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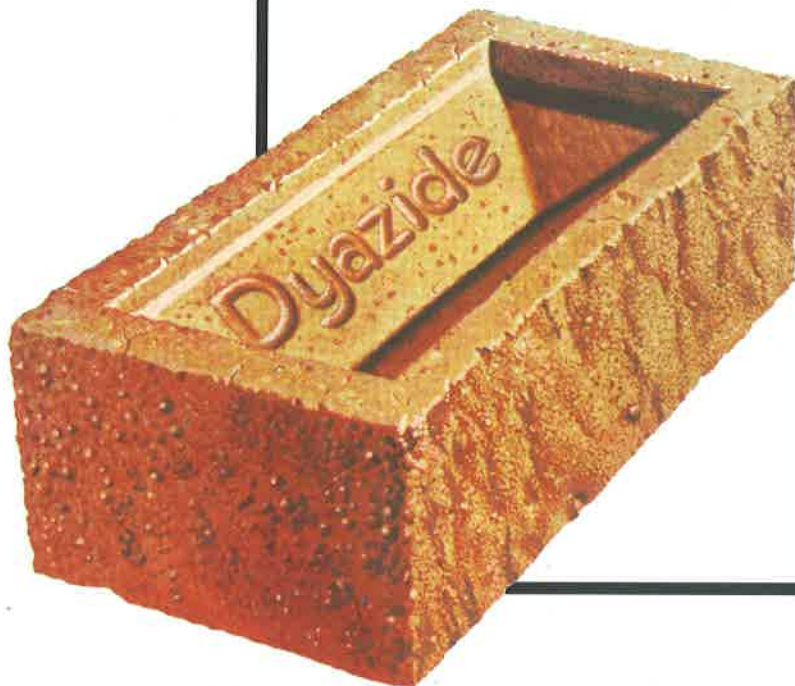
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THE SINGAPORE FAMILY PHYSICIAN

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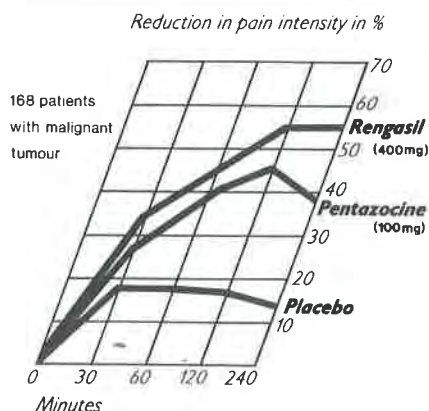
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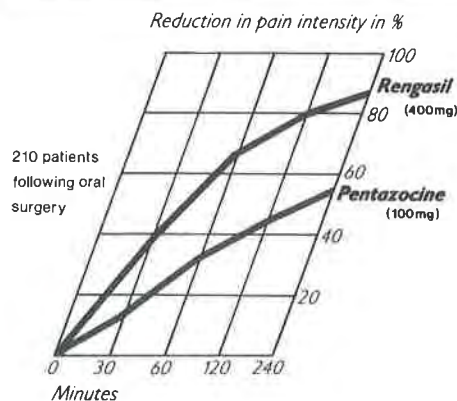
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² Sperr W. : Int. Symp., 1Xth Europ. Congr. Rheumatol., Wiesbaden 1979.

EDITORIAL

Medical Audit in General Practice

The term medical audit is one familiar to nearly everyone in the medical profession. The term itself is not exactly new, having been in use for a number of years and ever since 1969 nearly five hundred articles on the topic have appeared in the *Index Medicus*. Yet despite its wide usage there is still considerable ambiguity as to the true meaning of the term. To some it is equated with professional re-assessment, or re-certification, which is a periodic review of a doctor's knowledge and professional competence to allow him to continue in his medical practice.

The need for professional accountability has been advanced in some quarters as necessary to ensure that professional standards are maintained. There is always the fear that doctors who have graduated for some time and have not bothered to keep up with recent advances in medicine may not be practising medicine in the best interests of both the patient and the profession.

This view of medical audit is only one of the many held on the subject. Other terms like audit of structure, internal audit, external audit, tissue audit, self assessment and peer review show the diversity of viewpoints on the topic. The Royal College of General Practitioners came to the conclusion that there was no universally agreed meaning of the term.

Why the need for audit?

The necessity for keeping up with modern medical advances is not the sole purpose for medical audit. In fact there are some who think that programmed post-graduation education in the form of seminars and clinical sessions could do this effectively enough.

The term medical audit was actually first introduced in the United States to monitor the financial side of medical practice. Wild claims on medical insurance, exaggerated professional fees and unwarranted or unnecessary surgical interventions had made it necessary for many medical insurance companies to keep a close tab on medical expenditure and claims. These insurance firms kept a practice audit of the doctors who attended to the clients of the insurance companies, and

those doctors who sent in outrageous bills for medical treatment had to explain the reasons for the higher incurred costs before their bills were accepted or approved.

In countries where other forms of communal health care or insurance are in practice, it has also become important to keep a watch on expenditure for medical treatment. The phenomenal costs of maintaining the British national health service, the Australian medibank, and the American medicare, have all pointed to this need for the medical profession to have an accountability of the costs and efficacy of modern medical treatment.

Is there a need for medical audit in Singapore?

From the viewpoint of the health of our people has there been sufficient cause for concern to warrant a closer supervision and check on the medical profession here? This is easily answered in one word — No.

The health of the people of this country has in fact never been better. The average life expectancy of our average citizen is now close to seventy years, and compares favourably with affluent countries like Japan and the United States. Our infant mortality is also appreciably low and compares favourably with countries like Australia and the United Kingdom.

Although complaints of poor treatment do appear in our local press from time to time, it is generally true that most of those who are ill and seek treatment either from the doctors in the public or private sector, are efficiently and competently attended to.

As for the need to monitor or audit the costs of medical treatment, nowhere else in the world is it possible to obtain medical treatment in general practice for so little cost, and with such speed and efficacy.

Upgrading standards in general practice

The need to continually upgrade one's medical knowledge has long been recognised, and Osler reminds all of us of the need for what he calls a "quinquennial brain-dusting."

It is with this in mind that the College conducts regular refresher courses for general practitioners. It is perhaps wise here to borrow a different term other than audit from our friends the professional accountants. In their professional bodies they use the term C.P.D., not like we do to refer to cephalo-pelvic dysproportion but to "continuing professional development." Members of the profession are required to attend a stipulated number of hours of refresher courses, and points are awarded for attending these talks or seminars.

Medical knowledge alone of course does not provide all the answers to the proper care and management of an ill patient. In general practice there are so many other unquantifiable items in the care of a patient that a purely book bred academic doctor will find it difficult to understand. It is not always the doctor who is most adept at passing examinations who makes the best personal physician. Examinations do not assess a doctor's patience, honesty or rapport with his patient. Yet it is not unknown for bad doctors to be especially good at passing exams. The College believes however that despite its limitations, exams do have their use and a good knowledgeable doctor is preferable to a good unknowledgeable one.

In the application of one's medical knowledge a good general practitioner will often see that he does what is best for his patient, not merely what is right from the point of view of investigations and treatment. The tendency to pursue investigations purely for the sake of academic interest should be treated with caution. There is a growing trend in some countries for a doctor to order investigations not in the patient's interests, but for his own protection or curiosity. Shaw deplores this form of practice of "defensive medicine".

One of the dangers of medical audit is that it puts the practising doctor to scrutiny to account for his treatment and management. Stevens likens this to practice in a gold fish bowl. When a person is placed on stage, there is always the temptation to play up to the gallery.

In the practice of medicine a doctor must not play to an audience. What he does must firstly and lastly be governed by the welfare and interests of his patient. He must always practise medicine according to his own conscience, and here perhaps lies the best and most reliable form of medical audit.

The Middle Man

The general practitioner has been known by many names in his time — family physician, pri-

mary care doctor, GP., but to be known as the middleman, this is certainly quite a unique first.

There is nothing wrong in being known as the middle man if it means the man in the centre where all the action is, but it is doubtful this was what the press had in mind. To them he seems to be the redundant figure, a person whose sole existence is to increase medical costs, an extra palm waiting to be crossed with silver.

To be fair to them this is not an original concept. In the United States there was a time when the general practitioner was regarded as a supernumerary with all the specialists around. If one had a headache one could easily choose from a neurologist, psychiatrist or brain surgeon, all of whom would be within easy reach of anyone who needed one or all three. Then general practitioners soon became a rare breed and after this people found to their regret that it was neither simple nor cheap to have to decide which specialist to see. So the corner drugstore took the place of the family doctor's clinic and the friendly corner druggist gave helpful advice as to whether a seltzer pill or a bufferin tablet would help the headache. He did this without extra fee if the consultation took place over his soda counter. By the time the ordinary sick person clamoured for the return of his friendly GP it was a little late in the day, and United States medical schools by now produced five specialists for each generalist to look after the sick.

Whether or not we in Singapore should learn from this painful lesson is a moot point, but to say that general practitioners want to stop the public from direct access to specialists here is quite another matter. Medical specialists except those in Government service, have all along been able to see patients off the streets without letters of referral from general practitioners. There never was, or is ever likely to be objection from general practitioners on this. The matter of the medical signboard and the specialist registry is something which the Singapore Medical Council will have to decide taking into account the convenience of the public in mind.

The relationship between the general practitioner and the specialist in this country has always been good and friendly, and should continue to be so. It is in the interests of the patient that he should have a doctor he can trust, and whose advice he values. Whether this doctor is a specialist or generalist is of little importance to the profession so long as the patient gets well as soon as he is able to.

E.K.

Views expressed in the Editorial are not necessarily the official views of the college.

STATEMENT FROM THE EDITORIAL BOARD OF THE SINGAPORE FAMILY PHYSICIAN ON UNIFORMITY OF CHINESE NAMES IN BIOMEDICAL JOURNALS.

The Editorial Board of the Singapore Family Physician subscribes to the Singapore Medical Journal's statement on "a unified system of indexing Chinese names in biomedical journals". It has decided to adopt the following system for Chinese names: —

- for scientific articles, the author's **initials** will be followed by the **surname** e.g. E K Koh
(No period is put after each initial)
- for reference, the **surname** precedes the **initials** e.g. Koh E K
(Again no period is put after each initial)
- for Chinese authors with Christian names e.g. James Chang Ming Yu will be written as JMY Chang (and in the case of reference Chang JMY)
- In addition to the above, Chinese contributors to our journal are urged to be consistent in using their names. If an author uses his Christian name in one article, he is well advised to use it consistently and NOT to omit it in subsequent articles so as not to triplicate his identity.

e.g.	Peter Lim:	P Lim
	Peter Lim Huat Chye:	P H C Lim
	Lim Huat Chye:	H C Lim

A Study of Vaginal Trichomoniasis in a Family Practice

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SUMMARY

A study of 706 cases of vaginal discharge over a 3 year period revealed that 63 cases (8.9%) were due to Trichomoniasis. An analysis of results showed that this condition occurred in sexually active women. Promiscuity on the part of the patient or the sexual partner could not be established in the majority of cases. A diagnosis could be made clinically in only 78% of the cases. 22% were diagnosed only after microscopic examination of the vaginal discharge. All cases were confirmed by examination of the vaginal discharge diluted in N saline. Specific treatment with metronidazole or tinidazole provided excellent cure rates. It was felt that for a condition as gratifying to treat as Trichomoniasis, a definite diagnosis should be made by microscopy and the concomitant treatment of the sexual partner confidently embarked upon.

INTRODUCTION

Vaginal discharge is a common complaint in general practice. The majority of such discharges, particularly if unaccompanied by pruritus or offensive odour, were physiological and happily could be confirmed as such by the history, vaginal examination and microscopic appearance of the vaginal smear. Vaginal discharge which produced pruritus and/or offensive odours were assumed to be pathological, though this might not necessarily be so without a study of the vaginal smear. Treatment tended to be blunderbuss, with the use of broad spectrum regimens. In our present study, we attempted to find out the correlation between our clinical judgement of Trichomoniasis and its microscopic diagnosis.

MATERIALS AND METHODS

All cases of vaginal discharge over a 3 year period from January 1979 to December 1981 were subjected to a full clinical examination. A high vaginal swab was made through a vaginal speculum, using a cotton-tipped applicator stick. This was

diluted in N saline and a drop was examined under both low and high power microscopy.

A clinical diagnosis of Trichomoniasis was made based on the following criteria:

1. Pruritus vulva with nocturnal exacerbation.
2. Foul odour of the "fishy" type.
3. Vaginal discharge which is thin, frothy and yellowish-green.
4. Excoriation of the vulva.

RESULTS

An analysis of the causes of vaginal discharge in our patients is shown in Table 1. There were 63 cases of Trichomoniasis, giving a percentage of 8.9%. 49 cases were diagnosed on clinical grounds. 14 others were picked up after microscopy. This gave a failure rate of 22%. There were 7 cases of mixed infection i.e. Moniliasis and Trichomoniasis.

TABLE 1 Causes of vaginal discharge in 706 cases

Cause	Number	Percentage
Normal	306	43.8
Moniliasis	247	35.0
Trichomoniasis	63	8.9
Non-specific Infections	94	13.3
Total	706	100

The age distribution of the patients may be seen in Table 2. 29 cases (46%) were between 21 and 30 years. The youngest was 16 years and the oldest 55. All the cases had a history of being sexually active.

An admission of promiscuity was made in 7 cases. 8 patients proclaimed their sexual partners to be promiscuous and responsible for their symptoms. 13 patients suspected their sexual partners to be promiscuous. The majority (55.6%) of the

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cases were ignorant of the probable origin of the disorder. 6 cases (9.6%) of the patients were pregnant when the diagnosis was made.

There was no significant concomitant disease in the 63 cases. There was no correlation between the onset of symptoms and the use of public toilets, swimming pools or common towels. One patient had a pregnancy terminated 4 weeks prior to being seen. Another patient had vaginal hysterectomy performed 2 weeks prior to the consultation.

TABLE 2 The age distribution of patients with Trichomoniasis

Age	Number	Percentage
11-20	8	12.7
21-30	29	46.0
31-40	17	27.0
41-50	7	11.1
51 and over	2	3.2
Total	63	100

Table 3 shows the presenting symptoms of Trichomoniasis. Foul discharge and vulval pruritus were complained of by about half the cases. Soreness over the vulva was complained of by a fifth of the cases.

TABLE 3 The presenting symptoms in Trichomoniasis

Symptoms	Number	Percentage
Pruritus vulva	32	50.8
Foul discharge	35	55.6
Vulval soreness	14	22.2
Burning sensation	4	6.4
Dyspareunia	4	6.4
Dysuria	1	1.6

Table 4 shows the nature of the discharge as to its presenting colour and appearance. In about half the cases the discharge was both frothy and yellowish-green. The vagina was hyperaemic and inflamed in 57.1% of the cases. The characteristic "fishy" odour of the discharge was noted in 68.3% of the patients and may be related to the amount of the discharge and to whether the patient has washed herself just before the examination.

TABLE 4 The nature of the vaginal discharge

Nature of discharge	Number	Percentage
White	12	19.0
Yellow/green	31	49.2
Frothy	31	49.2
Milky	4	6.4

DISCUSSION

Specific infective agents causing vaginitis include viruses, bacteria, protozoa and fungi, of which the latter two cause the vast majority (Wright, 1976). The commonest infective agent found to cause vaginitis in our study was monilia. Infection due to the protozoa *Trichomonas vaginalis* accounted for 8.9% of our cases. Teoh and Tan (1976), in a survey of 388 patients who had vaginal swabs taken regardless of their symptoms, found 4% to be harbouring *Trichomonas* in the vagina. In a larger series, Gaudefroy and Lobbe (1968) found the incidence to be 6.4% of 15,819 women examined. It is significant to note that the incidence of Trichomoniasis varies, depending on the type of patients studied. Whittington (1957) reported in his birth control clinic an incidence of 5.3%, his gynaecological clinic, 12.8% and his venereal disease clinic, 21.3%.

The protozoa *Trichomonas vaginalis* is easily recognised under the microscope. It is a pear-shaped organism, approximately 15 μ in length. Its size is variable and sizes between 10-30 μ have been reported (Chandler & Read, 1961). This makes the protozoa about the size of a leucocyte and about half the size of a vaginal epithelial cell. The organism usually inhabits the vagina, hence its name, but it may also live in the urethral glands and other parts of the female urogenital system. In the male, it inhabits the prostate and urethra. Its motility makes it easily recognisable on the wet film of a freshly made saline suspension of a drop of vaginal discharge. It has jerky, non-directional movements which can be detected in the low power of the microscope.

Infection in the female produces the purulent vaginal discharge characteristically described as frothy, yellowish-green and of a "fishy" odour. The discharge often dates from menstruation. The organism may be a silent carrier in the vagina until conditions become favourable for it to become infective, for example the lowering of the general or local resistance. The elevation of the vaginal pH during menstruation predisposes to the pathogeni-

city of the organism. Though the discharge may be tinged with altered blood from the hyperaemic vaginal mucosa and appear brownish, several cases of "normal" looking white discharge have surprised us with the presence of Trichomonads under the microscope.

The mode of transmission from host to host is venereal in the majority of cases. All the cases in our series were women who were sexually active. Despite our inability to prove promiscuity in most of our cases, it is our suspicion that promiscuity is the likely cause. The non-venereal modes of transmission include the use of public toilets, swimming pools, shared towels and bedclothes. Trichomonads have been found to remain viable for 45 minutes on toilets seats (Whittington, 1957). Satti and Honigberg, 1959, showed that survival of the protozoa is possible up to 24 hours on damp cloth. The occurrence of the infection in children from families where adult female members were infected, suggests the possibility of such modes of transmission (Chandler & Read, 1961). Since the presence of *Trichomonas vaginalis* in the male is generally asymptomatic, only rarely causing urethral discharge or balanitis, the male consort seldom seeks treatment on his own.

With the use of systemic metronidazole, 200mg t.i.d. (Flagyl, May & Baker) for a week, or tinidazole 2g as a stat dose (Fasigyn, Pfizer), we have found the results to be most encouraging. Since the diagnosis was confirmed by microscopy in every case, we have insisted that the male consorts be given treatment simultaneously. We usually treat the males with tinidazole because of the ease of administration and the assurance of compliance.

The use of Mysteclin-F (Talsutin, Squibb) in the form of vaginal pessaries was found to be less effective against Trichomoniasis (Chee, Chong & Lean, 1970).

From our present study, we find that Trichomoniasis is readily amenable to treatment once the diagnosis is made. It is our impression that intractable cases of this infection in the female are due to failure to eradicate the infection from the male sexual partner. Our study also showed that the clinical suspicion of the infection was insufficiently accurate to pick up all cases. A failure rate of 22% would have occurred had we relied solely on the clinical criteria stated without the benefit of a microscopic diagnosis.

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Management of Hypertension in Pregnancy

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Pregnancy induced hypertension remains an enigma in contemporary obstetrics. While maternal mortality from eclampsia is diminishing, there has been little reduction in fetal morbidity. In the developing world, pregnancy induced hypertension is the most important obstetric problem contributing to maternal death (eclampsia) and fetal wastage.

Hypertension in pregnancy can be defined as in the non-pregnant state as a blood pressure at least two standard deviations above the mean of a normal population. This is an arbitrary definition as in large population studies, a significant relationship can be seen between blood pressure from levels as low as 115/70, and perinatal mortality rates. Blood pressure studies during pregnancy in Asian countries have yet to be documented.

In Singapore, deleterious effects of hypertension become apparent at diastolic blood pressure levels above 90 mmHg (which is two standard deviations above the mean of the normal third trimester population), and this is used as the arbitrary dividing point.

AETIOLOGY OF HYPERTENSION IN PREGNANCY

The causes of hypertension are all those which can affect a female population with the addition of pre-eclampsia (see Table 1). It includes those cases seen commonly and some which, although rare, are most serious for mother and fetus. Some of these can be excluded by history and physical examination when the patient is first seen; others must await definitive diagnosis postpartum.

Table 1

Causes of Hypertension in Pregnancy	
Pregnancy	— induced hypertension (pre-eclampsia)
Essential hypertension	
Vascular	— Renal artery stenosis
	— Coarctation of aorta
Chronic renal disease	
Cushing's Syndrome	
Pheochromocytoma	

CLINICAL METHODS

History

Gestation at which hypertension first documented: Pregnancy-associated hypertension rarely appears before 24 weeks of amenorrhoea, whereas other causes of hypertension frequently ante-date pregnancy.

Personal and family history: The patient should be questioned about symptoms suggestive of renal disease, coarctation of the aorta or an endocrine cause of hypertension. Any family history should be elicited as this may be a pointer, particularly towards chronic essential hypertension.

PHYSICAL EXAMINATION

This includes palpation of peripheral pulses and measurement of blood pressure in both arms (to exclude coarctation of the aorta). The abdomen should be carefully examined for renal masses, for example, polycystic kidneys.

The optic fundi should be inspected for hypertensive retinopathy, or of the arteriolar spasm so characteristic of severe pregnancy-associated hypertension or evidence of previous hypertensive disease. Careful daily examination of the abdomen to ascertain whether uterine size is compatible with the duration of amenorrhoea and signs of fetal growth retardation are cardinal features of management.

RELEVANT INVESTIGATIONS

Maternal — Renal Function

Some of the investigations can be performed during pregnancy without danger to mother or baby. Renal function should be evaluated fully to assess the extent of effect of renal decompensation and extent of hypertension. Proteinuria occurs in five per cent of all pregnant women, and complicates 20 per cent of those with hypertension. Its significance depends on accurate determination of a 24-hour collection. All patients with proteinuria should have a urinary tract infection excluded by microscopic examination and culture.

Glomerular filtration rate can be measured by creatinine clearance. Values for pregnancy are on

average 25 per cent higher than in the non-pregnant state, (range 130-200 ml/min/1.73m²). Glomerular function should be performed as early as possible in pregnancy, and a rough guide to glomerular filtration rate may subsequently be gained by serial measurement of serum creatinine levels. The appearance of proteinuria in a hypertensive woman is an indication of immediate admission to hospital and monitoring of both maternal and fetal welfare. The observance of this simple rule has led to a dramatic decline from eclampsia in Singapore.

If the glomerular filtration rate is below 70 per cent of normal non-pregnant levels (that is, less than 70 ml/min/1.73m²) in the first trimester of pregnancy, this is indicative of pre-existing severe renal disease, and termination of pregnancy may need to be considered. Hyperuricaemia in a hypertensive pregnant woman predates acceleration of hypertension and it also correlates well with fetal outcome and is therefore a most valuable parameter.

It is known that there is significant plasma volume expansion in normal pregnancy. Reduction in plasma volume is a feature of both chronic and pregnancy-associated hypertension. The extent of haemo-concentration is related both to intrauterine growth retardation and to severity of hypertension. It may be estimated readily by weekly changes in venous haematocrit.

It is now realised that disseminated intravascular coagulation can be a feature of pregnancy-associated hypertension. The platelet count is monitored regularly in those with severe clinical disease and may be an early warning sign of impending problems.

FETAL WELFARE

Fetal growth is assessed by clinical examination, more accurately by measurement of abdominal girth and fundal height. Serial ultrasound measurement of the fetal biparietal diameter or crown rump length in hypertensive women, who are at increased risk of intrauterine growth retardation is the most reliable method.

The perinatal mortality rate in severe hypertensive disease in pregnancy has fallen from 80% to 5-10%. Because of a documented fall in placental blood flow with lowering of the blood pressure in the experimental animal, there has been reluctance to give antihypertensives to the hypertensive pregnant women. It has now been realised that this fear is unfounded, and that treatment of hypertension can not only reduce the perinatal mortality rate significantly, but can be associated with improved fetal nutrition and growth in-

utero. This does not allow the obstetrician to use hypotensive drugs "Willy Nilly" but on severe cases in specialised units.

Assessment of fetal welfare has advanced considerably in the past decade and allows more rational decisions about the timing of delivery. The most frequently used parameters are:—

OESTROGEN ESTIMATION

- (i) Serum or urinary feto-placental hormone estimations: Serial measurement of 24 hour urinary oestriol excretion or of plasma levels is a useful adjunct to management in the third trimester of pregnancy. A sustained fall in either, suggestive of impaired placental function, is indicative of increased risk of perinatal morbidity, and a relative fetal indication for delivery.

USEFULNESS OF ULTRASOUND

- (ii) Serial ultrasound examination: This is a more sensitive estimate of fetal size than clinical examination and as the appearance of intrauterine growth retardation is a feature of the placental insufficiency associated with hypertensive pregnancy, serial ultrasound examination will allow earlier detection of this.

ANTEPARTUM CARDIOTOCOGRAPHY

- (iii) Antepartum fetal heart rate monitoring: In the third trimester of pregnancy, certain fetal heart rate patterns in response to Braxton-Hicks contractions or various stimuli have been observed to correlate with fetal well-being. Oxytocin challenge testing involves assessment of alterations in fetal heart rate in response to uterine contractions stimulated by intravenous infusion of small quantities of oxytocin. Results have been shown to correlate closely with fetal prognosis in-utero and an abnormal (positive) result is a relative fetal indication for urgent delivery. There are many recent publications assessing this test and its less invasive companion, unstressed fetal cardiotocography, observing the fetal heart rate response to fetal movement and/or spontaneous Braxton-Hicks contractions, an extremely valuable adjunct to the management of hypertensive pregnancy, particularly from about 30 weeks of gestation onwards. It is essential that the recording obtained be of high quality, and scrutinised by an experienced observer, if reliable results are to be obtained.

Post-Natal Investigations: All patients with chronic hypertension, renal disease or who remain hypertensive three months postpartum, should be investigated. These investigations should include renal function testing and intravenous pyelography, and other appropriate tests in a specialised unit.

TREATMENT

Rest & Sedation

Bed rest continues to be the sheet anchor of treatment of hypertension in pregnancy. Rest in bed in the lateral position will result in a significant drop in blood pressure in a significant proportion of patients and improve utero-placental blood flow.

Sedatives are not indicated but often used in the control of hypertension in pregnancy. They are really indicated if there is evidence of exaggerated reflexes or other neurological abnormality. Barbiturates will cause less fetal depression than will diazepam, and the most commonly used agent is sodium phenobarbitone or Valium.

Hypotensives

If the diastolic blood pressure is persistently above 100 mmHg despite adequate rest, oral antihypertensive agents should be prescribed. Favourable results have been reported with Aldomet, Oxprenolol and more recently Labetalol. With adequate therapy, it is possible to reduce perinatal mortality, and intrauterine growth retardation, and more important, morbidity in the low birth weight infants.

Diuretics

It is now realised that there is very little place for the use of diuretics in the treatment of hypertension in pregnancy. They will aggravate existing plasma changes of pre-eclampsia and decrease placental perfusion. This worsens the hypertension. In addition, the hyperuricaemia caused by the thiazide diuretic may lessen the prognostic changes related to pregnancy-associated hypertension.

Termination of Pregnancy

Maternal indications for delivery constitute deteriorating renal function (drop of more than 40 per cent in glomerular filtration rate), and the development of significant coagulation abnormalities. A steadily increasing blood urea level and uric

acid of more than 3 mg signify not only maternal but fetal danger.

Delivery for fetal reasons, if there is evidence of growth retardation or fetal distress. This is most readily detected by falling oestriols daily and fetal heart rate monitoring.

Intrapartum Care

Hypertension worsens (aggravating) during labour is common and where possible, analgesic drugs which may depress the neonate should be avoided. Continuous epidural analgesia provide excellent pain relief in addition to a drop in blood pressure secondary to sympathetic blockade. Continuous cardiotocography in labour would detect any problems early which necessitate operative intervention. Ergometrine is avoided in the third stage because of its pressor effects and syntocinon is the best oxytocin.

Hypertensive Crisis

A diastolic blood pressure in excess of 110 mmHg at any stage of gestation constitutes a maternal indication for parenteral antihypertensive therapy. The most commonly used agents are intravenous hydralazine (either as an infusion or as bolus injections) and intravenous diazoxide (either as a single large bolus or repeated small bolus doses), both vasodilating agents.

Intramuscular clonidine may also have a place but has not been quite so closely investigated. Anticonvulsant drugs are reserved for those with manifestations of neurological hyperactivity.

In Singapore, we have confidence in the use of an infusion of Librium and Nepresol for such patients. While delivery will be performed in the majority of patients shortly after such therapy, in individual cases, it may be desirable and possible to continue pregnancy with oral antihypertensive therapy.

Summary

In good centres, with care and adequate treatment of the hypertensive pregnant woman, it is possible to achieve a satisfactory result in terms of both fetal and maternal welfare. Such patients should be managed in special units with adequate facilities and expertise in management of the pregnant hypertensive and of the sick premature neonate. Improvement in neonatal paediatrics has made delivery early with good fetal outcome.

Groin Herniae

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INTRODUCTION:

To enjoy positive health and to be fully active, the patient with a groin hernia wants to be rid of his ailment. He often seeks advice from his family physician who must be fully appreciative of present day standards of hernia surgery before he can advise an operation. It is to aid the General Practitioner in this regard that we have undertaken this review of the surgery of groin herniae at the Dept of Surgery, Changi Hospital over a 3 year period with a detailed analysis of the results of treatment.

MATERIAL AND METHOD:

The case reports of 200 patients with groin herniae who were referred to and treated at the Surgical Dept. of Changi Hospital between 1979 and 1981 were analysed.

RESULTS: (Graph I, Tables I, II, III)

Over a 3 year period, 200 patients underwent a total of 227 operations for groin herniae. Two hundred & twenty-two were inguinal herniorrhaphies or herniotomies, while there were only 5 femoral hernia repairs. The 27 additional operations were due to: repair on the opposite side for those with bilateral herniae (25) and recurrent herniae following the first repair (2). Of the inguinal hernia patients the majority (160) had indirect herniae. Three of the patients with femoral herniae were females. There were 180 males and 20 females. The age range was between 1.5 to 79 years. Graph I was constructed by plotting frequency against decade periods. It showed that there were 2 age peaks during which groin herniae present most commonly; during the first decade of life and towards middle age. There were 132 Chinese, 43 Malays, 20 Indians and 5 Eurasians.

The commonest mode of presentation was groin mass in 191 cases. The remaining 9 were discovered on routine medical examination. Pain as an associated complaint was present in only 60 patients; however, in only four of these were the

herniae irreducible. The hernia was on the right side in 101 instances & on the left in 74. Bilateral inguinal herniae were present in 25 patients but there were no bilateral femoral herniae. All herniae were reducible except in the 4 emergency admission cases presenting with pain. The latter were all of the indirect inguinal type. Predisposing factors i.e. chronic cough & signs & symptoms of prostatism were found in only 4 and 3 patients respectively.

GRAPH I: HERNIAE & AGE PERIODS

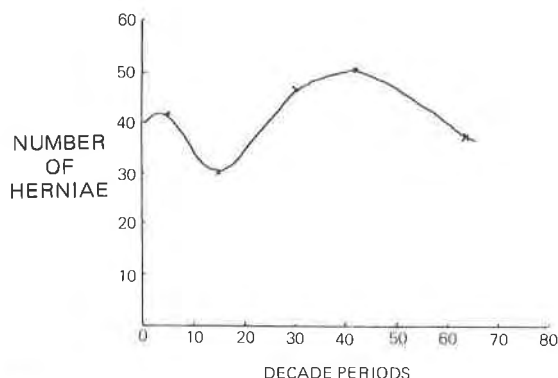


TABLE I: PATIENTS & HERNIAE

200 patients	unilateral inguinal herniae :	195
	bilateral inguinal herniae :	25
	unilateral femoral herniae :	5
	recurrent herniae :	2
total number of herniae treated: 227		

TABLE II: PRESENTATION

Elective (reducible)	— mass only	131
	— mass with pain	56
	— asymptomatic	9
Emergency (irreducible)	— mass with pain	4

TABLE III: COMPLICATIONS

Early complications:			
Minor	— local — infection	: 15	Major: Nil
	— haematoma	: 7	
	— sinus	: 1	
	— systemic — chest	: 2	
Late complications:			
	Recurrence	: 12	

Surgical Technique & Anaesthesia: A herniotomy was the only form of surgery performed for patients with inguinal herniae who were below the age of 25. A modified Bassini type repair was adopted for both direct & indirect inguinal hernia patients above this age. Only the inguinal approach of Lotheissen was used in the femoral hernia repairs. The suture material utilised in all the operative procedures was monofilament nylon. Bilateral herniae were repaired in stages (i.e. 2 separate operations) in the interest of safety. Gut resection was required in the 4 irreducible herniae because strangulation was noted at the time of surgery.

147 operations were done under spinal regional anaesthesia while a general anaesthetic was employed in 80 cases — 42 of these were children 10 years of age and below.

Hernial Sac Contents: In 12 herniae viable small bowel was present within the sac and in 3 of these the hernia was considered to be a Richter's type i.e. only a portion of the circumference of the intestine was affected. Gangrenous small bowel was the finding in the 4 cases which required resection. Viable colon was observed in 2 patients (1 sigmoid, 1 caecum) while the sac contained part of the bladder in 3 cases. These 5 cases presented with huge inguino-scrotal herniae. Omentum alone was found in 42 sacs. In 17 instances fluid only was seen within the sac. An empty hernial sac was the finding in the rest of the 147 patients.

Mortality/Morbidity: The early complications of operation were: wound infections 15, of which 2 followed emergency operations; chest infection 2; wound haematoma 7; persistent sinus 1. Recurrence of hernia occurred in 2 cases within a 2 year period of follow-up.

The length of stay in the hospital averaged 5 days. Period off work ranged between 10 days to 4 weeks with a mean of 2 weeks away from all occupational activities.

There were no deaths in this series.

DISCUSSION:

In this series of patients with groin herniae, the majority (75%) were of the indirect inguinal type. 22.5% were direct inguinal herniae while 2.5% were femoral herniae. McVay¹ reported corresponding figures of 80%, 16% and 4% in 1965. Our higher incidence of direct herniae may be due to the fact that the patients with this type of hernia were over 45 years of age and were mainly employed as heavy manual workers in the local community. Indeed, all the 25 cases of bilateral herniae came from within this group of 35 patients with direct herniae. Although this study confirms that femoral herniae are more commonly found in women, the commonest hernia affecting both sexes is still the inguinal type.

Patient presentation conforms fairly closely with accounts given in standard texts but it is worth noting that the oft quoted associations of chronic cough & prostatism² were observed to be infrequent in our series. The peak periods when herniae were found viz. childhood & towards middle age correspond to periods of life when the incidence is expected to be higher; in the former period congenital factors are operative while the latter period is the most active in the life of any individual.

Our complication rate (excluding recurrences) of 12.5% is higher than the 7% reported by Gallagher & Earley (1980)³. However on breaking this percentage down, we note that the complications were minor in nature and that wound infection accounted for 7.5% and wound haematoma 3.5%. The other local (sinus) and systemic (chest infection) complications were too insignificant to warrant comment. Better preoperative skin preparation & improved handling of tissue at operation should decrease the incidence of septic wounds. We still believe that good surgical principles should resolve this problem rather than the indiscriminate exhibition of antibiotics. We feel that the cause of postoperative wound haematoma may be the liberal use of spinal regional anaesthesia which is known to induce some degree of hypotension during surgery. Minor bleeding points may therefore not be recognised at operation because of this relative hypotension. When the blood pressure returns to normal in the recovery room, slight oozing from this source probably caused the haematomata.

In comparison, our recurrence rate of 1% is low; recurrence rates ranging from 1.4 to 3.2% have been reported with other methods of repair. However, a longer period of follow-up is necessary before our good results in this respect can be deemed valid. The absence of any mortality is

also encouraging when compared with mortality rates of 1.25 to 10% of others³. The length of hospitalisation of 5 days in this series compares favourably with that of the 10 days reported by Davies & Barr⁴ (1965).

CONCLUSION:

With present day preoperative care and anaesthesia, the indications for hernia surgery have become wide; age limits have been largely removed and the results of operation for all grades and type of groin herniae as revealed by this study generally good. Early operation should therefore be confidently recommended so that the fear of strangulation can be totally eliminated.

The truss, a palliative and useful form of therapy in the 'dark ages' of anaesthesia & surgery has little place to play in present day management of groin herniae.

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The diagnosis and management of swelling of the scrotal contents

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Introduction

Swelling of the scrotal contents often has to be considered an emergency. Delay of proper treatment, either by failure of the patient to seek medical attention promptly or by time consuming referral patterns or by the decision to treat the condition expectantly, may lead to an unsatisfactory end result.

Differential diagnosis of intrascrotal swelling

The causes of swelling of the scrotal contents can be categorized in 5 groups:

1. malignant disease of the testis
2. inflammatory disease of testis and epididymis
3. torsion of the testis
4. trauma of the testis
5. other causes

1. Malignant disease of the testis

Testicular carcinoma usually occurs in men of between 18 and 35 years of age. Although the disease constitutes about 2% of all malignancies in males, in the age group of 20 to 30 years it is the most common tumor in males. Definite causes for the disease have not yet been established, but cryptorchidism appears to be a significant etiological factor: the chance of a maldescended testis to develop a tumor is about 35 times the chance of carcinoma affecting the normally descended testis. The most important presenting symptom is painless enlargement of the testis. This is usually an accidental discovery, sometimes following a minor injury, sometimes the sexual partner is the first to notice it. The tumor can also announce itself simulating an acute epididymitis with pain, scrotal swelling and redness, and fever. As a rule however, the urinary tract infection usually found in true epididymitis, will be absent. An early, but seldom recognized symptom is gynecomastia in patients whose tumor produces gonadotrophin. Hydrocele, varicocele and haemospermia are occasionally seen as presenting symptoms. In some cases abdominal discomfort caused by retro-peritoneal metastases first brings the patient to the doctor. In a small proportion of

patients testicular carcinoma occurs bilaterally.

On examination one can find an enlarged testis with an irregular surface. The testis gives an impression of being 'heavier' than normal. The typical testicular pain sensation on squeezing the organ is often absent. Testis and epididymis cannot easily be separately palpated. The spermatic cord is normal. Routine urinalysis usually shows no abnormalities. Gonadotrophin producing tumors can cause a positive pregnancy test. Blood tests typically show a raised ESR and a raised LDH. Metastases are looked for by chest X-ray, lymphangiogram, IVP, CAT scan and certain tumor specific blood tests.

Since the introduction of radiotherapy and, later, of cytostatic chemotherapy in the treatment of testicular carcinoma the prognosis of the disease has dramatically improved. Still, the first step of any therapeutic approach is inguinal orchidectomy. Most testicular tumors metastasize along the spermatic bloodvessels to the paraaortic lymphnodes. It is therefore important to emphasize that when suspicion of testis tumor exists, biopsies, aspiration and exploration through the scrotal wall should be avoided in order not to involve the inguinal lymphnodes which are part of the drainage system of the scrotum. If the scrotal tissues are incriminated, later radiotherapy will have to include the groin area as well.

2. Inflammatory lesions of testis and epididymis

Epididymitis is no doubt the most important differential diagnosis in this group. The typical history is a rapidly developing painful swelling in one half of the scrotum, usually together with urinary tract infection or prostatitis and fever. The scrotal skin is swollen, red, painful and hot. The creases have disappeared. Transillumination is negative. During the first few hours the testis can be palpated separately but soon this organ will become involved in the inflammatory process resulting in just one big painful lump. The spermatic cord and more specifically the vas deferens are swollen and painful on palpation. Sometimes there is a secondary hydrocele which makes palpation even more difficult. During the

first few hours the ESR is not yet raised but leukocytosis is usually present. On urinalysis one can often find signs of urinary tract infection. Treatment is aimed at the infection with appropriate antibiotics and at the local discomfort with scrotal support and icebags. When the acute episode has passed further investigation should be done in order to establish the cause of the epididymitis. This will usually be found to be infravesical urinary obstruction (e.g. prostatic disease, urethral stricture).

Acute orchitis is less common than epididymitis. It also is a rapidly developing painful swelling in one half of the scrotum which is red and edematous. Testis and epididymis cannot be separately palpated and transillumination is negative.

Sometimes there is a concomitant or recent infectious disease, like parotitis. Rare causes of orchitis are tuberculosis, syphilis, actinomycosis, filariasis, malakoplakia and sarcoidosis. Granulomatous orchitis, as most of the previously mentioned types of orchitis, cannot be distinguished from testicular carcinoma on examination and is not usually diagnosed until after orchidectomy has been performed.

Treatment should be directed at the underlying cause of the disease, and in most cases can only start after orchidectomy. Local treatment is aimed at making the patient more comfortable with scrotal support, icebags and pain killers.

3. Torsion of the testis

This is no doubt a true urological emergency. Often there is a history of several previous short attacks of pain in the same testis that used to disappear spontaneously. Testicular torsion causes a sudden acute pain in the scrotum, followed by rapidly developing swelling of the testis that soon becomes indistinguishable from the epididymis on palpation. Transillumination is negative. Often the pain radiates to the abdomen along the course of the spermatic cord which is also swollen. The affected testis is usually pulled up towards the neck of the scrotum. Leukocytosis is common, urinary tract symptoms are not. It is important to examine the other testis also and to note its position in the scrotum. In patients with torsion, the unaffected testis often shows a long mesorchium and is more or less horizontally positioned, rather than 'standing up' in the usual way. This long mesorchium has allowed the affected testis to twist.

The condition is so painful that the patient will hardly allow the doctor to examine his

scrotum. In such case it is worthwhile to inject some local anaesthetic in the spermatic cord, because in some cases the testis can be saved by direct detorsion. It is a well documented fact that when torsion has existed for more than 6 hours the testis will be infarcted beyond repair. This is what makes torsion an urological emergency and the condition should be treated without delay. At the same session it is wise to perform an orchidopexy on the other testis as well since the long mesorchium allows the unaffected one to twist easily too.

4. Trauma of the testis

Testicular trauma is uncommon, mainly because the scrotal tissue is lax enough to allow free movement of its contents. The trauma itself is the main diagnostic datum. The trauma usually results in a hematoma, surrounding and compressing the testis. This results in swelling and pain. Transillumination is negative. Surgical decompression is indicated as an emergency since fertility is best preserved in this way. A rent in the visceral layer of the tunica is often found and this must be closed after removing all devitalized tissue.

5. Other causes of swelling in the scrotum

In many cases the scrotum is enlarged because it contains fluid.

Hydrocele is the most common example of this condition. It is a collection of clear, yellow fluid within the tunica vaginalis. In idiopathic hydrocele the cause that makes the tunica vaginalis secrete this fluid is not clear. Symptomatic hydrocele is caused by an inflammatory or tumorous process involving the testis or the epididymis.

In those cases the fluid may be cloudy or bloody or it may contain pus. The symptoms consist of a usually slowly progressive painless swelling of the scrotum. On palpation the testis appears to be completely embedded in the fluid and cannot be palpated properly. Fluctuation is always present. Positive transillumination confirms the diagnosis.

In newborn babies there is a good chance the hydrocele will disappear spontaneously. In children aspiration of the fluid under aseptic conditions is often followed by complete cure. In adults the recurrence rate after aspiration is considerable and operative treatment should be carried out after the second recurrence. Careful palpation of the testis immediately after aspiration of the fluid is necessary.

Hematocele refers to a usually traumatic hemorrhage in a pre-existing hydrocele. Trans-

illumination becomes negative. Treatment is by surgical exploration and repair.

Spermatocele is a thinwalled cystic structure originating from the upper testicular pole. Its fluid contains protein and immobile sperm cells. It is due to a congenital abnormality of the Mullerian duct. Spermatoceles do not usually reach the same size as hydroceles. Transillumination and fluctuation are positive and the swelling is painless. The testis can be separately palpated. The indication for surgical removal is the degree of discomfort it causes.

Varicocele is a scrotal swelling caused by varicose dilatation of the veins in the spermatic cord, the pampiniform plexus. The causes are either incompetence of the valves in the internal spermatic vein (idiopathic varicocele) or seldom a renal tumor that is obstructing the renal vein. Hemodynamic conditions cause the idiopathic varicocele to occur mainly on the left side. Therefore, an IVP is indicated in a right sided varicocele. Varicocele can cause oligoasthenospermia with infertility, a condition that often improves after surgical intervention. Idiopathic varicocele is treated by retroperitoneal ligation of the internal spermatic vein, a relatively minor operation.

Scrotal abscess causes a painful swelling and often the scrotal contents are not separately palpable. Transillumination is negative. There is redness of the scrotal skin and fluctuation. Treatment is by incision and drainage.

Scrotal hernia usually has a long history. Often it is easily reducible and not painful. Transillumination is negative. In some cases the diagnosis is easy because peristalsis can be heard or seen over the scrotum. Treatment is by hernia repair.

Some very uncommon conditions could also be mentioned like torsion of hydatid of Morgagni, tumor of the epididymis, tumor of the paratesticular soft tissues and accessory spleen. These are extremely difficult to diagnose preoperatively.

Conclusion

Many of the causes of intrascrotal swelling require surgical intervention. Some of these conditions are frank emergencies. Torsion of the testis, traumatic rupture of the testis, scrotal abscess and traumatic hematocele must be operated on immediately. Orchidectomy in carcinoma of the testis should be considered a semi emergency. Some conditions like epididymitis, orchitis and torsion of a hydatid of Morgagni can simulate torsion of the testis so closely that in the equivocal case it may be safer to surgically explore the scrotal contents than to treat conservatively: less harm is done by surgical exploration in a case of epididymitis than by treating a torsion conservatively. A detailed history, physical examination, including transillumination in a darkened room, and simple laboratory tests will generally lead to an accurate diagnosis in scrotal enlargement.

Colonoscopy: Technique & Results at the Changi Hospital

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INTRODUCTION:

Colonoscopy has recently been introduced as another important gastroenterological investigative procedure¹. Because it requires considerable skill for its performance, it has been suggested that it should not be used as a routine screening investigation but should be utilised to supplement adequate air contrast radiology of the large bowel². In this paper the experience gained during the first 70 colonoscopic examinations undertaken at the Dept of Surgery, Changi Hospital is reported. Key points in the technique³ are emphasized, and its indications in routine clinical practice discussed.

MATERIAL & METHOD

Patients: All patients included in this study were inpatients at the Dept of Surgery, Changi Hospital during the period Feb'81 to Feb'82. There were 48 males & 22 females & their ages ranged from 23 to 81 years. A barium enema study was undertaken in all patients either before colonoscopy was done or after the procedure. The only patients who were not considered suitable for inclusion in this study were patients with severe cardiopulmonary disease.

Patient preparation: Patients were restricted to a fluid diet 3 days prior to the endoscopy and the colon was washed out with soap enema, twice on the day before and once on the morning of the intended examination. Just prior to the colonoscopy itself, the patient is given a simple tap water enema. Initially patients were premedicated with Valium 10 mg but subsequently administration of pethidine permitted better patient co-operation. When significant colonic spasm was encountered an intravenous injection of hyoscine N-butylbromide was used to relax the bowel.

The instrument: The Fujinon COL-M Measuring 1340 mm long & with a 105 degree angle of view was used in all examinations. The 'leading tube' was used only once and it was discarded after it produced the only case of perforation in this series.

The examination: A rectal examination was first performed. Then a well-lubricated instrument was inserted with the patient lying in the left lateral position and being subsequently moved as necessary to assist its ease of passage. Fluoroscopic control was not used because the radiological equipment was not available. Despite this disadvantage, difficulty to negotiate the rectosigmoid loop was encountered in only one case (with a tense, ascitic abdomen). Passage to the ascending colon and caecum was attempted in all cases.

Photography/biopsy/polypectomy: All cases were photographed and lesions visualised were usually subjected to biopsy. Polypectomy was performed in 20 cases using the same instrument and without the aid of carbon dioxide gas insufflation.

Aftercare: All patients were returned to the ward and discharged only after a day's observation. A chest Xray was routinely done for all cases subjected to polypectomy after the procedure was over in order to exclude gas under the diaphragm.

RESULTS:

The success rate for total or partial colonoscopy is shown in Table I. Passage to the ascending colon and caecum was accomplished in 30% of the cases while the splenic flexure was visualised in 40% of patients. The endoscopy was completed from between 15 minutes to one & a half hours depending on whether intubation down to caecum was achieved or polypectomy also done.

The indications for the examination are shown in Table II and the diagnoses made at colonoscopy in the 70 patients appear on Table III. Generally, good correlation between colonoscopic finding and the contrast radiology report was obtained. However there were 7 cases (10%) where a barium enema contrast study did not reveal a lesion demonstrated by colonoscopy. The only failure to negotiate the sigmoid loop was in the patient previously mentioned to have gross ascitis and the single case of perforation was caused when the leading tube was used.

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TABLE I: TOTAL/PARTIAL COLONOSCOPIES

Ascending colon & caecum reached	— 21 cases (30%)
Splenic flexure seen	— 28 " (40%)
Partial colonoscopies	— 21 " (30%)

TABLE II: INDICATIONS

Persistent symptoms despite neg or equivalent Ba enema	— 23 cases
Xray neg rectal bleeding	— 15 cases
Radiological diagnosis of Chr inflamm bowel disease	— 2 cases
To exclude Ca in segment of diverticular disease	— 5 cases
Examination of post operative bowel	— 1 case
To perform colonic polypectomy	— 20 cases
Altered bowel habit with palpable mass	— 3 cases
Gross anemia wth palpable mass	— 1 case
total	70 cases

TABLE III: DIAGNOSES

carcinoma	12
polyps	20
radiation colitis	2
non specific colitis	4
amoebic colitis	1
ischaemic colitis	1
whipworm infestation	1
diverticular disease	5
no lesions seen	24
total	70

DISCUSSION:

Having thus reviewed our experience with colonoscopy at our Dept of Surgery, we confirm the high diagnostic accuracy of the technique in establishing large bowel disease. Its use is definitely justified because of its added accuracy and the opportunity it gives to get a tissue diagnosis by biopsy. If colonic polyp be the most likely diagnosis, then its performance provides the opportunity for transendoscopic removal by snare polypectomy and the avoidance of formal surgery.

Like others however, we emphasise the need for excellent bowel preparation⁴, skill & experience⁵ required for its successful performance. In our indications we have adhered to fairly standard practices⁶ and have not found cause for altering these in the future. Our good results with polypectomy conform with those of our colleagues

overseas^{7,8}; the only difference in our technique being our avoidance of carbon dioxide insufflation. In our hands the excellent bowel preparation and replacement of colonic air with room air was sufficient to eliminate any explosion hazard.

We have discarded the use of the leading tube⁹ to facilitate speedy negotiation of the signomidal loop because of the one case of perforation we encountered when using this accessory piece of instrument.

Finally, our success rate in getting to the Caecum (30%) and splenic flexure (40%), compares favourably with that of Cowen² (20% & 50% respectively) and makes it unnecessary to acquire a colonoscopy greater in length than our medium range instrument.

CONCLUSION:

Colonoscopy today should be available to all institutions where colorectal surgery is being performed. Although it is not a screening procedure, it should be used if the clinical or radiological features strongly suggest colorectal disease which cannot otherwise be confirmed by simpler techniques eg. proctosigmoidoscopy¹⁰. Complications do occur at colonoscopy but they are so infrequent that the flexible fiberoptic endoscopy can be safely recommended providing that a highly skilled and experienced colonoscopist is available, and no unnecessary manipulations eg. use of leading tube in the absence of fluoroscopic facilities be performed.

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ORIFICE OF SIGMOID
DIVERTICULUM



WHIPWORM IN THE CAECUM



RADIATION COLITIS

TYPICAL COLONOSCOPIC PICTURES



CHRONIC INFLAMMATORY
DISEASE OF COLON



RECTOSIGMOID JUNCTION



DESCENDING COLON



A RED PEDUNCULATED
COLONIC POLYP



TRANSVERSE COLON



CAECUM



SNARED SESSILE COLONIC
POLYP



ANNULAR CONSTRICTING
CA.COLON

Immunology & Microbiology for Family Physicians*

* * DR E H SNG MBBS, Dip Bact.

MICROBIOLOGY

Basic aspects

Bacteria	—	mucoprotein in cell wall
Viruses	—	ribonucleic acid or deoxyribonucleic acid
Fungi	—	yeast or mold
Commercial	—	part of normal flora may be pathogenic
Pathogen	—	capable of causing disease patients with reduced immunity susceptible to opportunistic infection.

Pathogenesis

Colonisation	—	overcome host immunity (adherence)
invasion	—	enzymes (hyaluronidase)
tissue damage	—	toxins enzymes inflammation immune mechanisms

Role of Laboratory Investigation

For the family physician the areas where the laboratory may have a role in the management of a patient with infectious disease are:

- Establishing the aetiological diagnosis. This is usually unnecessary, but may be important in special situations, eg typhoid.
- Choice of antimicrobial agent for treatment, especially where use of second line drugs is necessary.
- Assessing the response to treatment, especially where the disease may be sub-clinical, eg syphilis.
- Determining the source of infection, eg sex contact of patient with a sexually transmitted disease.

Though it is ideal to investigate patients whenever in doubt, it is often not practical because of various factors such as cost of investigation and delay in getting the results. A discussion on some of

the more common ailments will illustrate certain principles which will help to indicate those patients who are more likely to benefit from investigations. Also, laboratory investigation involves a series of stages where errors can occur. Careful observance of certain procedures will ensure optimal utilization of laboratory tests.

Selection of Patients for Investigation

(a) Diarrhoea

Besides microbial aetiology, there are other causes of diarrhoea, such as chemicals, drugs, extraintestinal diseases, etc. Of the microbial aetiology, viruses (rotavirus) is probably the most common in children, especially in developed countries. In developing countries bacterial (*E. coli*, *V. parahaemolyticus*) and parasitic agents (*E. histolytica*) have a more significant role. Bacteria cause diarrhoea by two main mechanisms — by the production of an enterotoxin (*V. cholerae*, *E. coli*) or by invasion of the submucosa (*shigellae*, *salmonellae*). Although there are epidemiological (consumption of sea-food, etc) and clinical differences (fever, nature of stool, etc) between these two groups of diarrhoeas, it is usually not possible to clinically differentiate the types of infection within each group. In deciding to investigate a patient with diarrhoea the following points should be borne in mind.

- As most microbial agents are likely to be viral, most diarrhoeas do not require antimicrobial agents. There are only few specific bacterial infections (cholera, shigellosis) where antibiotics are of some use. For some infections (salmonellosis) antibiotics may even delay clearance of the pathogen.
- Since the different pathogens have different requirements for their isolation, it is important to indicate the likely pathogen suspected based on epidemiological and clinical data. The traditional pathogenic *E. coli* does not usually cause diarrhoea.

*Dr Sng Ewe Hui is the Senior Consultant Bacteriologist at the Singapore General Hospital, Singapore 0316.

- (iii) Investigation is best indicated for patients who are suspected of having cholera, parasitic infestation (*E. histolytica*, *Giardia lamblia*) or whose diarrhoea persist beyond one week without improvement.

(b) Respiratory Tract Infection

It has been estimated that viruses may be responsible for 70-90% of the cases. Most of the viruses are RNA viruses like rhinovirus, respiratory syncytial virus, influenza virus, parainfluenza virus and corona virus. Of the DNA viruses, the adenovirus is the most important. The diagnosis of a viral infection is usually based on epidemiological and clinical data. In Singapore the highest incidence of influenza usually occurs around May.

Of the bacteria responsible for upper respiratory tract infection, the *Streptococcus pyogenes* is the most important, since it may give rise to rheumatic fever or acute glomerulonephritis. It is important therefore that this infection should not be missed. For the lower respiratory tract the pneumococcus is the most common pathogen. Other indigenous bacteria such as the *Staphylococcus aureus*, *H. influenzae* and *K. pneumoniae* may also give rise to infections in patients whose immunity is compromised. *Mycoplasma pneumoniae*, which is caused by a bacteria *M. pneumoniae*, is often underdiagnosed. It is frequently mistaken for viral pneumonia. Tuberculosis should always be considered in a patient with persistent cough.

In considering laboratory investigation, a few points should be borne in mind.

- (i) Most infections are viral in nature, and laboratory investigations for bacteria will therefore yield negative results.
- (ii) Most bacteria responsible for acute respiratory tract infections are susceptible to penicillin, erythromycin or tetracycline. When patients are not responding to these drugs, investigation may be desirable.
- (iii) Patients with depressed immunity are prone to infection by a wide range of indigenous flora. As these patients may be quite ill, and the bacteria have varying spectrum of susceptibility to antibiotics, investigation is usually advisable.

Selection of Test

No laboratory test is 100% sensitive or 100% specific. This being so it means that if a patient population is being investigated (screened) for a disease which they are unlikely to have, then their chances of getting false positive results are very high. The use of clinical judgement will reduce this considerably.

For microbiology the range of test is usually limited to a few types: microscopic examination, culture and serology. For those with their own laboratory the microscopic examination of the gram smear is very valuable. It is not only simple, quick but it allows one to differentiate the commensals from pathogens by interpreting the various cellular elements. The use of test kits is generally preferred because the reagents come prepared and standardised.

The following are a few tests which have been wrongly used:

Gonococcal complement fixation test — under-sensitive and nonspecific

- | | |
|---------------------|---|
| Collodial gold test | — nonspecific |
| FTA-ABS test | — for confirmation of diagnostic problem; not for follow-up of patient |
| Culture | — for diarrhoea and respiratory tract infections bacteria is usually not the primary pathogen and culture is not necessary. |
| Serology | — paired sera usually necessary. |

Collection and Handling of Specimen

To minimise errors precautions should be observed in the following areas:

- (a) **Blood for culture:** Disinfect skin and external surface of rubber cap with alcohol. Bottle may be kept at room temperature. Anaerobes require special medium.
- (b) **Sputum:** Send only purulent or mucopurulent sputum. Avoid sending saliva.
- (c) **Urine:** Mid-stream urine is preferred; should reach laboratory within two hours. Use of dip-slide is recommended.
- (d) **Pus:** Culture for the gonococcus should preferably be by direct streaking on to Thayer-Martin medium with presence of carbon dioxide. Culture for anaerobes requires of pus which should reach the laboratory within an hour.
- (e) **Serology:** Dry syringe and bottle should be used to prevent lysis.

Interpretation of Test Results

(a) Isolation of Pathogen

The significance of the result has to be interpreted in the light of the clinical features, since pathogens may be found in various tissues which have little clinical significance.

Brief episodes of bacteraemia may also occur in normal people. False negative results may occur especially if the patient has just been given an antibiotic. In doing a test of cure, it is advisable where possible to carry out the investigation a few days following cessation of chemotherapy.

(b) Antibiotic Susceptibility Test Results

The final outcome of chemotherapy is dependent on the interaction between the patient, drug and pathogen. In vitro susceptibility test depends only on the interaction between drug and pathogen. Hence the test result should be interpreted in the light of this, and the following guideline is suggested:

- (i) Starting patient on antibiotic — refer to results
- (ii) Patient responding to antibiotic:
 - (a) no reason to change drug — ignore results
 - (b) desires to change drug (adverse effect, cost, administration) — refer to results
- (iii) Patient not responding to antibiotic — refer to results.

(c) Serology

This depends on the ability of the patient to form antibody in response to infection. False negative result usually occurs because the blood has been taken during the early phase of infection. A false positive result may occur because of previous immunisation, a cross reaction with other bacteria or an anamnestic response. Such errors can usually be reduced if paired sera are taken to detect rising antibody titres.

IMMUNOLOGY

Specific response to foreign antigen.

Lymphocytes — B (bursa of Fabricius) & T (thymus) cells.

Clinical Aspects

Deficiency	— infection
Hypersensitivity	— adverse effect

Autoimmune diseases	— direct against self (loss of tolerance)
Immunoproliferation & tumour	— loss of immunological surveillance
Transplantation	— rejection.

Major Responses

I Humoral antibody

Passive transfer by serum

Pyogenic infection

Immunoglobulin — heavy chain (5 classes)
light chain (2 types)

IgG : 75% serum Ig
extravascular; passes through placenta; chronic infection; immune complexes

IgM : intravascular — red cell antibody
does not pass through placenta; congenital infection; early antibody (of value in the diagnosis of rubella)

IgA : mucosal secretion; locally produced; T-piece — resist digestion; localised infection

IgE : cell-bound; parasitic infestation; anaphylaxis; asthma

IgD : role unknown.

II Cell-mediated immune response

Passive transfer by cells

Cytotoxic lymphocytes; macrophages

Tuberculosis; gram-negative bacteria; fungus; virus

Contact dermatitis.

Diagnosis

Clinical: family history; age of onset; frequency, severity and type of infection; occupation; chemicals; hobby.

Skin tests: immediate type (asthma)
Arthus phenomenon (hypersensitivity pneumonitis)
delayed-type hypersensitivity (contact dermatitis.)

Laboratory: Serum Ig quantitation
autoantibody; IgE antibody; T cell enumeration and function.

* Lecture delivered at the In-Depth Course in Minor/Ultra Specialities in Family Medicine on Friday, 11 September 1981.

Clinical Biochemistry for Family Physicians*

* * DR EDWARD JACOB PhD, MCB, FRIC

INTRODUCTION

Clinical Biochemistry may be defined as the development and application of chemical laboratory knowledge or methods to : diagnosis, prognosis, control of treatment and prevention of disease. The laboratory deals with the analysis of chemical components present in various body fluids/ tissues e.g. blood; urine; sweat; CSF; pleural, ascitic, gastric fluid; various tissue obtained by biopsy and stool.

MULTIPLE FUNCTIONS OF LABORATORY TESTING

- (a) Assisting in the diagnostic process in a patient known to be sick.
- (b) Providing data that are of value in assessing the severity of disease, and so helping in the formulation of the prognosis.
- (c) Providing an indication as to whether or not a disease is present in its early or subclinical stages in otherwise healthy persons.
- (d) Monitoring the response to treatment.
- (e) Providing data that may indicate whether or not disease might develop at some future time, that is, delineation of risk factors.

PRE-ANALYTICAL FACTORS

There are many non-analytical factors that can cause changes in laboratory data that are sufficiently large that misinterpretations could arise if they were ignored. The following are important considerations:

- (a) **DIET.** e.g. variations can affect plasma cholesterol, the response to glucose tolerance tests, plasma triglycerides, urea.
- (b) **DRUGS.** These can have marked effects on chemical analysis e.g. oral contraceptives affect total thyroxine values.
- (c) **MENSTRUAL CYCLE.** Several substances show variation with the phase of the cycle. e.g. plasma iron, pituitary gonadotrophins, ovarian steroids and their metabolites.
- (d) **MUSCULAR EXERCISE.** e.g. plasma creati-

nine kinase activity.

- (e) **POSTURE.** Several proteins and protein-bound constituents show significant differences in concentration between blood samples collected from upright and from recumbent individuals; e.g. plasma albumin, calcium, cholesterol, cortisol.
- (f) **TIME OF DAY.** Several plasma constituents show diurnal variation e.g. plasma cortisol.
- (g) **VENOUS STASIS.** Prolonged stasis can falsely raise plasma protein levels, calcium, lipids, thyroxine i.e. protein bound substances.
- (h) **HAEMOLYSIS.** Erythrocytes contain very different concentrations of many substances from those of the surrounding plasma e.g. K^+ concentrations are about 25 times as high. If haemolysis occurs the contents will 'leak out' and false answers will be detected by the laboratory e.g. SGOT, LDH.
- (i) **AGE, RACE, SEX.** Several measurements showed marked physiological variation with age e.g. plasma urea, alkaline phosphatase activity; racial differences have been described for plasma cholesterol and protein.

In interpreting results it should be borne in mind that the Reference Range (Normal Range) only indicates the probability of a result being normal or abnormal, and that there are physiological differences in reference ranges and physiological variations from day-to-day. There are small day-to-day variations in results due to technical factors and reference ranges may vary with the laboratory technique employed. The analytical reliability with which measurements are made varies considerably. Poor standards of precision widen the reference range for the substance being determined, while poor accuracy affects the level at which the mean value is set.

In general, laboratory tests are costly and doctors are requested to be selective when making requests for investigations.

PLASMA ENZYMES IN DIAGNOSIS

Plasma enzyme levels depend on:

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- (a) rate of release from cells, in turn dependent on rate of cell damage
- (b) extent of cell damage
- (c) rate of enzyme excretion and catabolism.

e.g. in viral hepatitis — rapid damage of relatively few cells causes very high enzyme levels; whereas the liver may be more extensively involved in advanced cirrhosis, but the rate of cell breakdown is often low and enzyme levels may be only slightly raised.

Following major surgical procedures or after extensive trauma, levels of lactate dehydrogenase (LDH), aspartate transaminase (SGOT), and creatine kinase may be raised.

If circulatory failure is present, due to cardiac failure or shock, and especially after cardiac arrest, very high levels of several enzymes may occur. When unexplained raised levels (especially of lactate dehydrogenase) are found, the possibility of malignancy should be considered.

Alanine transaminase (SGPT) and LDH occur only in the cytoplasm, while glutamate dehydrogenase occurs only in the mitochondria and SGOT occurs in the cytoplasm as well as the mitochondria. Thus different relative plasma levels indicate different types of disease.

NON-SPECIFIC CAUSES OF RAISED ENZYME LEVELS

- (a) Newborn — levels of some enzymes such as SGOT are raised in neonates.
- (b) Childhood — Alkaline phosphatase levels are high until after puberty.
- (c) Pregnancy — in the last trimester levels of alkaline phosphatase are raised.
- (d) Enzyme induction by Drugs — some drugs, particularly diphenylhydantoin and barbiturates may stimulate the production of enzymes e.g. Alk P'tase, SGOT, SGPT.
- (e) Haemolysis — haemolysed samples, in general are unsuitable for enzymes.

MYOCARDIAL INFARCTION

Enzyme estimations of greatest value are creatine kinase (CK), SGOT AND LDH.

Enzyme	Starts to rise (hours)	Peak elevation (hours)	Duration of rise (days)
CK	4-8	24-48	3-5
SCOT	6-8	24-48	4-6
LDH	12-24	48-72	7-12

The height of the rise is a rough index of the

extent of damage. A second rise in enzyme levels indicates extension of the infarct. Levels in angina are usually normal.

Some confusion may arise if the patient presents with cardiac failure and secondary liver involvement, with raised transaminase and LDH Levels. Evaluation of the two processes is assisted by estimation of isoenzymes e.g. HDB and the rise in SGPT.

ENZYMES IN LIVER DISEASE

- (a) rises of SGPT, SGOT, isocitrate dehydrogenase and to a lesser extent, LDH, are indices of liver cell damage.
 - levels are raised in the prodromal phase of viral hepatitis and reach their maximum after the onset of jaundice, thereafter to return to normal.
 - very high levels occur associated with toxic hepatic necrosis.
 - in early extrahepatic cholestasis enzyme increases are minimal, but if obstruction persists cell damage with consequent rise in enzyme levels occur.
- (b) Alkaline phosphatase, gamma-glutamyltransferase and 5'-nucleotidase are useful mainly as indicators of cholestasis.
 - biliary cirrhosis produces very high levels; intrahepatic cholestasis in hepatitis is associated with a 2-3 times normal rise.
 - space-occupying lesions in the liver may produce raised levels of ALP without a corresponding rise in bilirubin.
- (c) Cholinesterase levels are decreased with liver cell dysfunction.

BIOCHEMICAL TESTS FOR LIVER DISEASE

- (a) Tests for liver cell damage: e.g. transaminases released from damaged cells (see above).
- (b) Tests for liver cell dysfunction:
 - bile pigment metabolism. Essential tests to assess jaundice are estimation of plasma bilirubin (conjugated and unconjugated) and qualitative tests for urinary bilirubin and urobilinogen. Raised levels of unconjugated bilirubin only indicate excessive red cell destruction, defective entry of bilirubin into liver cell or defective conjugation of bilirubin. In cholestasis conjugated bilirubin predominates. Bilirubin in the urine means that there is an increase in circulating conjugated bilirubin and is always pathological. Complete absence of urobilinogen from urine in a case of jaundice indicates complete cholestasis.

- bromsulphthalein excretion. Less than 5% of an injected dose of BSP remains in the circulation 45 minutes after administration. Increased retention of BSP is a sensitive index of hepatocellular dysfunction. False positive results occur where there is impaired circulation in the liver, e.g. in congestive cardiac failure, or if biliary obstruction is present. This is a sensitive test of liver function, when other tests are normal, but is unnecessary when the patient is jaundiced.
- (c) Test of synthetic function. Albumin is catabolised at a rate of about 4% of the body pool daily; decreased synthesis is reflected in reduced plasma levels. Hypoalbuminaemia may occur in both acute and chronic liver disease.
- (d) Tests for cholestasis. Raised alkaline phosphatase levels in jaundice generally indicate cholestasis, although moderately raised levels, as in hepatitis, may be a result of liver cell damage. The higher the level of alkaline phosphatase, the greater the likelihood of extra-hepatic cholestasis.

The following are useful tests in individual conditions:

Suspected acute hepatitis: plasma bilirubin, SGPT or SGOT, urinary bilirubin and urobilinogen.

Suspected chronic hepatitis: SGPT (SCOT may be normal), protein electrophoresis.

Suspected cirrhosis: plasma albumin and electrophoresis. If this condition is suspected and if none of the biochemical findings are abnormal, a BSP excretion test should be done.

Suspected cholestasis: alkaline phosphatase, bilirubin (especially the conjugated fraction).

Suspected primary hepatocellular carcinoma: SGOT and alkaline phosphatase.

RENAL FUNCTION TESTS

1. URINALYSIS

The most common urinary abnormality that suggests renal disease is proteinuria.

- (a) Appearance: normal urine is yellow to amber in colour; cloudiness or turbidity on standing is secondary to the precipitation of urates and phosphates; blood, haemoglobin and myoglobin impart a red or reddish brown colour; foaming is a clue to proteinuria; yellow foam suggests the presence of bile salts and bile pigments.
- (b) pH: urine is almost always acid except when there is infection with urea-splitting

organisms. Urine is alkaline in renal tubular acidosis.

- (c) Glucose: methods that employ glucose oxidase (e.g. dipstick) detect only glucose, whereas other methods detect not only glucose but other reducing substances e.g. salicylates, dextran, urates, pentose sugars and thus produce false-positive results.
- (d) Other substances: ketonemia results in a positive finding for acetone in the urine; this occurs most commonly in diabetic Ketoacidosis; ketonuria alone may be found in starvation or fasting.
- (e) Proteinuria: This is usually the first and occasionally the only abnormality in patients with renal disease; the major protein in urine is albumin; the 24 hour protein excretion is of utmost importance; proteinuria is considered significant when excretion exceeds 15% mg./24 hr.

2. CREATININE CLEARANCE

The best guide for evaluation of renal function is the creatinine clearance as this estimates the glomerular filtration rate (GFR); clearance procedures are useful in detecting early renal function impairment and in following the course of renal disease. Clearance is defined as the volume of blood cleared of a substance per minute of time. It is reported in milliliters per minute. Most men excrete at least 1000 mg. of creatinine in 24 hours, and women more than 700 mg. in the same period.

Reference Values for creatinine clearance:

Men	85 – 125 ml/min.
Women	70 – 120 ml/min.

GFR declines slowly above the age of 40. By the age of 70, creatinine clearance may be 50% of normal even in the absence of renal disease.

3. UREA

Reference range: 15 – 40 mg/100 ml.

Urea is not a good test for detecting early renal function impairment because it may be normal with as much as a 50% reduction in GFR. It is affected by diet. High protein diet tends to increase serum urea.

4. CREATININE

Serum creatinine is a more useful guide to the GFR than urea

Reference range: 0.5 – 1.6 mg/100ml.

Not affected by diet.

INCIDENTAL ABNORMAL FINDINGS IN RENAL FAILURE

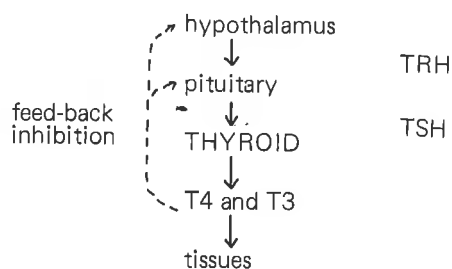
Plasma urate (uric acid) levels rise in parallel with plasma urea, and a high level does not indicate primary hyperuricaemia. Plasma phosphate levels rise and those of calcium fall.

THYROID FUNCTION TESTS

The two important circulating thyroid hormones are thyroxine (T4) and triiodothyronine (T3). Both hormones are tightly bound by thyroid binding proteins; the binding proteins are: **thyroxine binding globulin (TBG)** — 75% circulating T4 is bound to this protein; **thyroxine binding prealbumin** — 15% of T4 is bound to this; **albumin** — 10½% of T4 is bound to this fraction. More than 99% of both hormones are bound to protein. It is the less than 0.1% of the free hormone which is active.

CONTROL OF THYROID HORMONE PRODUCTION

Pituitary thyroid-stimulating hormone (TSH) controls output of T4 and T3. TSH output is controlled by thyrotrophin-releasing hormone (TRH) from the hypothalamus. There is a feed-back inhibition by the circulating T4 and T3. It is the free form of the hormones which bring about the feed-back inhibition.



TOTAL THYROXINE LEVELS

Total thyroxine (T4) levels in plasma can be measured by radioimmunoassay (RIA). T4 is high in hyperthyroidism and low in hypothyroidism. However as more than 99% of measured T4 is protein bound, values depend on the level of thyroxine binding proteins. In practice the commonest sources of potentially misleading results for plasma total T4 occur in:

- Pregnancy and in patients on estrogen therapy, including women on the pill. On average, the total T4 is 30 — 40% higher in pregnant than in non-pregnant women.
- Elderly ill patients, who often have low plasma TBG and therefore low T4.

In hypothyroidism, plasma T4 is usually low. However it is less sensitive than plasma TSH for this condition.

TOTAL T3 LEVELS

The main value of plasma total T3 is in the diagnosis of hyperthyroidism. In most cases of thyrotoxicosis, both T4 and T3 are raised, but in a small percentage of cases who are clinically thyrotoxic the T4 may be normal but the T3 is elevated. This condition has been termed T3 — toxicosis.

PLASMA THYROID HORMONE-BINDING CAPACITY

This test has been referred to as 'T3 uptake test', T3 or T3 resin test. These names are misleading and do not measure the hormone T3. The test should be referred to as the serum uptake test, and is a measure of the unsaturated thyroid hormone binding capacity. This measurement allows for the calculation of the free thyroxine index.

Plasma free thyroxine (free T4) provides the most accurate in vitro test of the thyroid status. This estimation is difficult but the free thyroxine index correlates well with direct measurement of free T4. Calculation of this index (FTI) from the total T4 and the serum uptake test, tends to correct the plasma total T4 for variations in plasma TBG.

PLASMA THYROID STIMULATING HORMONE (TSH)

TSH may be assayed by RIA. Estimation is of value in the diagnosis of primary hypothyroidism. In this condition, plasma T4 and T3 are usually normal in the early stages of the disease whereas TSH is invariably raised in cases due to primary thyroid disease.

GLUCOSE TOLERANCE TEST

The glucose tolerance test is performed to assess the response to glucose.

Upper Limits of Normal Glucose Tolerance
(mmol/L with mg./100 ml in brackets)

	Fasting	1 hour	1½ hour	2 hour
Whole Blood (capillary)	5.6 (100)	10.0 (180)	7.8 (140)	6.7 (120)
Whole Blood (venous)		8.9 (160)		6.1 (110)
Plasma or Serum	6.4 (116)	10.3 (185)	9.0 (162)	7.8 (140)

Types of GTT curves

- (a) The 'normal' GTT.
- (b) The diabetic GTT curve. The most significant finding is the failure of glucose levels to fall below 6.7 mmol/L (120mg/dl) (capillary) or 6.1 mmol/L (110mg/dl) (venous) by two hours. The peak level is often above normal and the fasting levels may or may not be raised. Glycosuria is present.
- (c) Lag storage curve. The peak level may be higher than normal but the 2-hour value is

within normal limits, or often low. This implies a delay in early compensatory mechanisms ("lag") without necessarily impairment of insulin response. Such a curve may be found in:

- apparently normal individuals (reactive hypoglycaemia)
- after gastrectomy
- in very severe liver disease
- rarely in thyrotoxicosis.

*Lecture delivered at the In-Depth Course in Minor/Ultra Specialities in Family Medicine on Friday, 18 September 1981.

NEWS FROM THE COUNCIL

Annual General Meeting

The Eleventh Annual General Meeting of the College was held on Sunday, 23 May 1982. As the present Council (1981-83) was elected for a two-year term no elections were held at this meeting and the present office-bearers will carry on for another year.

Tenth College Examination

The Tenth College Examination for Diplomate Membership will be held on:

Sunday, 24 October 1982 — Theory
Sunday, 31 October 1982 — Clinicals

Five candidates will be taking the examination.

In-Depth Course in Surgery

The Continuing Education Unit of the College is organising an In-Depth Course in Surgery to be held from 2 July 1982. The programme is as follows:

PROGRAMME

THEORY SESSIONS: Friday evenings, from 9.00 to 10.30 p.m., at Academy of Medicine Lecture Theatre, Alumni Medical Centre, 4A College Road.

Date	Topic:	Lecturer:
2. 7. 82*	Neurosurgical disorders of interest to the family physician	Mr Gopal Baratham
9. 7. 82	The Breast	Mr James J Murugasu
16. 7. 82	Dysphagia	Mr Chan Kong Thoe
23. 7. 82	Acute Abdomen	Mr Yahya Cohen
30. 7. 82	Chronic Dyspepsia	Assoc Prof Ti Thiow Kong
6. 8. 82	Large Bowel Tumours	Mr R Nambiar
13. 8. 82	Anal Conditions	Assoc Prof Abu Rauff
20. 8. 82	Male External Genitalia	Prof Foong Weng Cheong
27. 8. 82	Haematuria	Assoc Prof Foo Keong Tatt
3. 9. 82	Paediatric Surgery	Mr V T Joseph

* This session will be held at the Pathology Lecture Theatre, Spore Gen. Hosp.

CLINICAL SESSIONS: Sunday afternoons, from 2.30 to 5.00 p.m.

Date:	Topic:	Venue:
8. 8. 82	Lumps and Bumps Breast Examination	Surgical Unit 'A' OPD Singapore General Hospital.
	Thyroid Gland and Cervical Gland Management	
	Practical Wound Management	
22. 8. 82	The Abdominal Mass	—do—
	External Genitalia including Hernias	
	Anal Conditions including Ano-rectal Examination	
5. 9. 82	Local/Regional/Intravenous Anaesthesia	Anaesthetic Unit Singapore General Hospital.



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¹ Acta Paediatrica Scand. 1979; 68: 851-5; 441-2, 813-17.

² Codex Alimentarius Commission Joint FAO/WHO food standards programme. Recommended international standards for foods for infants and children. CAC/RS 72/74 - 1976. Rome: Secretariat of the joint FAO/WHO food standards programme, 1976.

³ American Academy of Pediatrics. Committee on Nutrition. Commentary on breast-feeding and infant formulas, including proposed standards for formulas. Pediatrics 1976; 57: 278-85.

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References: 1. Brest, A. N.: Hemodynamic response to antihypertensive drug therapy, J. Amer. med. Ass. 192:41-44, April 5, 1965. 2. Tarazi, R. C. and Gifford, R. W., Jr.: Drug treatment of hypertension, in "Drugs in Cardiology," E. Donoso (ed.), vol. 2, New York, Stratton Intercontinental, 1975, pp. 1-41. 3. Brest, A. N.: Hemodynamic effects of methyldopa, in "Methyldopa in the Management of Hypertension," R. W. Gifford, Jr. (ed.), West Point, Pa., Merck Sharp & Dohme, 1972, pp. 27-34. 4. Onesti, G.: When hypertension is complicated, Drug Therapy 5:66-78, June 1975.

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