature showed that many drugs had been used in the past to treat benign prostatic hyperplasia. Drugs like estrogen-androgen combination were used by Kauffman and Goodwin with little beneficial effect; anti-androgens like 17-hydroxy progesterone, medrogestone, cyproterone acetate and flutamide were used by several investigators and again with no significant improvement of symptoms.

Perhaps the most important development in the medical treatment of benign prostatic hyperplasia was the recognition of the presence of alpha-adrenergic receptors in the prostate by Caine et al in 1975. They demonstrated that the tone of smooth muscle of the prostate and the capsule is under the influence of the alpha-adrenergic receptors. Blockade of these receptors with drugs such as phenoxybenzamine (alpha 1 and alpha 2) or prazosin (alpha 1) results in reduction of flow resistance of the prostatic urethra. Hence it becomes clear now that in patients with benign prostatic hyperplasia, in addition to mechanical obstruction, there is also a neurogenic or dynamic component which contributes to outflow obstruction. The rationale of medical treatment in benign prostatic hyperplasia is tus aimed at abolishing this dynamic component.

Caine et al showed that 80% of their patients treated with phenoxybenzamine had improvement of obstructive symptoms. However, 30% of patients developed side effects of the drugs like dizziness, weakness, palpitation and syncope. In 10% of patients treatment had to be terminated due to severe side effects. Brooks on the other hand when using phenoxybenzamine 10 mg/day for his patients, reported no beneficial effect. More recently, prazosin, a selective alpha one blocker has been used by several workers and reported good symptomatic relief following treatment. Both Hedlund and Kirby showed improvement of maximum flow rate in 60% of their patients with minimal side effect.

Both phenoxybenzamine and prazosin are effective in relieving obstructive symptoms but prazosin gives the least side effect due to its selective alpha one blockade. Phenoxybenzamine has been shown recently not proven in men, it is probably safer to use it only on short term basis.

It is known that the symptoms of benign prostatic hyperplasia might wax and wane and are not always progressive. Hence, in those patients with mild to moderate symptoms with no renal impairment and no urgent indications for surgery, treatment with alpha blocking drugs would be appropriate. It is also beneficial to those patients awaiting surgery to temporarily relieve the symptoms of bladder outlet obstruction. Another category of patients who might benefit from this regime of treatment are those who are not fit for surgery either temporarily or permanently due to several underlying medical diseases. However, one has to be aware that these drugs might be contraindicated in patients with cerebrovascular accident, severe ischaemic heart disease and recent myocardial infarction.

SURGICAL ASPECTS OF BENIGN PROSTATIC HYPERPLASIA

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INDICATIONS FOR SURGERY

Acute retention of urine:

One episode of acute retention of urine is enough indication for surgery. Even though 50% of patients deny any previous history of difficulty in passing urine, after surgery many of them will experience improved urine flow as if they were young again!

Acute retention of urine is an agonising condition. The ideal management would be for the Primary Care physician to insert an indwelling catheter in the clinic and send the patient on to the emergency department for admission to the urology ward. Before catheterisation, the urethra should be properly anaesthetised with 2% lignocaine jelly and if there is difficulty encountered, the procedure should be abandoned and the patient sent speedily to the hospital. If urethral catheterisation fails, percutanous suprapubic cystostomy can now done in the ward.

For those patients who refuse or who are not fit for surgery, the catheter can be removed after 4 days if their renal functions are normal, and conservative treatment with alpha adrenergic blockers can be tried. A successful patient is sent home with an IVU appointment to assess the degree of bladder outlet obstruction. If there is significant degree as shown by dilated ureters and marked residue urine, the patient should be advised strongly to have surgery.

Symptoms of bladder outlet obstruction (Prostatism)

Hesitancy, poor stream and intermittency are symptoms specific to bladder outlet obstruction. Frequency per se is not. In this group of patients, IVU should be done before referring the patients to the urology clinic for further assessment. Uroflow study can now be done to measure the flow rate more objectively. A flow rate of less than 10ml/sec. is evidence of significant outlet obstruction and surgery would strongly be indicated.

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Other indications:

The other indications are recurrent urinary infections, presence of bladder stones in about 10% of our patients and painless gross haematuria in about 5%. Patients with enuresis due to high residue urine and overflow incontinence would also require surgery. With better medical care the incidence of chronic retention of urine with associated renal failure is not common (about 1% of patients).

PRE-OPERATIVE MANAGEMENT

General Assessment: In our previous study, slightly more than 60% of our patients are in clinical grade 2 and 3, i.e. patients who are above the age of 70 or those with associated hypertension, diabetes, chronic obstructive airway disease, ischaemic heart disease, previous myocardial infarction or cerebrovascular accident. Ideally those with recent myocardial infarction or cerebrovascular accident should wait at least 3 to 6 months before surgery.

Specific Assessment: Pre-operatively urinary infection if present should be controlled with appropriate antibiotics. The electrolytes should be normal with serum sodium at least above 130mEq/L. In patients with chronic renal impairment one should wait until the urea and creatine levels stabilise.

OPERATIVE PROCEDURES

Transurethral resection of prostate is the

procedure of choice for removal of the obstructing prostate because of the many advantages. If properly done, the mortality and morbidity are low. Patients can generally be discharged within a week and return to normal activities within another 2 to 3 weeks. The main advantage to the patient is lack of post operative pain. The offending pathology is dealt with directly without having to cut through unnecessary tissues. Therefore the metabolic upset to the patient is minimum. Thus even the old and infirm could tolerate this procedure well.

Open surgery for removal of the prostate should not be done nowadays except for the occasional big prostate associated with big or multiple bladder stones.

POST OPERATIVE MANAGEMENT.

The patient is put on continuous bladder irrigation with normal saline for 24 hours. The indwelling catheter is removed on the 2nd or 3rd day and the patient is discharged the day after if there are no complications.

Patient is reviewed at 6 weeks and then 6 months post- operatively. By 6 weeks the post operative symptoms of frequency, urgency and occasional haematuria should disappear. During this period, the General Practitioner has an important role to play in reassuring the patient and to treat him if the symptoms are severe. Constipation should be avoided as straining at stool can give rise to secondary haemorrage, though urinary infection is generally thought to be the main cause. If urinary infection is suspected, the urine is sent for culture and the appropriate antibiotics given. The rewiew at 6 months is to detect the possibility of urethral stricture or bladder neck stenosis in about 5% of patients.

COMPLICATIONS

Mortality: The mortality is about 1 to 2%. The commonest cause of death is acute myocardial infarction post operatively because of the group of old patients we are dealing with. Thus one should be cautious in advising patients with severe ischaemic heart disease or recent myocardial infarction to have surgery.

Morbidity:

Sexual dysfunction: A high percentage (54%) of patients will develop retrograde ejaculation after surgery but the sexual potency usually should not be affected. (4%). The patient should be warned about the dry ejaculation and be reassured that it would not affect his health, but only affect his fertility which is usually not important in this age group. However in younger patients, sexual dysfunction may be an important consideration and if their bladder outlet obstruction is not severe, surgery can be postponed.

Post-operative retention of urine: (5%) This can be distressful. This is managed by further period of catherisation for 4 to 5 days. If the patient is still unable to pass urine, then recystoscopy is done to exclude mechanical causes of obstruction such as remnant apical lobe which needs to be removed. If there is no mechanical obstruction, the retention is assumed to be due to poor detrusor tone and the patient is treated with further period of catheterisation and cholinergic agents (urocholine, carbacol). Occasionally some patients with added neurogenic bladder problem may require prolong period of catheterisation before they recover.

Incontinence of urine: Total permanent incontinence should be rare, less than 1%. Temporary stress incontinence is more common (5%) and fortunately most of them recover in time as the prostatic urethra heals.

Infections: post operative urinary infection is common (25%). The infection usually responds to the usual antibiotics. Septicaemia and epididymo-orchitis sometimes can occur.

Secondary Haemorrage: (7%) This occurs within 2 to 3 weeks of surgery and is probably related to infection and constipation. If mild, it can be managed with high fluid intake and reassurance. If severe with clots, the patient needs to be readmitted to hospital for bladder washout and possible cystodiathermy to control the bleeding.

Post-operative urethral strictures and bladder neck contracture: (5%) Patient will give a typical history of deterioration of urine stream after initial improvement. This usually occurs within 3 to 6 months. Patients will

respond well to treatment with optical urethrotomy or bladder neck resection.

CONCLUSION

Transurethral resection of prostate (TURP) is the treatment of choice for obstructing prostate. The mortality and morbidity are low and the benefit is high especially for those with retention of urine . For those patients with less severe symptoms and who are not keen on surgery, conservative treatment with alpha adrenergic blockers may have a role to play. However this group of patients need to be monitored closely for possible ill effect of obstructive uropathy and also carcinoma of the prostate need to be excluded.

PROSTATITIS

Dr IR Rekhraj *MBBS, FRACS, AM*

The term prostatitis is used to describe any condition associated with prostatic inflammation or prostatic symptoms.

Despite recent advances regarding features and sequelae of inflammatory conditions of prostate, many urologists and physicians have been perplexed about the diagnosis and management of prostatitis. This state has emerged in the past because of varied criteria to define and classify prostatitis; the difficulty in localising and identifying causative organisms, and the lack of understanding of pharmakokinetics of antibiotics acting on the prostate.

INCIDENCE

The true incidence of prostatitis is still undetermined. However, indirect studies relating to autopsy findings have led to an estimated incidence of 4-5% of all men in the general population. The incidence is said to increase to as high as 16% in advanced age.

CLASSIFICATION

The classical work of Stamey et al in 1978 on quantitative bacteriological localisation cultures, and on microscopy of prostatic expressate by other workers, have led to the present classification of the disease. Although several distinct types of prostatitis or prostatic syndromes occur, the most prevalent conditions are :

* Bacterial Prostatitis :
  - Acute
  - Chronic
* Nonbacterial Prostatitis
* Prostatodynia

The less common types of prostatitis include gonococcal, tuberculous, mycotic, non-specific granulomatous, and parasitic.

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BACTERIAL PROSTATITIS

Bacteriology

The pathogens responsible for bacterial prostatitis are common gram −ve organisns which usually affect the rest of urinary tract:- E. coli, klebsiella, Proteus, Enterobactor, Psuedomonas, and Serratia. E. coli is the commonest pathogen among all the gram −ve bacilli. Of the gram +ve enterococci, Str. faecalis is the only pathogen which may cause chronic bacterial prostatitis.

Although most infections are caused by single pathogens, mixed infections by two or more bacteria is not unknown in bacterial prostatitis.

SYMPTOMATOLOGY

Acute bacterial prostatitis is the only condition which has general constitutional symptoms of malaise, chills, and fever in addition to the local and bladder symptoms.

Local symptoms are pain in the perineum, medial aspect of thighs, low back ache or pain in the groins. Painful erections and painful ejaculation are common in Nonbacterial prostatitis and in Prostatodynia.

Bladder irritative symptoms constitute frequency, dysuria, and urgency while obstructive symptoms could be hesitency, poor stream and rarely retention of urine.

METHODS OF DIAGNOSIS

Present methods of diagnosis are based on two main tests :
(i) Microscopy of prostatic expressate and (ii)

quantitative bacteriologic localisation cultures. X-ray, cystocopy, prostatic biopsy, or even rectal examination of the prostate cannot differentiate the most common types of non-acute prostatitis.

In carrying out the above mentioned tests, the patient is made to void the first 10 ml of urine in a container (VB1) – urethral sample; followed by the collection of midstream urine (VB2) – bladder sample; the prostatic secretions expressate (EPS) by prostatic massage – prostatic fluid; and the first voided 10 ml of urine immediately after prostatic massage (VB3) – prostatic fluid sample. The samples are examined (i) microscopically for WBCs and lipid-laden macrophages (oval fat bodies) and (ii) cultured for bacteria.

The finding of >10 WBC/HPF and the presence of abnormal number of macrophages in the prostatic expressate are sure signs of prostatic inflammation. (Exclude: urethritis, stricture, expressate within 3 days of ejaculation).

The bacteriologic cultures specifically localise the infection to the prostate if the EPS and VB3 cultures exceed by ten fold compared to other specimens. However, when the two tests are positive along with VB2 (bladder specimen), the patient is treated for one week with antibotics which attain high urinary concentration but low level in prostatic secretions (eg: Nitrofu rantoin). The bacteriologic localisation test is then repeated. In cases of bacterial prostatitis, the prostatic pathogens can still be recovered.

TREATMENT

The treatment of acute bacterial prostatitis is much the same as for other urinary tract infections. General supportive measures, urinary diversion if acute retention of urine occurs, and appropriate antibotics usually result in a good response and cure. The inflammatory reaction, fortunately, disturbs the barrier between plasma and prostatic epithelial membrane and permits adequate levels of most broad spectrum antibiotics to diffuse into the area of infection. Ampicillin with gentamycin are recommended initially until the culture and sensitivity results are known when appropriate oral therapy is started and continued for further three weeks. Alternatively, therapy with TMP-SMX (Trimethoprim – Sulfa methoxazole) can be initiated if the clinical condition permits and the frug continued for a full four weeks to ensure a cure and prevent the development of chronic bacterial prostatitis.

The treatment of Chronic bacterial prostatitis poses problems due to plasma – prostatic fluid barrier to antibiotics. Although bacteria affecting the prostate are highly sensitive to the antibiotics in-vitro sensitively studies, they are unable to reach the site of bacterial infection in chronic prostatitis. The factors that determine the diffusion and concentration of drugs between the compartments are: lipid solubility, high ionisation (pka), low protein binding property of antibiotics, and a pH gradient difference of at least 1. The drugs that meet with these criteria are :-

(i) Trimethoprim – Sulfamethoxazole
(ii) Carbenicillin indanyl sodium
(iii) New tetracyclines: menoxycycline, Doxycycline

It is important to continue the treatment with the chosen antibiotics for at least 12 weeks to achieve a cure. About 75 – 90% achieve a clinical cure and 40 – 75% a bacteriologic cure. Relapses can be controlled by repeating the course with appropriate antibiotic. Men who are not cured by medical therapy can be kept relatively comfortable with use of continuous, low dose, daily suppressive therapy.

The role of TURP in chronic bacterial prostitis with prostatic calculi is unresolved. About 30% are said to benefict from the procedure. The calculi lie in the deep part of the gland and TUR does not eradicate them. Only total prostatectomy can effect a cure. But this operation has its own serious complications.

NON-BACTERIAL PROSTATITIS

Nonbacterial prostatitis, a syndrome of uncertain cause, is the most common type of prostatitis seen today. A definitive therapy of this condition is difficult. If there is a suspicion of Chlamydia or Ureaplasma, a clinical trial using one of the new tetracyclines or erythromycin may be given for two weeks. If there is no improvement, the antibiotics

should not be repeated and the patient treated symptomatically. Reassurance and full explanation of the syndrome may alleviate the anxiety that accompanies this condition. Bland diet, warm sitz bath and anticholinergics and anti-inflammatory drugs may relieve the irritative symptoms and pain.

PROSTATODYNIA

Prostatodynia is again a very difficult syndrome to treat. Tranquilisers and alpha-sympathetic blockers have been tried with some success. Antibiotics and analgesics have no beneficial role in the treatment of this condition.

UPDATE ON PROSTATIC CANCER

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The incidence of prostatic cancer in Singapore is only 8 per 100,000 population or predicted to have 91 new cases in the year 1990. This is a very low incidence when compared to USA where the incidence is 40 per 100,000. In the States, it is the second commonest cancer among the male population after lung cancer and the commonest cancer in man over 50. In Singapore it ranks ninth among the male population. There is a significant familial incidence which suggests a genetic component.

Clinical Features

The majority of the patients (75%) will present with symptoms of outflow tract obstruction similiar to that of Benign Prostatic Hyperplasia (BPH). Approximately 10 to 20% will present first to the orthopaedic surgeon with bony lesions. Uraemic symptoms would be a late feature when bilateral ureteric obstruction occurs.

Rectal examination is the most important step in the diagnosis of prostatic cancer. An indurated area and/or obliteration of the median groove are significant findings. It would progress to the classical bony hard prostatic enlargement with features of fixity.

1. **Anaemia** may occur at a late stage when a bone marrow is replaced by tumour.
2. **Uraemia** may set in when bilateral urateric obstruction occurs.
3. **Serum Prostatic Acid Phosphatase** is important in the diagnosis and staging of the prostatic cancer. It is also useful in monitoring the effectiveness of treatment.

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It is elevated in 70% of patients in Stage C and D diseases but often remains normal in Stage A and B diseases. Elevated levels can also be found in 6% of patients with BPH and about 5% with non-prostatic cancer.

4. **Serum Alkaline Phosphatase** elevation is evident with bony metastases. It reflects the osteogenic activity of the cancer. With effective therapy, this level will return to baseline.
5. **Prostate Specific Antigen (PSA)** is present in the serum in 75% of patients with Stage A and B cancer. However, it lacks sensitivity and specificity to be used as a screening test. It has been used in monitoring the disease process.
6. **Intravenous Urogram (IVU)** may show ureteric obstruction as well as metastases to pelvic bones and lumber spine.
7. **Transrectal Ultrasound** of the prostate has not been proven to be sufficiently reliable for routine detection of early cancer. Detection of hypoechoic lesions in patients with normal digital examination is followed by needle biopsy under ultrasound guidance with 5 to 10% subsequently proven to be carcinoma. Since 30 to 40 %of prostatic cancer are isoechoic lesions, these will escape detection by ultrasonography. Previous surgery, inflammation, stones and cysts will interfere with this investigation.
8. **Transrectal Needle Biopsy** can be performed in the clinic without anaesthesia.

Staging Investigations

1. **Lymphangiography** is used soley to detect lymph node involvement. Its accuracy is in the region of 80 to 90%.
2. **CT Scan** can determine the local extent of the disease as well as lymph node involvement.

3. **Bone Scan** Technetium-99m labelled Polyphosphate is used to detect bony metastases.

4. **Magnetic Resonance Imaging (MRI)** is the latest diagnostic tool. It can similarly determine the local spread of the cancer as well as lymph node involvement. It is particularly useful in detecting bony metastases.

TREATMENT

The scheme in Table I acts as a general guide for treatment of prostatic cancer at different stages of the disease (see Table II). The age and the grading of the tumour would influence the choice of treatment.

Table I – Table I Treatment of Prostatic Cancer

Stage A	
Af	Observe
A1, A2	RP/DXT
Stage B	RP/DXT
Stage C	DXT
Stage D	Hormonal Manipulation 1. DES 1 mgm T..D.S 2. Orchidectomy 3. Estramustine 4. LHRH analogue 5. Antiandrogens Steroidal – Cyproterone acetate Non-steriodal – Flutamide DXT to bony metastases Chemotherapy ± Hormonal therapy

Key: RP = Radical prostatectomy
DXT = Deep Xray Therapy

Orchidectomy: It is safe, has few side effects and gives rapid results. There is no question of therapeutic compliance. However, it causes the loss of libido and impotence.

Oestrogen Therapy: It reduces the pituitary release of L.H., thereby removing the central stimulation for testes to produce testosterone. Castrate levels of testosterone are usually achieved in 7 to 21 days when oral doses of $\geq$ 3 mgm. of diethylstiboestrol (DES) or its equivalent are delivered. It may cause nausea, vomiting, headaches and fluid retention. Long term side effects consists of gynaecomastia, loss of libido and potency and an increase of serious cardiovascular events.

LHRH analogues paradoxically during chronic administration causes the drop of sex steriods to castrate levels. They do not effect adrenal androgen production. It has few cardiovascular complications and lower incidence of gynaecomastia. Being degraded orally, it has to be given daily either subcutaneously or by nasal spray.

Antiandrogens are a class of compound that peripherally inhibit the action of dihydrotestosterone.

Steroidal agents are cyproterone acetate (CPA) and medroxyprogesterone acetate (MPA). Its central effect decreases LH production while peripherally it competes with dihydrotestosterone. It has less cardiovascular toxicity compared with DES.

Non steroidal antiandrogens such as flutamide have little central effect but do have potent peripheral effects. Potency is preserved as serum testosterone levels are not effected. It can cause flushing, diarrhoea and gynaecomastia.

Transurethral Resection of Prostate (TURP) is only required when there is significant outflow obstruction at any stage of the disease. Coring a passage through the tumour would be sufficient. It also provides tissues for histological confirmation.

In summary, the digital examination is the most important step in the diagnosis of prostatic cancer.

If the cancer is **not clinically overt** on digital examination, then the diagnosis is often made incidentally from histological studies of tissues obtained following a transurethral or open prostatectomy performed for B.P.H. Such patients are often of the disease. Those patients with focal or well differentiated tumours are at best observed closely without further treatment. Otherwise a more aggressive and radical approach is undertaken particularly in patients who are younger or suffering from a poorly differentiated tumour.

For clinically overt cancer, the diagnosis could be easily confirmed with a transrectal biopsy. The decision to do a TURP procedure would therefore depend on obstructive symptoms and urodynamic assessment. For

Stage B tumours. radical prostatectomy could be considered in centres experienced with this form of surgery. Otherwise, the althernative is irradiation with an acceptable 70% 5-year survival rate.

For Stage C tumours, irradiation would be the treatment of choice with a 40% 5-year survival figure.

With **advanced Stage D** disease, hormonal therapy has been shown to result in remarkable regression of the cancer with marked symptomatic improvement. Bilateral orchidectomy is advisable as it avoids the thrombo-embolic complications of oestrogen therapy. Chemotherapy would be considered when all other modalities of treatment fail. The result of chemotherapy has not been encouraging. Irradiation alleviates severe pain from bony metastases.

Unfortunately only 10% of men with prostatic cancer presents at an early stage when radical surgery would offer a reasonable hope of cure. At least half of these men would be over the age of 70 and are therefore not candidates for radical procedures. Thus an annual careful digital examination of man over 50 would be useful screening procedure. This is particularly so in man with a strong family history of prostatic cancer. Digital examination is still the most efficient and cost-effective approach for detection of the disease in an early and curable stage.

TABLE II STAGING OF PROSTATIC CANCER

	Rectal Exam	Acid P04	LNS	Metastases
STAGE A Early lesions				
Af Focal	N	N	–	–
A1 One lobe	N	N	–	–
A2 Multifocal, Diffuse	N	N	–	–
STAGE B Confined within capsule				
BN Solitary nodule < 1.5 cm.	AbN	N	–	–
B1 One lobe	AbN	N	+	–
B2 Diffuse	AbN	N	++	–
STAGE C Through Capsule	AbN	±	+++	–
STAGE D Through Capsule	AbN	++	+++	+

HOME STUDY SECTION

NON-SEDATING ANTIHISTAMINES

Dr Omar B.S.T.
MBBS (S'pore) MCGP (S'pore) FRACGP

The term antihistamine is rather unsatisfactory because the drug has numerous other actions. This partly derives from the fact that there is a considerable similarity of structure amongst such local hormones as histamine, adrenaline, serotonin and acetylcholine. A compound that may block the action of one substance may also be capable of blocking the action of another. Thus the H1-antihistamines may also have anticholinergic or sometimes a-adrenoceptor antagonist effects, and anticholinergic drugs may exhibit some antihistaminic actions. The H1-antihistamines are therefore used as hypnotics, antiparkinsonism preparations, antitussives and expectorants; all these actions are not obviously related to antihistaminic effects. These unwanted features are a disadvantage when H1-antihistamines are used specifically to counteract the effects of histamine, e.g. for allergies. The introduction of H1-antihistamines largely free of sedative and anticholinergic effects [terfenadine, astemizole, mequitazine] has been a useful advance.

Each of the the newer antihistamines is different in origin, chemical structure and specificity of action, and each is different in solubility and metabolic effects. However, they have in common the property of not readily penetrating the blood-brain barrier in the usual therapeutic dosages. In contrast, most of the older antihistamines are highly lipid-soluble and thus readily cross the blood-brain barrier. In crossing the blood-brain barrier antihistamines cause significant and sometimes troublesome CNS effects. The most common is sedation but others include appetite stimulation, mood disturbances, dizziness, tinnitus, poor coordination and visual disturbances.

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TERFENADINE [Teldane]

It is of interest to note that some of the new non-sedating antihistamines, and in particular terfenadine, were developed as an offshoot of the search for drugs with improved selective central effects in the treatment of anxiety and depression. Many antidepressants and tranquillisers are powerful antihistamines. However, terfenadine is an exception in that it was found to have no central effects but retained its antihistamine properties.

Terfenadine is perhaps the most specific of the H1-histamine receptor antagonists currently available. There is no evidence of cholinergic, serotonin or adrenergic antagonism. It does not readily cross the blood-brain barrier, in clinical dosage, but it binds to both peripheral and central H1-histamine receptors to a similar extent.

Terfenadine is rapidly absorbed, reaching peak plasma concentrations one to two hours after an oral dose. It undergoes rapid and extensive first-pass metabolism in the liver, and its metabolites are excreted in the urine [primarily] and faeces. Its half-life of about 20 hours allows a bd dosage.

Terfenadine is essentially devoid of CNS effects [either depression or excitation] when administered in high or low dosages. It neither impairs psychomotor performance nor adversely affects subjective feelings, nor enhanced the depressant effects of concomitantly administered alcohol or benzodiazepines. Although the UK Committee on Safety of Medicines has received several reports of terfenadine causing drowsiness and headache in some patients, controlled studies have shown the incidence of sedation due to terfenadine was comparable with that of

placebo and significantly less than with conventional antihistamines.

Terfenadine has been demonstrated to be of value in the symptomatic treatment of allergic rhinitis, hay fever, allergic rhinoconjunctivitis, acute pollenosis and perennial rhinitis. It is also effective in the treatment of histamine-mediated allergic skin disorders including urticaria and angioneurotic oedema. Terfenadine has also been demonstrated to be of value in protecting against exercise-induced asthma when given orally in a single dose of 120 to 180 mg; however further studies are required to properly assess its role in this area.

In common with other non-sedating antihistamines, terfenadine does not alleviate pruritus associated with non-allergic skin conditions in which conventional antihistamines are effective. The new H1-histamine receptor antagonists may relieve itch of peripheral origin when it is due to histamine release, but may not relieve itch of central origin.

Terfenadine is generally well tolerated. In controlled studies the incidence of adverse reactions in patients receiving terfenadine was similar to that reported in patients receiving placebo. Headache, sweating, dryness of mouth and mild gastrointestinal disturbances have been infrequently reported.

ASTEMIZOLE [Hismanal]

The available evidence indicates astemizole penetrates the blood-brain barrier only to a small extent and acts primarily on H1-histamine receptors. It has virtually no affinity for cholinergic receptors. In high dosages [not used clinically] it may have alpha-adrenoceptor blocking and antiserotonergic effects. As dosage increases receptor binding is no longer reversible and dissociation from receptors takes place only very slowly. This "insurmountable" antagonism is not seen with conventional antihistamines; it occurs with astemizole at therapeutic dosages, but with terfenadine only at very high dosages.

Astemizole is well absorbed, reaching peak plasma concentrations two to three hours after an oral dose. Its action begins slowly but persists up to four days after a single dose. The plasma half-life of unchanged drug is about five days but a major metabolite which also antagonises histamine has a plasma half-life of about ten days. A steady state may therefore not be reached for several weeks.

The recommended adult dose of 10mg suppresses skin weal and flare responses to histamine for several days. The usual dose is 10mg once daily, but doses as high as 20mg do not seem to adversely affect vision or performance.

The efficacy of astemizole has been convincingly demonstrated in allergic rhinitis [seasonal and perennial]. Additionally it has beneficial activity against the symptoms of allergic conjunctivitis and chronic urticaria [but not atopic dermatitis].

The side effects profile of astemizole is similar to that of terfenadine [described earlier]. Additional astemizole has occasionally been known to increase appetite and bodyweight during prolonged treatment. Astemizole, as is also terfenadine, is best avoided in women who are pregnant; very high doses of these drugs have increased foetal loss in rats.

MEQUITAZINE [Primalan]

Mequitazine appears to have greater affinity for peripheral than central H1-histamine receptors. It also crosses the blood-brain barrier poorly. Plasma concentrations peak at about 6 hours after an oral dose and the drug is cleared from the body about 38 hours after ingestion.

Sedation apparently does not occur at the optimum recommended dose of 5mg twice a day, although some CNS effects with impairment of performance have been documented at 10mg bd. It has some anticholinergic activity.

There is no doubt that the new non-sedating antihistamines are a valuable adjunct in the treatment of the allergic patient particularly in whom sedation and anticholinergic effects may be especially bothersome or detrimental. Barring unexpected findings with wider clinical use, non-sedating antihistamines could well become the "drugs of choice" in many patients in whom a H1-histamine receptor antagonist is indicated.

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5. Sutherland, D: Antihistamines in clinical practice Australian Family Physician June 1985.

X-RAY QUIZ

Contributed by **Dr K Param**

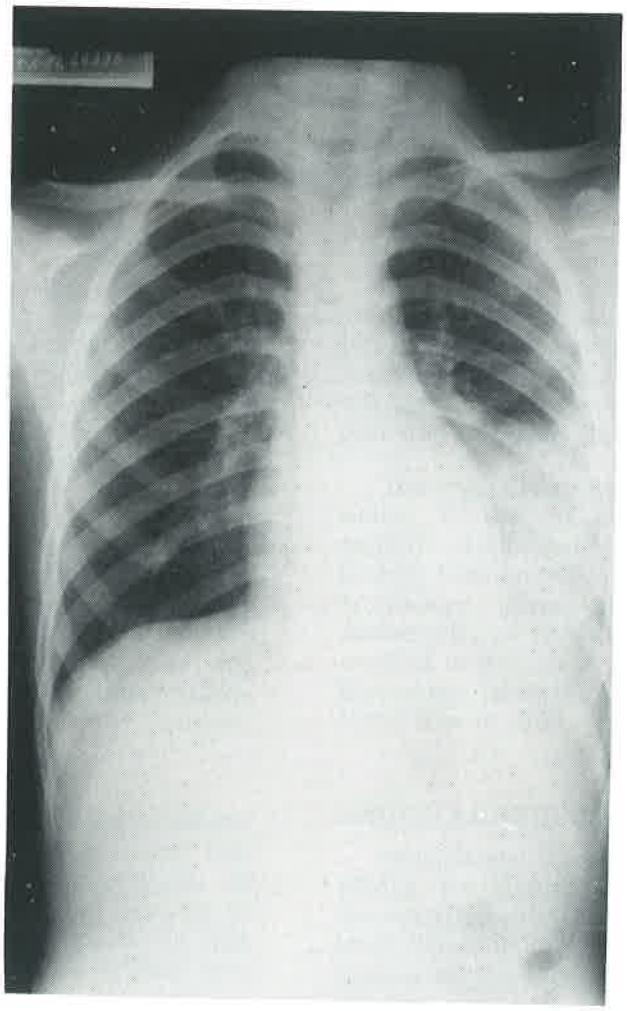


FIG I

Fig 1 is a chest X-ray of a young adult presenting with fever and cough.

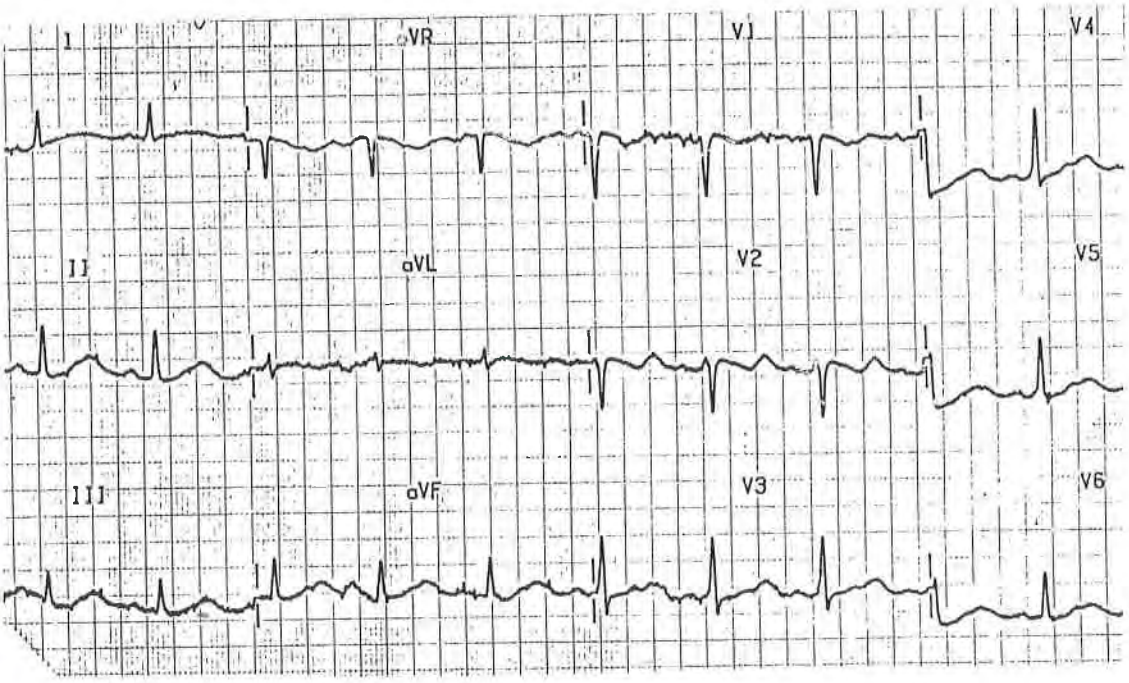
What abnormal features can you see in this CXR?

Where do you think the lesion lies?

ECG QUIZ

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

What prominent abnormality is present in the ECG shown? What is your diagnosis?



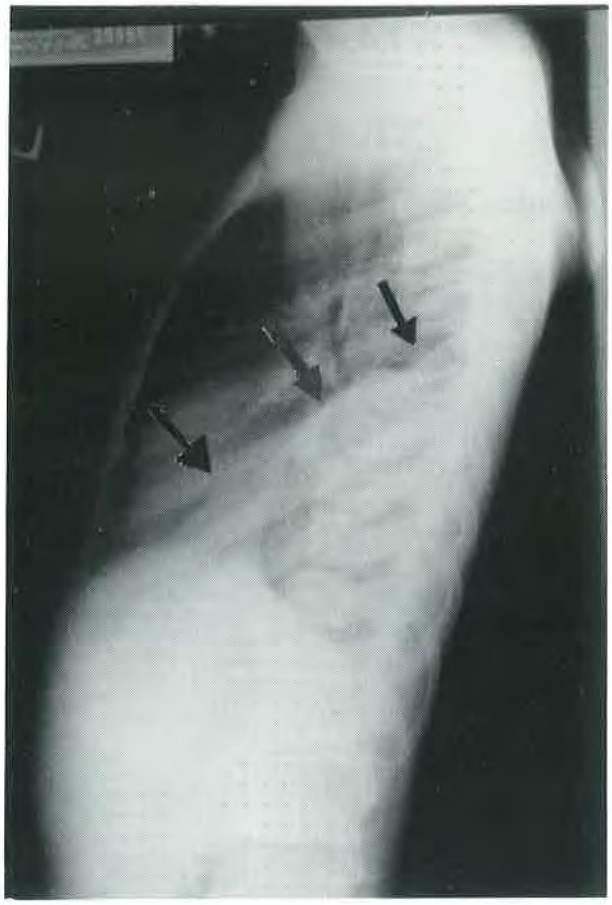


Fig 2 is a left lateral view of the chest.

It shows an homogenous opacification of the left lower lobe as indicated by the arrows.

DIAGNOSIS: COMPLETE PNEUMONIC CONSOLIDATION OF THE LEFT LOWER LOBE.

DISCUSSION

The PA view of the chest shows confluent shadowing of the left lower and mid zones with obliteration of the left hemidiaphram. However, the left cardiac border appears clear and distinct. This would indicate that the lesion lies behind the heart and therefore in the lower lobe. If the lesion lies anteriorly, for example, in the lingular segments of the left upper lobe, the cardiac border will be indistinct. This is called the "Silhouette Sign".

In this case, there was consolidation with no significant collapse of the left lower lobe. When there is collapse the left lower lobe shrinks behind the heart and presents as shadow behind the heart. If the collapse is complete, it may be difficult to demonstrate this. A left posterior oblique (LPO) view with adequate penetration would be useful.

Confirmatory signs of lower lobe collapse include downward shift and rotation of the hilum and lateral spread of the upper lobe blood vessels.

ANSWERS

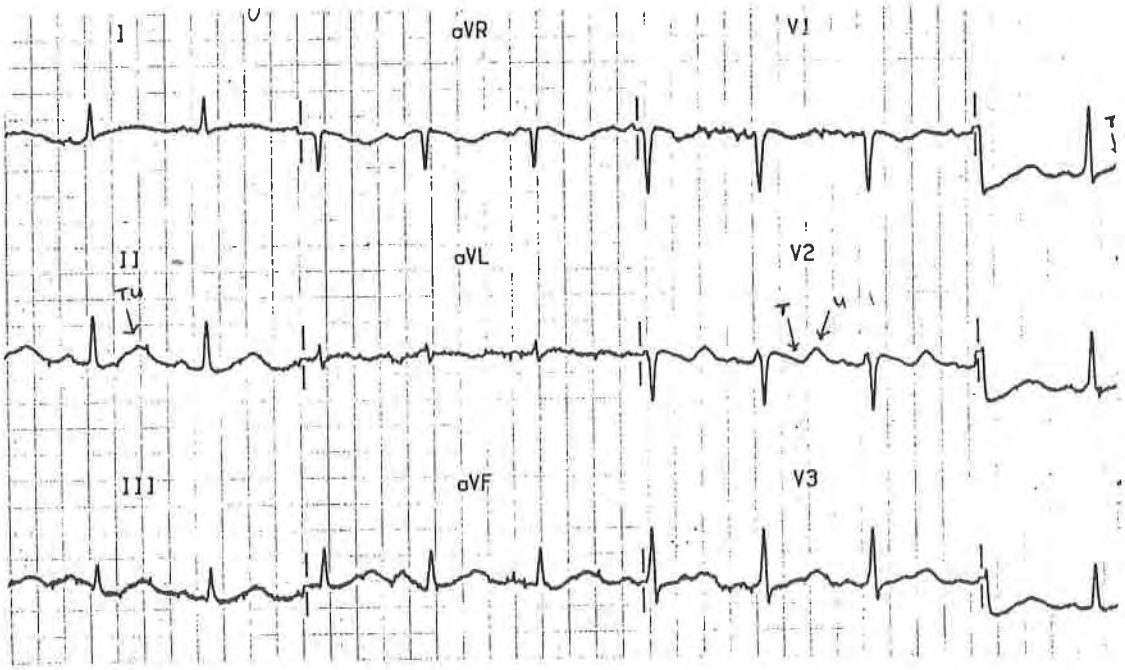
This ECG belongs to a patient who was admitted for diarrhoea.

Prominent U waves are seen following the T waves in V3, V4, V5 , V6. In II, III, AVF, the U waves are fused with the T waves to form a large TU wave.In V2 the T waves is inverted and U wave upright. The patient had hypokalemia.

Serum potassium was 2.1 meq/L.

The changes found in hypokalemia (in decreasing order offrequency) are:

1. S-T segment depression, decreased amplitude of Twaves, increased U wave height.
2. Cardiac arrhythmias.
3. Prolongation of QRS duration, increase in P wave amplitude and duration.



BOOK REVIEW

PRACTICAL MANAGEMENT OF ISCHAEMIC HEART DISEASE

author: Graham Jackson FRCP
publisher: Martin Dunitz

Most books on cardiology are written with physicians or cardiologists in mind, as a result of which they are usually too esoteric for the average GP PRACTICAL MANAGEMENT OF ISCHAEMIC HEART DISEASE isn't one of these. It has been written specifically for the GP and the junior hospital doctor finding his feet in a cardiology unit. This isn't a book that is likely to stay on the bookshelf for a long time to be used only for that occasional reference. It is intensely practical and readable from cover to cover.

Dr Jackson is a practising cardiologist at King's College and Lewsham Hospitals in London. He has edited both Cardiology in Practice and the British Journal of Clinical Practice. His wide experience as a clinical teacher and writer accounts for his didactic style. This book brings us right up to date with the current thinking on the practical management of ischaemic heart disease which has seen rapid advances in recent years. The author makes no apologies for presenting only his own point of view in matters which have yet to be settled by the pundits. He feels that theoretical arguments (which are bound to change with time anyway) are not likely to be relevant to the decision making process of those at the sharp end of patient care. However, he does provide adequate references at the end of the book to support his line of thinking and for those who wish to delve into the various topics at greater depth.

This 230-page hardback is copiously illustrated with diagrams, ECGs and photographs, most of them in full colour. The text, most of which is in the form of short captioned paragraphs, is punctuated by useful flow charts. The salient points in each chapter are summarised and tabulated into a blue box for easy reference. The twenty-one chapters deal with topics such as: pathology, epidemiology (risk factors), symptoms, primary prevention, clinical evaluation and management of angina, unstable angina, variant angina and coronary artery spasm, management and secondary prevention of myocardial infarction, cardiac rehabilitation, silent ischaemia and chest pain with normal coronary arteries. Most of these topics are essential reading for the GP although some of us may rarely see some of these conditions in our practice. An excellant feature of this book is, I feel, the way it lucidly puts across the state-of-the-art in this increasingly important area of cardiology to those of us whose experiences of acute coronary care have long since become *passe*.

ESK

NEWS

VISIT OF PRESIDENT OF THE ROYAL COLLEGE OF GENERAL PRACTITIONERS

It is not everyday that the President of a Royal College pays us a courtesy visit accompanied by a high powered team from the College Council.

We were very fortunate to have been accorded this honour when the President of the Royal College of General Practitioners Prof Michael Drury called on us accompanied by Prof Denis Pereira-Gray, Chairman of Council, Dr Bill Styles, Honorary Secretary and Dr Colin Waine, Chairman of the Communications Division.

This distinguished group paid a visit to our College premises and spoke to some of our clinical tutors on General Practice Learning and Training.

They also visited the Dept of Community, Occupational and Family Medicine of the National University of Singapore where they gave a much appreciated talk on "General Practice Education and Training: The British Experience" to postgraduate students of the department. Later they were taken to lunch by Prof Lee Hin Peng, Head of the Department, where they enjoyed both the meal and view from atop the Premier revolving restaurant.

A significant moment of their visit must be their trip to see the new polyclinic at Toa Payoh. Here they were met and personally taken around by Dr Chen Ai Ju, Deputy Director of Medical Services [Primary Care] together with Dr Lim Hai Chiew.

Prof M Drury relived a little of the past when he visited Alexandra Hospital where he had worked before as a British Army surgeon. The team was warmly welcomed by the Medical Director of the hospital, Dr Ng Yook Kim.

Although their stay was short here, we were however able to show our visitors a little of Singapore. They had lunch on our new waterfront cataraman and also were taken on a ride on our MRT. The President of our College, Dr Lee Suan Yew, hosted a dinner in honour of our guests and it was a most convival occasion where professional problems were mostly set aside.

Our visitors later left for Australia where they attended the Australian bi-centennial celebrations organised by the Royal Australian College of General Practitioners.

Dr Bill Styles echoes the sentiment of his colleagues when he wrote back to say "I myself have learnt a great deal about the organisation and postgraduate education in other countriess and seeing how well you are doing things in Singapore".

This is praise indeed, from a much senior sister College.

NEWS FROM THE COUNCIL

1. Visit of delegates from the Royal College of General Practitioners.

Our College had the pleasure of welcoming four members of the council of the Royal College of General Practitioners (UK) who visited us recently, namely, Prof VWMD Drury, President, Prof D J Pereira, Chairman of the Council, Dr WMcN Styles, Honorary Secretary of the Council and Dr C Waine, Chairman of the Communications Division. The delegation were in Singapore from 30 August to 1 September 1988.

The delegates paid a visit to our college and spoke to some of our clinical tutors on the following topics.

"Recent changes in the Undergraduate Curriculum"
"Continuing Education with particular reference to performance review"
"Vocational Training"
"Standards of Care"

There was active discussion from the floor not withstanding that it was 11pm.

Dr Koh Eng Kheng, Vice-President of our College gives a more detailed account of their visit to Singapore on page 145.

2. First Annual Scientific Conference

The College's First Annual Scientific Conference will be held on 12 and 13 November 1988. The Organising Committee has been busy planning and preparing for the countdown. Concurrently, an exhibition of medical equipment and books will be staged.

Highlights of the Conference:

— 1988 Sreenivasan Oration
— 4 Scientific Sessions
  * New Perspectives in Patient Care
  * New Perspectives in Practice Management
  * New Perspectives in Record Keeping
  * What's New in ....
    - Thyroid Disease
    - Diabetes Mellitus
    - The Eye in Diabetes Mellitus
    - Bronchial Asthma
    - Surgical Treatment in IHD
— Annual Dinner

3. Continuing Medical Education

The CME module on "Update on Cardiovascular Disease" commenced on 26 August 1988. Details of the course programme are provided below:

Date	Topics	Lecturer	Moderator
26.08.88	Auscultation of the Heart – Finer points	Prof Chia Boon Lock	Dr Hia Kwee Yang
02.09.88	The Surgical Management Congenital Heart Disease	Dr Ong Kim Kiat	Dr Lee Suan Yew
	Surgery for Valvular Heart Disease	Dr Tan Ngoh Chuan	Dr Lee Suan Yew
09.09.88	Vascular Disease – Surgical Options	Dr Lim Yew Cheng	Dr Goh Lee Gan
	Surgically Treatable Chest conditions	Dr Tan Ngoh Chuan	Dr Goh Lee Gan
16.09.88	Coronary Angioplasty – Current State	Dr Leslie Lam	Dr Lim Kim Leong
	Coronary Artery Surgery for IHD	Dr Tong Ming Chuan	Dr Lim Kim Leong
23.09.88	Medical Management of Chronic Heart Failure	Dr Charles Toh	Dr Henry P H Yeo
30.09.88	Medical Management of IHD	Prof Arthur Tan	Dr Chang Ming Yu
07.10.88	Primary Cardiomyopathy	A/Prof Maurice Choo	Dr Alfred W T Loh
14.10.88	Cardiac Arrhymthmias – Basic aspects & pharmacological intervention	Dr Koo Chee Chong	Dr Soh Cheow Beng

4. Family Medicine Teaching Programme

Module 1 had just been completed with a total of 36 participants. Module 2 commenced on 17 September 1988. Details of the module are provided below:

SUBMODULE	THE CHILD AND ADOLESCENT
Concepts in FM	17.09.88 Common problems in childhood 01.10.88 Behavioural problems in the child and adolescent 15.10.88 Normal & abnormal development; the handicapped child
SUBMODULE	**GASTROINTESTINAL DISORDERS**
Case Discussions Journal Club	24.09.88 Jaundice in General Practice 09.10.88 Lower GIT problems in General Practice 22.10.88 Upper GIT problems in General Practise
SUBMODULE	**PRACTICE MANAGEMENT**
Practice Management; medico-legal & ethical topics	05.11.88 The GP's responsibility in — notification — certification — dispensing Medical negligence

5. New Members

The College welcomes the following colleagues who have recently joined the College:

Dr Ong Teck Thian	Ordinary Membership
Dr Ian Lee Pheng Lip	Associate Membership
Dr Carol Lim Kah Choo	Associate Membership
Dr Neoh Swee San	Associate Membership
Dr Daniel Ong Kian Giap	Associate Membership
Dr Poon King Hou	Associate Membership
Dr Ramsay Catriona Margaret	Associate Membership
Dr Tan Lay Wee	Associate Membership
Dr Tan King Suan	Associate Membership
Dr Cecilia Tan Swee Lian	Associate Membership
Dr Tay Sok Hoon	Associate Membership
Dr Joseph Varghese	Associate Membership
Dr Karen Wee Ian Lin	Associate Membership
Dr Wong Song Ung	Associate Membership
Dr Yeo Lock Peow	Associate Membership
Dr Karen Yin Ee-Hian	Associate Membership

THE SINGAPORE FAMILY PHYSICIAN
Guidelines For Authors

Authors are invited to submit material for publication in the Singapore Family Physician on the understanding that the work is original and that it has not been submitted or published elsewhere.

The following types of articles may be suitable for publication: case reports, original research work, audits of patient care, protocols for patient or practice management and review articles.

PRESENTATION OF THE MANUSCRIPT

The whole paper

* Normally the text should not exceed 2000 words and the number of illustrations should not exceed eight.
* Type throughout in upper and lower case, using double spacing, with three centimetre margins all round. Number every page on the upper right hand corner, beginning with the title page as 1. Make all necessary corrections before submitting the final typescript.
* 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.
* Send three copies of all elements of the article: summary,text, references, tables and illustrations. The author should retain a personal copy.

The title page

* The title should be short and clear.
* Include on the title page first name, qualifications,present appointments, type and place of practice of each contributor.
* Include name, address and telephone number of the author to whom correspondence should be sent.
* Insert at the bottom: name and address of institution from which the work originated.

The summary

* 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.

The text

The text should have the following sequence:

* Introduction: State clearly the purpose of the article.
* Materials and methods: Describe the selection of the subjects clearly. Give references to established methods, including statistical methods; provide references and brief descriptions of methods that have been published but are not well known. Describe new or substantially modified methods, giving reasons for using them and evaluate their limitations. Include numbers of observations and the statistical significance of the findings where appropriate.

  Drugs must be referred to generically; all the usual trade names may be included in parentheses. Dosages should be quoted in metric units.

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

  Do not use patient's names, initials or hospital numbers.
* Results: Present results in logical sequ-

ence in the text,tables and illustrations.

* Discussions: Emphasise the new and important aspects of the research and the conclusions that follow from them. Indicate the implications of the findings and limitations. Relate the observations to other relevant studies.

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.
* Each illustration must carry its appropriate Figure number and the top should be clearly labelled.
* Figure legends, typed (double-spaced) and each on a separate page should be no more than 45 words.

Tables

* Any table must supplement the text without duplicating it.
* Each should be numbered, typed on a separate sheet with an appropriate title.

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Place these at the end of the text, before references.

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References should be double spaced and arranged alphabetically by author. Personal communications are not acceptable as references. Unpublished material should be included only if an address can be given from which a copy of the material cited is available.

Authors are responsible for accuracy of references, which should conform to the Vancouver style (see Further reading). List all authors (include all initials) when there are six or fewer; when seven or more list the first three and add et al. Give the title of the paper cited in full, the title of the journal abbreviated according to Index Medicus (if not listed by Index Medicus spell in full); the year; the volume number and the first and last page number of the article.

Editing

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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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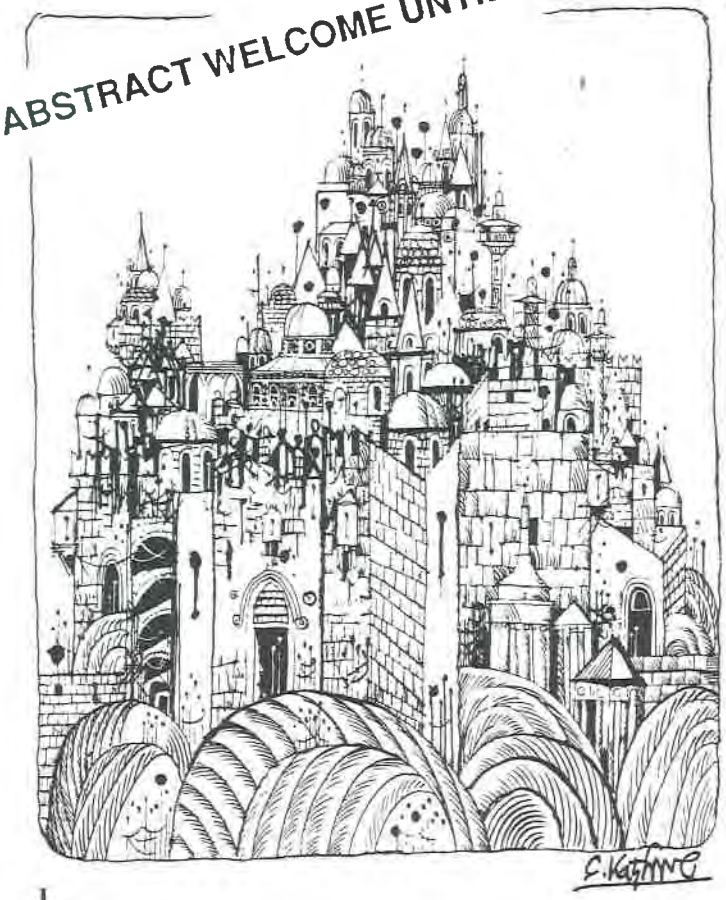

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