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Editorial

Post-Graduate Medical Education and Examinations

by A. A. Sandosham

MEDICINE is an ever advancing discipline with new-discoveries, new ideas and new techniques being introduced continuously. Post-graduate medical education has to be a continuing process if our doctors are to keep abreast with the phenomenal advances in medicine. A certain amount of self-education is undertaken by doctors who peruse some of the ever-growing output of medical literature.

Organised facilities are provided by Medical Associations and Societies, large hospitals and teaching institutions in the form of clinical meetings, ward rounds, workshops, seminars, refresher courses and lectures by eminent clinicians and research workers. These activities, however, are confined to the larger towns and only relatively few of the busy practitioners take full advantage of these opportunities. There is need for extension of this programme by providing better facilities in the form of lecture halls, facilities for the projection of medical films and tape recordings of lectures at a time and place best suited for most of the practitioners.

This is an age of specialisation and to supplement the activities of the Malaysian Medical Association, the Academy of Medicine and the University of Malaya there have come into being Organisations to cater for the special needs of surgeons, physicians, obstericians and gynaecologists, general practitioners, oto-rhino-laryngologists, ophthalmologists, anaesthesiologists, psychiatrists, pediatricians, radiologists, urologists and the like. Some of these Organisations are designated Colleges, and in addition to providing the facilities for keeping their members informed of advances in their particular fields they are talking of conducting examinations in their specialities and awarding diplomas and degrees rather like those granted by the Royal Collges in Britain and Australia.

It has been, and to large extent still is, the practice for Malaysian Medical graduates to go abroad to UK, Australia and USA for post-graduate studies. This is not an altogether satisfactory arrangement because of the differences in culture and disease patterns in these foreign countries. Besides, it is a costly undertaking involving travelling with or without their families and maintenance abroad for prolonged periods with all their attendant problems. It must be remembered that these trainees during their period of apprenticeship render considerable service to the hospitals and the people of the countries where they study. This is a great loss to Malaysia with its insufficient medical manpower, and every effort should be made for our graduates to obtain their post-graduate training locally. Some effort has been made to reduce the time they have to spend abroad by instituting a training programme during their registrarship in the big hospitals and laboratory postings at the Institute for Medical Research. This, however, is inadequate to serve our purpose. While advocating training locally it is not suggested that a visit abroad is not desirable. In fact, it is necessary to give our graduates the breadth of view which can only be obtained by brief visits to centres of advanced learning. The best time, when they are most likely to benefit from such a visit, would be after our doctors have obtained post-graduate experience and degrees locally irrespective of whether the post-graduate examinations were held under the auspices of the Royal Colleges or not.

At the moment, the Institute for Medical Research, Kuala Lumpur is the national centre for training and research of the Central Coordinating Board for Tropical Medicine of the Southeast Asian Ministers of Education Council which has been conducting post-graduate courses leading to the Diploma in Applied Parasiotology and Entomology. The Board on Post-graduate Medical Education has started at the University of Malaya courses for the Diploma in Public Health, Pathology and Psychological Medicine. It is contemplating running courses in Paediatrics and Obstetrics and Gynaecology.

The Board on Post-Graduate Medical Education has also arranged for the holding locally of examinations of the Royal Colleges of Physicians, Surgeons and Obstetrics and Gynaecology of UK and Australia and short courses have been held in the Faculty of Medicine, University of Malaya in preparing candidates sitting for these examinations. For running these courses the Board has been almost solely dependant on the staff of the Faculty of Medicine, University of Malaya whose terms of appointment include teaching at the post-graduate level as well. There is no doubt, however, that there are a number of specialists in Government service, in the Universiti Kebangsaan and in the private sector who are fully competent to teach at the post-graduate level and whose services are not utilised at the moment.

Perhaps, the situation can be remedied by setting up a new Board on Post-Graduate Medical Education with powers to requisition the services of all available talent in the country. As at present constituted the personnel of the Board is practically solely drawn from the Faculty of Medicine, University of Malaya with the Dean as Chairman. The new Board could be set up as an independent Statutory Body with better representation from the Faculty of Medicine of Universiti Kebangsaan, the Ministry of Health, the Academy of Medicine, the Malaysian Medical Association and other interested organisations. Such a body could be held responsible for planning all post-graduate medical education in the country taking into consideration the future needs of the country and making full use of the resources available.

Besides determining the specialities in which training could be developed locally and where courses could best be conducted, the Board could decide on the disciplines in which post-graduate examinations are to be held in the country. The question of our ability to maintain adequate and comparable standards at local examinations should be seriously considered lest our graduates suffer from an inferiority complex. It is not desirable that every 'College' that considers itself competent to do so should automatically be entrusted with the power to hold post-graduate examinations and award diplomas and degrees.

Media Systems for Education and Training in the Allied Health Sciences

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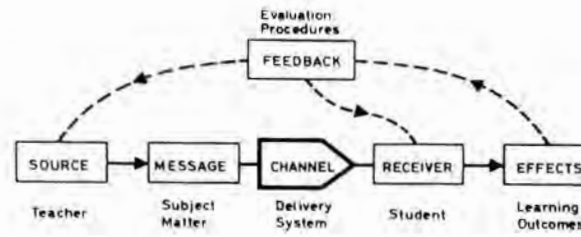
Introduction

THE TECHNIQUES involved in education and training are essentially techniques of communication of knowledge, skills and attitudes from one group of persons (teachers) to other groups (students). However complex the system of communication may be, the elements involved can be reduced conceptually to a simple model, the S-M-C-R-E model (modified from Rogers and Shoemaker, 1971) as depicted in Fig. 1. This shows the basic components of the process of communication. The boxes contain words denoting the communication process while below are shown terms relating to the context of education. In each case, the process starts with a source having a message to pass on to a receiver through a channel. Upon receipt of this message, the receiver responds and effects are generated accordingly. A feedback pathway is usually incorporated to allow the source to monitor the success or failure of his communication and also for the receiver to check upon the results of his reception of the message. In educational terms the process would involve a teacher having a unit of instruction to transmit to a student through a delivery system. The student, upon receiving the unit of instruction, exhibits learning outcomes that can be assessed by relevant evaluation procedures. This generates feedback both for the teacher (in terms of how effective his "teaching" has been) and the student (how successful he has been in his "learning")

When this model is applied to the education and training of medical, para-medical and auxilliary health personnel, the link that may be explored further in the light of advances in media technology



S-M-C-R-E MODEL OF COMMUNICATION

is the *channel* by which the unit of instruction is "transmitted" to the student. In educational terms, this is the delivery system.

The term "media" refers to "any means of presenting stimuli" (Briggs et al. 1966) and "media technology" is the employment of technology (whether graphic, mechanical, electric or electronic) in the creation of formats and devices for the presentation of stimuli. "Media systems" are therefore procedures associated with a single medium or combination of several media with the attendant technological processes that are used for the transmission of stimuli particularly in an educational setting.

Objective

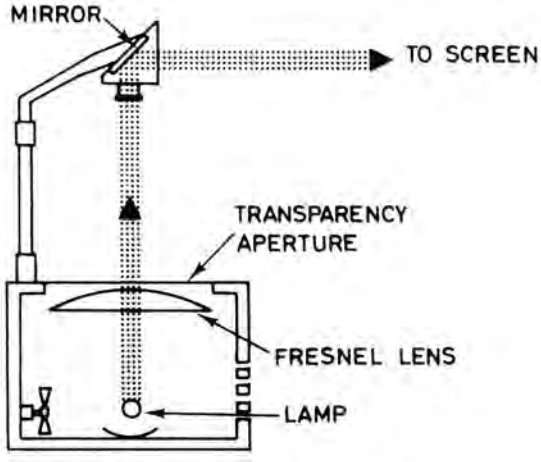
The spoken and printed word, patients, cadavers, lantern slides and models have long been used in education and training in the allied health science field. More recently, the 35 mm slide has become a common means of presenting data or illustrations

and many 16 mm movie films are available for medical teachers who wish to use these either to supplement or to replace the traditional lecture.

Newer media systems have now been created and are available for more effective delivery of subject material to students. In the Malaysian context, some of these are already in use, but others are being tried out only experimentally. Further, the manifold potentialities of some of the systems already in use have still not been fully exploited.

The objective of this paper is to draw the attention of educators in the field of the health sciences in Malaysia to some of these newer media systems.

(a) *An overhead projector (OHP)* (Fig. 2) is a device that throws an image of an 8 inch by 10 inch transparency "over the head" of the teacher on to a screen behind him. This device can be operated by the teacher alone facing the audience, and can be used in a normally lighted room. The OHP comes in several models with varying power in the light source. Newer models employ quartz-iodine lamps which emit a brighter light with less heat production. A portable model is also available in a package slightly larger than a brief-case.



OVERHEAD PROJECTOR (OHP)

The transparencies that are projected by the OHP can be obtained in sets that have been prepared and tested by the manufacturers and a wide range of subjects in the health sciences may be purchased as "teaching packages" complete with worksheets and teacher's guide. These professionally prepared transparencies are in colour and are usually of high quality. They also incorporated "overlays" (one transparency on top of another) in order to introduce a subject sequentially or to show by superimposition the relation of one factor to another. However, most of these teaching packages have been prepared in a non-Malaysian context and caution has to be exercised when they are used locally.

Transparencies for the OHP can also be prepared locally by drawing on clear acetate sheets or imprinting by means of an infra-red thermocopying machine upon special heat-sensitive sheets of clear acetate from paper sheets with pencilled words or diagrams. Rolls of clear acetate are also available and can be fitted to the OHP for use as a writing surface by the teacher. As more space is required, the used part can be rolled away from the transparency aperture to be replaced by fresh writing surface. Clear acetate sheets are relatively expensive and a cheap and effective substitute may be obtained from discarded X-ray films bleached by immersion in iodine solution.

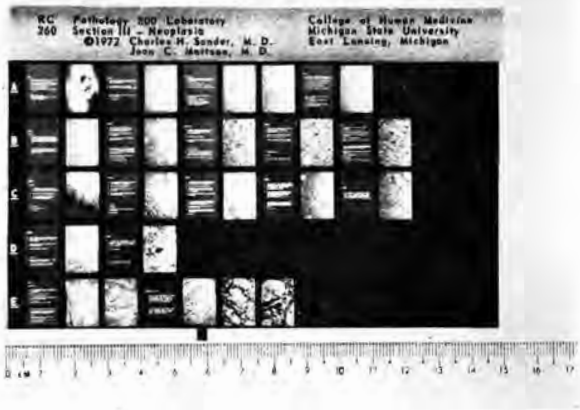
(b) *Audiotapes* are now available in open-reels, cassettes or cartridges. Lectures or articles from journals can be recorded on audiotape and these can be borrowed by the students and played back at their convenience at home, in the library or even in the motor-car while commuting if cassettes are used. Certain medical journals are already issued in this form, for example, the American College of Cardiology Extended Learning (ACCEL) circulates a "multimedia journal" in cassettes accompanied where necessary with illustrative printed material, for example electrocardiogram tracings.

(c) *Tape-slide presentations* are produced by combining the commentary, narration or lecture on an audiotape with a series of 35 mm slides that serve to illustrate visually the presentation. These presentations may be synchronised – the slides changing by a recorded pulse from the audiotape.

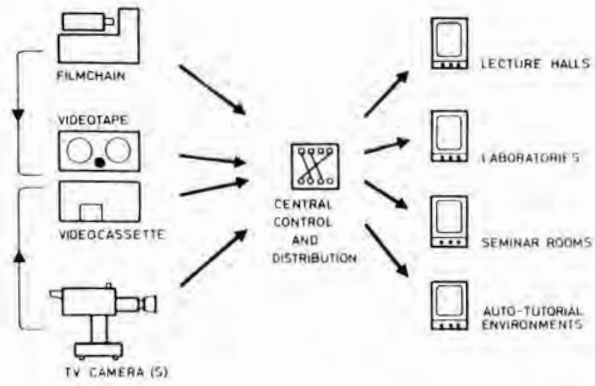
If automatic slide projectors are not available, manual projectors or battery-powered viewers can be substituted for small group or individual viewing. Learning packages can be made available through libraries or circulation. These presentations are quite easily available, for example, the Royal College of General Practitioners in the United Kingdom in conjunction

with the Medical Recording Service Foundation citercusla a large stock of tape-slide packages on a wide range of medical and health subjects. A number of these will shortly be available in the Medical Library of the University of Malaya.

(d) Insome medical schools, *microfiche* have replaced microscope slides as a means of illustrating phoblogic changes in tissues. Microfiche are made of photographically exposed films, 4" by 'a' with a maximum capacity (in this form) of sixty frames, projected for viewing by a reader machine. In Fig. 3, each picture is accompanied by questions with answers given below. Microfiche are not difficult or costly to prepare, although those requiring illustrations and compactly stored and are virtually indestructacte if handled in the proper manner. Reader machines, however, vary in price depending on the degree of resolution obtained and degree of automation required.



(e) *Television* has been used in education for some time. Closed circuit television (CCTV) systems are the most widely used, with the programs being distributed through cables. A possible CCTV system is depicted in Fig. 4. The source of the program may be pre-recorded videotapes, video-cassettes, or live productions from a television studio. Live productions can be simultaneously recorded on videotapes for repeated showings. A film-chain which allows slides or movies to be shown through television can also be linked with the CCTV system and a central control and distribution panel incorporated to direct the programs to the appropriate viewing areas.



CLOSED CIRCUIT TV PRODUCTION / DISTRIBUTION SYSTEM

CCTV can be used for recording events, experiments, or patient interviews on videotapes for future viewing and discussions, for handling overflows from lecture halls or for providing close-ups of anatomy demonstrations, post mortem examinations or surgical operations for large groups of students. Because video recordings can be sent by post, they serve to extend a teacher in space and audience miles apart can view the same presentation for a fraction of the cost and time spent if the teacher were to travel around giving the same lecture. Various institutions, for example the Network for Continuing Medical Education (NCME) in New York and the British Postgraduate Medical Federation in London, offer videotapes either in reel or cassette form on a rental basis to medical schools. Several NCME programs have been televised by the CCTV system in the Faculty of Medicine.

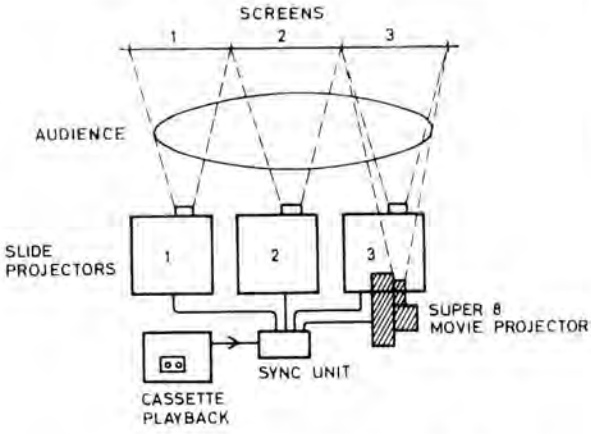
An important asset of CCTV systems is the capability of instant replay of a recording. An event, such as a teaching session or a psychiatric interview, can be recorded and immediately replayed for discussion. Although CCTV has a lot to offer as a medium in education, it is expensive to set up a system which will exploit its potentiality.

(f) *Super 8 mm films* have been used extensively for educational purposes having the advantage of being cheap to produce. Film loops, each illustrating a single topic such as the technique of venepuncture, lumbar puncture or vaccination, are encased in plastic cartridges which can be repeatedly played without the need to rewind or rethread the projector reducing damage to the film. It is possible to add a

sound track to the film making the loop a complete learning package. Loop-film learning packages have been produced and are currently being used experimentally in the Faculty of Medicine (*Chan*, **1971**).

A more recent development of the Super 8 mm film is the Programmed Individual Presentation (PIP) system described by Wittich and Schuller (1973). The film is placed in a cassette and the narration is recorded on a separate audio cassette on which a separate track controls the speed of the film. The film can be run at normal speed, slowed to show motion in extended time, or stopped at a single frame for longer narration. This system, although allowing flexibility in the design of a learning package, is expensive and requires expertise to produce.

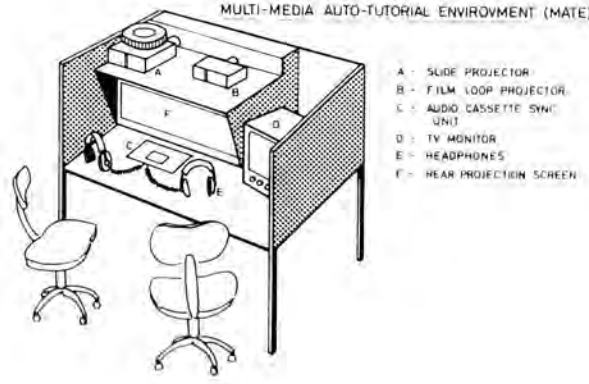
(g) Combination of the above media systems can be used for certain presentations and specially designed for high audiovisual impact on the audience or high affective power. A set-up for a *multi-media multi-screen* presentation is depicted in Fig. 5. This employs three slide projectors and one movie projector which are synchronized by a control (or "sync") unit, with a cassette playback machine supplying the audio component. With this system it is possible to illustrate different aspects of a topic simultaneously or with two slides showing descriptions and the movie illustrating these.



MULTI-MEDIA, MULTI-SCREEN SET-UP

(h) The *multi-media auto-tutorial environment* (MATE) provides the student with playback or monitor equipment for viewing and listening to learning packages. One such design is shown in Fig. 6. The MATE has also been called a "structured learning and teaching environment" (SLATE) or more simply an audiovisual carrell.

Planned as a replacement for or supplement to formal classroom teaching, MATEs have been widely used in medical and nursing schools in the United States and Britain. In the Faculty of Medicine, University of Malaya, MATEs are being used on an experimental basis. However, in order to utilize this multi-media system effectively, there must be a sufficient number of programs or packages produced, purchased or rented for the students. A media production unit should be at hand to develop programs to fulfil "local" needs, and the technical maintenance services must be available to ensure full function at all times.



Implications

With the availability of these media systems, the role of the educator in the allied health sciences will probably change from being a "teacher" in the traditional classroom sense to that of a "creator of learning situations" and a "co-ordinator of media systems". In this situation, teaching (i.e. the transmission and dissemination of knowledge, skills and attitudes) will not be aimed only at the level of the average student in the class, but will cater for the learning styles of each individual student by making available learning packages utilizing alternative media systems. This will mean that most students in the class will be able to master the subject matter presented in a way that is most *effective for himself*. "Mastery learning" (Bloom, 1968) will then be achieved and academic wastage in terms of failure or drop-outs should be cut to a minimum.

Acknowledgements

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*The Early Detection of Unsuspected Carcinoma of Cervix in Malaysia by Exfoliative Cytological Screening

by Prof. T. A. Sinnathuray and *Prof. K. S. Lau*

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CARCINOMA OF the cervix is the commonest cause of death from cancer in women in most countries of the world, and the pattern for Malaysia is no exception. It was 50 years ago, in 1923, that Papanicolaou (1943) began a comprehensive study of vaginal smears in normal and pathological women, and from these studies he realised that it was possible to detect desquamated cancer cells of the uterus by the screening of vaginal smears. He published his first paper in 1923 (Papanicolaou, 1943), but he was unable to convince the clinicians or pathologists of those days that vaginal cytology could in any way be useful in the earlier detection of carcinoma of the uterus. The value of exfoliative cervical cytological smear screening programmes in the early detection of unsuspected carcinoma of the cervix has now been firmly established, to justify the provision of such programmes within the national health services of a country.

Methodology

An exfoliative cervical cytological cancer screening service, based upon the Papanicolaou technique, has been provided for the patients of the Obstetrical & Gynaecological Unit of the University Hospital, University of Malaya, Malaysia since the inception of the Unit in March 1968. Initially, all patients who attended the Obstetrical & Gynaecological Unit, irrespective of their ages, had vaginal and cervical cytological smears taken. This was done so as to teach our medical undergraduates this investigatory procedure, and it was made possible by the fact that the cytology screening unit of our Pathology Department was initially able to cope with all the patients that we screened. However, after the first year (1968) of running, the rapid increase in patient turn-over in the Obstetrical & Gynaecological Unit had made it necessary to restrict the screening service to high risk women, aged 25 years and over.

The technique of smear-taking was as follows: One end of the wooden spatula dipped into the secretions of the posterior vaginal fornix was smeared onto one end of a clean glass slide. The squamous-columnar area of the cervix was firmly scraped by the other end of the wooden spatula and smeared onto the middle portion of the same glass slide; and finally, a cotton wool swab from the endocervical canal was taken and smeared onto the other end of the same glass slide. The smeared slide was immediately fixed by immersing it into a bottle containing alcohol-ether solution. The fixed smear was subsequently stained in the laboratory by the standard Papanicolaou staining technique and screened for the presence of malignant cells.

Patients, from whom a positive smear is obtained, are admitted to the gynaecological ward of the Hospital for further investigations. Smears are repeated, and if these confirm the previous findings, usually a "cone-biopsy" of the cervix is taken for thorough histological examination. Treatment depends upon the histological findings – radiotherapy, Wertheim's Hysterectomy, or a combined attack in the case of the invasive Stage I lesions, and usually hysterectomy for the pre-invasive lesions.

*Paper read by first author at the 8th Singapore-Malaysia Congress of Medicine held in Singapore in July 1973.

Results

The experience of the cervical cancer screening programme over a 5-year period from March 1968 to February 1973 inclusive, and covering a total of 11,283 obstetrical and gynaecological patients, that were screened by exfoliative vaginal and cervical smears are evaluated and presented.

In Table I is presented the annual breakdown of all obstetrical and gynaecological patients that were screened, over the 5-year period of March 1968 to February 1973, together with the respective "Pick-up" rates for unsuspected carcinoma of the cervix. The large number of patients (2,727 patients) screened, together with the low "Pick-up" rate of 0.5% for the 10 month-period of March to December 1968, is because of the fact that all patients, attending the Unit were screened, without any prior selection. The high "Pick-up" rate of 1.6% for 2-month period of January to February 1973 is a chance distribution and not representative of the entire study. The average "Pick-up" rate for the entire study is 0.7%.

Table I
University of Malaya
University Hospital
"Pick-up" Rates on Annual Breakdown of All Obstetrical and Gynaecological Patients Screened for the Five-Year Period — March 1968 to February 1973

Year	No. of Patients Screened	No. of Un-suspected "Positives"	"Pick-up" Rates
1968 (March to Dec.)	2,727	14	0.5%
1969	1,711	18	1.1%
1970	1,889	11	0.6%
1971	2,015	19	0.9%
1972	2,561	7	0.3%
1973 (Jan. to Feb.)	380	6	1.6%
Total for 5 years	11,283	75	0.7%

In Table II is presented the break-down of "Pick-up" rates in the ante-natal patients by age-groups for the 5-year period. Except for the small group of 221 patients in the "40 to 49 years" age-group, where the "Pick-up" rate was atypically high (0.9%), the "Pick-up" rates for all other age-groups and for the whole of this sample was very low (0.2% to 0%). This is not surprising, as these ante-natal patients represent the relatively healthy members of the Malaysian community. There was no "Pick-up" in the age-group "under 25 years".

Similar study for the post-natal patients of this Unit is presented in Table III. The total patients in this post-natal group is very small (less than 2% of entire sample) ,and hence not representative for critical evaluation. The overall "Pick-up" rate amongst the 193 patients is 1.0%. The reason for the very small number of post-natal patients screened in this study is that most obstetrical patients would have already been screened during their ante-natal period, and these represent the small number of unbooked obstetrical patients. Again, there were no "Pick-ups" in the age group "under 25 years".

Table IV represents the combined results that have been presented in Tables II and III, and shows the "Pick-up" rates in all obstetrical patients by age-groups for the 5-year period of study. It is worthy of note that there were no "Pick-up" in obstetrical patients under 25 years of age, and the "Pick-up" rate for the total obstetrical patients (all ages) is very low (0.2%).

The "Pick-up" rates for all the gynaecological patients by age-groups in the study are presented in Table V. There are again no "Pick-ups" in the "under 25 years" age-group. However, in contrast to obstetrical patients, there is a 0.2% (2 out of 937 women screened) "Pick-up" rate in the "25 to 29 years" age-group. The "Pick-up" rates in the gynaecological patients, aged 30 years and over, are relatively high, 0.8% to 1.8%. The overall "Pick-up" rate for the total gynaecological patients is also relatively high – 1.0%.

Table VI represents the combined results that have been presented in Tables IV and V, and shows the "Pick-up" rates in the total obstetrical and gynaecological patients by age-groups for the 5-year period of study. There is an apparent steady rise in the "Pick-up" rates with increasing age-groups. The "Pick-up" rates are significantly high (1.4% to 1.8%) in the age groups of 40 years and over.

In Table VII is presented the histological diagnosis of the cervical lesions in the 75 positive "Pick-up" cases in this study. These 75 cases had cone-biopsy studies of the cervix undertaken to establish a histological diagnosis of the cervical pathology. In this study, it is apparent that 89.3% of the cervical lesions are carcinoma-in-situ (intra-epithelial carcinoma of cervix) and 10.7% are (pre-clinical) early unsuspected invasive squamous cell carcinoma of cervix.

The age-group distribution of the cervical lesions in the 75 positive "Pick-up" cases is presented in Table VIII, and the contents of this Table are self-explanatory. A critical evaluation of the 3 "Pick-up" cases in the "25 to 29 years" age group reveals the following:–

Table II
University of Malaya
University Hospital
"Pick-up" Rates in Ante-Natal Patients by Age-Groups for the Five-Year Period March 1968 to February 1973

Age-Groups Studied	Under 25 Years	25 to 29 Years	30 to 39 Years	40 to 49 Years	50 to 59 Years	60 Years & Over	All Ages
No. of Ante-Natal Patients screened	804	797	2,878	221	—	—	4,700
No. of Positive "Pick-ups"	0	1	7	2	—	—	10
"Pick-up" Rate	0%	0.1%	0.2%	0.9%	—	—	0.2%

Table III
University of Malaya
University Hospital
"Pick-up" Rates in Post-Natal Patients by Age-Groups for The Five-Year Period March 1968 to February 1973

Age-Groups Studied	Under 25 Years	25 to 29 Years	30 to 39 Years	40 to 49 Years	50 to 59 Years	60 Years & Over	All Ages
No. of Post-Natal Patients Screened	47	57	80	9	—	—	193
No. of Positive "Pick-ups"	0	0	2	0	—	—	2
"Pick-up" Rate	0%	0%	2.5%	0%	—	—	1.0%

Table IV
University of Malaya
University Hospital
"Pick-up" Rates in All Obstetrical Patients by Age-Groups for The Five-Year Period March 1968 to February 1973

Age-Groups Studied	Under 25 Years	25 to 29 Years	30 to 39 Years	40 to 49 Years	50 to 59 Years	60 Years & Over	All Ages
No. of All Obstetrical Patients Screened	851	854	2,958	230	—	—	4,893
No. of Positive "Pick-ups"	0	1	9	2	—	—	12
"Pick-up" Rate	0%	0.1%	0.3%	0.9%	—	—	0.2%

Table V

University of Malaya

University Hospital

"Pick-up" Rates in Gynaecological Patients by Age-Groups for The Five-Year Period

March 1968 to February 1973

Age-Groups Studied	Under 25 Years	25 to 29 Years	30 to 39 Years	40 to 49 Years	50 to 59 Years	60 Years & Over	All Ages
No. of Gynaecological Patients Screened	442	937	2,600	1,441	643	327	6,390
No. of Positive "Pick-ups"	0	2	20	26	9	6	63
"Pick-up" Rate	0%	0.2%	0.8%	1.8%	1.4%	1.8%	1.0%

Table VI

University of Malaya

University Hospotal

"Pick-up" Rates in Total Obstetrical and Gynaecological Patients by Age-Groups for the Five-Year Period

March 1968 to February 1973

Age-Groups Studied	Under 25 Years	25 to 29 Years	30 to 39 Years	40 to 49 Years	50 to 59 Years	60 Years & Over	All Ages
No. of Total Obstetrical and Gynaecological Patients Screened	1,293	1,791	5,558	1,671	643	327	11,283
No. of Positive "Pick-ups"	0	3	29	28	9	6	75
"Pick-pu" Rate	0%	0.2%	0.5%	1.7%	1.4%	1.8%	0.7%

Table VIII

University of Malaya

University Hospital

Age-Group Distribution of the Cervical Lesions in The 75 "Pick-up" Cases

Age-Groups Studied	Under 25 Years	25 to 29 Years	30 to 39 Years	40 to 49 Years	50 to 59 Years	60 Years & Over	All Years
Intra-Epithelial Carcinoma of Cervix (Ca-in-situ)	0	2	27	26	7	5	67
Early Unsuspected Invasive Squamous Cell Carcinoma of Cervix	0	1	2	2	2	1	8
Total No. of "Pick-up" Cases	0	3	29	28	9	6	75

Table VII
University of Malaya
University Hospital
Histological Diagnosis of Cervical Lesions in The 75 "Pick-up" Cases

Histological Diagnosis of Lesion	No. of Cases	%
Intra-Epithelial Carcinoma of Cervix (Ca-in-situ)	67	89.3%
Early Unsuspected Invasive Squamous Cell Carcinoma of Cervix	8	10.7%
Total	75	100%

1st Case: Eurasian, aged 26 years, para 8, married 10 years, presented in the first trimester of pregnancy with a benign-looking cervical erosion, contact bleeding and a positive Schiller's test. Repeated PAP smears revealed malignant cells. Colposcopy and punch biopsy of cervical lesion revealed a moderately well differentiated squamous cell carcinoma of the cervix on histological examination.

Diagnosis: Carcinoma of cervix Stage I (a). The case was treated by hysterotomy (for pregnancy termination) and full course of radiotherapy. Patient alive and well 5 years later.

2nd Case: Chinese, aged 28 years, para 4, married 9 years, presented at clinic with request for sterilisation. Repeated PAP smears revealed malignant cells. Cone biopsy of cervix confirmed carcinoma-in-situ. Treated by hysterectomy.

3rd Case: European, aged 25 years, para 2, married 3 years, but has had premarital sex for 9 years with both her children born illegitimately. Cervix revealed benign erosion. Repeated PAP smears revealed malignant cells. Cone biopsy of cervix confirmed carcinoma-in-situ. Refused hysterectomy in view of the fact that she had had no children by the present marriage.

Summary and Conclusions

1. The experiences of a cervical cancer screening programme at the University Hospital, University of Malaya, Malaysia over a 5-year period since its inception, from March 1968 to February 1973, and covering a total of 11,283 obstetrical and gynaecological patients, that were screened by exfoliative vaginal and cervical smears, are presented.
2. The overall gross "pick-up" rate is 0.7%.
3. The "pick-up" rate for all obstetrical patients (all ages) is very low – 0.2%, whereas that for all gynaecological patients (all ages) is high – 1.0%.
4. There were no "pick-ups" in the women in the age-group "under 25 years", and the "pick-up" yield in the age-group of "25 – 29 years" was also very low – 0.2%.
5. The "pick-up" yield was significantly high in the women over the age of 40 years – 1.4% to 1.8%.
6. It is recommended that ideally all women, who are aged 25 years and over, should have the benefits of a vaginal and cervical cytological cancer screening service.

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A Review of Radiation Hazards with Special Reference to Diagnostic Radiology

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Introduction

THE QUESTION OF radiation hazards has aroused public interest recently, as a result of publicity in the local press and the international controversy surrounding the French nuclear tests in the South Pacific. In view of the increasing clinical applications of ionising radiation, it is also important that doctors should have more than a casual knowledge of its potential dangers. It is felt therefore that a brief review of the subject will be timely and of general medical interest.

Exposure to radiation is by no means a new environmental hazard, since man has constantly been exposed to natural background radiation, both from cosmic rays and from radioactive material in the ground. But it is with 'man-made' radiation, and in particular medical radiation, with which we are concerned. A survey by the Medical Research Council of Britain (1960) revealed that the largest contribution to man-made radiation came from diagnostic radiology. This is not at all surprising because of the widespread availability of diagnostic radio-logical facilities and the frequent indications for their use.

For many years it has been known that radiation can produce deleterious effects in man. In the early days following the discovery of x-rays, the hazards of radiation were not appreciated and no precautions were taken to reduce occupation exposure. For instance, it was common for radiologists to test their x-ray beams by interposing their hands between the tube and a fluorescent screen (Stern and Lewis, 1970). This highly dangerous practice sometimes led to intractable skin burns and years later to malignant growths. Kerley (1961) analysed the causes of death amongst the early x-ray matyrs and reported that the great majority died from chronic radio-dermatitis and secondary malignant change. Other studies (Court Brown and Doll, 1957; MacMahon, 1962) have shown that radiation may induce leukaemia.

Biological Effects of Ionising Radiation

These may be broadly divided into: (1) somatic effects, i.e., those which directly affect the irradiated individual and (2) genetic effects, i.e., the effects on germ cells which may be transmitted to the progeny of the irradiated individual.

(1) Somatic Effects

Somatic effects may be acute or delayed.

(a) *Acute Effects*

These follow exposure to high doses and are manifest within a few weeks of the exposure. The effects are dose-dependent. The most sensitive change is a reduction in the lymphocyte count, which may occur with 25 rads of whole body exposure. Symptoms of the acute radiation syndrome become apparent with doses above 100 rads. Other effects include skin reactions, epilations, temporary sterility, and depression of the bone marrow. The lethal dose for man is in the range of 400 to 800 rads delivered to the entire body, death occurring from irreversible damage to the blood-forming organs (400 to 1200 rads), intestinal gangrene (1200

to 2000 rads) and central nervous system injury (above 2000 rads). These acute effects have been observed mainly in nuclear accidents and explosions, and will not occur with diagnostic x-ray exposure, where the absorbed doses range from a few millirads to perhaps 10 rads limited to a small part of the body.

(b) *Delayed Effects*

These may occur years after a single exposure to a large dose (as in nuclear accidents) or after chronic exposure to repeated smaller doses (as in occupational exposure). Delayed somatic effects include: (i) the induction of cancer; (ii) the production of developmental anomalies in the foetus; (iii) a non-specific reduction in life span; (iv) other effects, such as cataracts.

(i) (i) *Induction of Cancer*

A wide range of experiments with animals and observations on man provide convincing evidence that ionising radiation can cause cancer (International Commission on Radiological Protection, 1966). The most detailed studies relate to the induction of leukaemia.

Leukaemia

Studies of atomic bomb survivors and of patients irradiated for ankylosing spondylitis have shown that radiation exposure to high doses above 100 rads may result in leukaemia. The induction period has varied from about 15 months to 15 years. Only acute leukaemia and to a lesser extent chronic myeloid leukaemia have been induced in man. It has not been established that leukaemia in either children or adults can be caused through exposure to the small doses used in diagnostic radiology (Webster, 1971). There is however some evidence that leukaemia and other malignancies may develop postnatally after foetal exposure to these low doses (Stewart, Webb and Hewitt, 1958; MacMahon, 1962). The magnitude of the increased risk from leukaemia is indicated by the following figures. The risk of childhood leukaemia before age 10 is 44 per 100,000 in the absence of pre-natal x-rays, and 62 per 100,000 following pre-natal x-ray exposure. Thus about 30 per cent of the childhood leukaemia that develops in children who have been irradiated in utero appears to be attributable to the radiation. A typical foetal dose from a pelvimetric examination in the studies just mentioned was probably 2 to 3 rads. Hence the number of cases of leukaemia per million irradiated foetuses per rad is estimated to be 60 to 90.

There is no conclusive evidence of any relationship between current levels of occupational exposure and leukaemia. A study of causes of death amongst British radiologists (Court Brown and Doll, 1958) revealed no increased incidence of leukaemia or other cancers in those entering radiology subsequent to 1920, when the first radiation protection regulations came into force.

Other Cancers

Radiation is known to cause other malignancies in man. These include thyroid carcinoma following doses of over 100 rads to the thyroids of infants and children (Conti, Patton, Conti and Hempelmann, 1960; Latourette and Hodges, 1959; Saenger, Silverman, Sterling and Turner, 1960); bone sarcoma amongst employees in the luminising industry; bronchial carcinoma amongst cobalt and radium miners who were exposed to radioactive matter in the form of radon; and skin cancers in early radiation workers. In all these instances the exposures involved were well in excess of the present-day diagnostic range.

(ii) *Developmental Anomalies*

The Russels (1952) have shown that in experimental mice doses of 25 rads or more produced demonstrable changes in the foetus. It appears that irradiation before im-

plantation tends to produce death of the foetus; during the period of major organogenesis (2 to 6 weeks in humans) it tends to produce malformations and neonatal death, rather than prenatal death. In man, different abnormalities have been attributed to irradiation. Children exposed to irradiation in utero from the Hiroshima and Nagasaki bombs showed an abnormaly high incidence of microcephaly and mental retardation. Lejeune, Turpin Rethore and Mayer (1960) found a significant excess of heterochromic wedges in the iris of children who had been irradiated in utero. Whether any abnormalities can be produced by doses of the order of those given in the course of diagnostic radiography is uncertain, but caution dictates that any radiation exposure of the maternal abdomen during pregnancy should as far as possible be avoided.

(iii) *Non-specific Reduction in Life-span*

In addition to causing death from cancer there is some evidence that radiation may have a non-specific effect in reducing the life-span of experimental animals, exposed to large doses. But there is conflict of opinion about whether this effect is produced with lower doses, given either acutely or spread out over many weeks. Human data bearing on the problem are few. Court Brown and Doll (1958) in their study of British radiologists found no evidence of shortening of life span. Other studies quoted by Henry (1969) have shown that in fact radiologists have a somewhat increased longevity as compared with either physicians as a whole or the general population. In the light of experimental evidence, this observation may not be entirely fortuitous and may have rather interesting implications. It has been demonstrated in animal experiments that while exposures of more than 10 rads per day resulted in shortening of life span, smaller doses of the order of 5 rads per day led to increased longevity.

(iv) *Other Effects*

Cataracts have been observed following doses of x and gamma rays above 200 rads and a latent period of about 10 years. Interference with skeletal development in children likewise requires large doses beyond the diagnostic range. While gonadal exposures of about 200 rads may cause temporary sterility, those above 600 rads may lead to permanent sterility.

(2) **Genetic Effects**

The genetic risks of radiation, especially from small doses, are much more difficult to evaluate than somatic risks, and the subject is one of great complexity.

The following is a summary of some basic observations in the light of current knowledge.

(1) Radiation can produce mutations in experimental animals. However, no new mutations have been produced.

(2) The relative frequency of various recognised genetic lesions is the same for radiation induced and spontaneously occurring mutations.

(3) 30 to 80 rads is the most probable range of the dose which would double the spontaneous mutation rate in man (doubling dose). Therefore genetecists recommend that the dose to the general population from man-made radiation should not exceed 10 rads per generation.

(4) There appears to be no threshold for the production of mutations, i.e. regardless of how low the exposure level some mutations will be produced.

It is clear that any irradiation to the gonads should be avoided wherever possible, or when dictated by clinical necessity, kept to the absolute minimum.

Summary of Radiation Hazards from Diagnostic Radiology

From the data we have considered, the hazards from diagnostic radiology can be summarised as follows:

(1) Irradiation to the unborn foetus can lead to leukaemia and other childhood malignancies.

(2) Foetal exposure in early pregnancy may be associated with developmental anomalies.

(3) Pre-conceptional irradiation may produce genetic damage in the children subsequently born. Gonadal irradiation of males may also carry a very small risk of genetic abnormalities in their progeny.

(4) There is no conclusive evidence of a relationship between diagnostic radiation received postnatally and development of malignant disease or shortening of life-span, in the irradiated individual.

Radiation Hazards in Perspective

While we should all be aware of the possible harmful effects of radiation, any discussion of radiation hazards may be misleading if due emphasis is not also given to the beneficial effects of many procedures that involve radiation exposure. The hazards of radiation should also be considered in relation to other man-made environmental hazards such as atmospheric pollution, automobile accidents, drugs, chemicals, and cigarette smoking. No one would seriously suggest that the use of x-rays and other ionising radiation in medicine should be banned because of their potential dangers. For it is beyond dispute that the appropriate medical use of radiation in diagnosis and therapy far outweigh the hazards, and indeed modern medical care would be inconceivable without proper radiological facilities. What is important is that there should be adequate control and supervision of all radiation sources, adequate protection of staff and patients, and not least a proper understanding on the part of doctors of the indications and limitations of various radiological procedures.

Control of Radiation Sources and Protection of Staff

Detailed recommendations and procedures have been laid down by international bodies such as the International Commission for Radiological Protection, the International Atomic Energy Agency and the World Health Organisation, with regard to maximum permissible doses, safety standards for equipment, medical surveillance of radiation workers and other protective measures. These are mainly of interest to those who have administrative responsibility for radiation protection in institutions and are beyond the scope of our discussion.

Protection of the Patient — The Role of the Medical Practitioner

It is primarily the responsibility of doctors to safeguard the patient from the over-enthusiastic or inappropriate use of radiation, particularly in diagnostic radiology. The role of the radiologist in education, in ensuring high standards of safety and quality in radiological techniques, and in being vigilant against unnecessary or ill-advised requests for radiological investigations is obvious. But the co-operation of his other clinical colleagues is equally important, and the routine observance of a few elementary precautions can be of tremendous help. It is suggested that every doctor should ask himself the following questions before referring any patient for an x-ray examination.

(1) Is the examination essential to the management of the patient? In considering this, special care should be exercised in the case of pregnant patients, and in examinations of the abdomen, pelvis and hips where some gonadal irradiation is inevitable. If the answer to the question is no, the examination can only rarely be justified. Exceptions to this are: (a) chest radiographs for routine medical examinations and (b) skull x-rays following head injury which may be required for medico-legal purposes.

(2) What is the most appropriate examination in the light of the provisional clinical diagnosis? In case of doubt, one should never hesitate to consult one's radiological colleague. Providing adequate clinical information on the request form will also enable the radiologist to decide whether the procedure requested is indicated, and if not to suggest an alternative. This inter-departmental communication should be encouraged and will help to ensure that the best diagnostic information is invariably obtained for each radiation exposure of the patient.

(3) In the case of young female patients, is the patient pregnant. The referring clinican is in the best position to ascertain this, as inquiry into the last menstrual period could be easily included as part of the routine medical history. There appears to be a case for observing the 'ten day rule' (Rugh, 1968; Hoare, 1968). This states that all radiation exposures of the pelvis of the female of reproductive capacity should be limited to the first 9 or 10 days after onset of menstruation, unless such exposure is of immediate importance for proper medical diagnosis or therapy. In this way the exposure of an unrecognised pregnancy during the period of greatest radiosensitivity can be avoided.

Conclusion

(1) The risks from diagnostic radiology are small but it is wise to assume that any radiation, no matter how low the dose, is potentially harmful, especially in its possible genetic effects.

(2) Irradiation of the unborn foetus is particularly hazardous and should be avoided except in the presence of over-riding clinical indications.

(3) Although all reasonable precautions should be taken to see that patients are not unnecessarily irradiated, one should not forgo a radiological examination whenever this is judged after due consideration to be in the best interests of the patient.

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Some Clinical Problems of a Phychiatric Day Centre

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Synopsis

Some clinical problems related to a Psychiatric Day Centre are discussed. These problems include difficulty in getting suitable patients, dealing with the suicidal patient, the acting-out patient, the problem of dependency, and the need for family involvement. Some aspects of their management are included.

Introduction

THE ORIGIN AND further development of the Day Hospital has been well described by many authors (Bierer, 1951, 1959, 1961; Harris, 1967; Craft 1959; Farndale, 1961; Freeman, 1970).

A working definition of a day hospital is necessary, in view of the many diverse ways in which the day hospital has developed. A department of Health Report (1969) suggests that: "A day hospital is a special unit set apart for the use of patients who attend the hospital other than as out-patients but who return home at night."

A 'day centre' is generally considered to be a facility which provides occupation and social support for the handicapped (including the elderly) on a long term basis (Freeman, 1970). In Britain the day centres are mainly operated by local authorities or voluntary organisations.

As will be evident from what follows, the Psychiatric Day Centre of the Department of Psychological Medicine, University of Malaya, functions more as a day hospital than as a day centre.

This paper reports on the experiences gained, and some of the clinical problems encountered, in the management of day care patients.

The Setting

Physically, the Psychiatric Day Centre is sited in the rehabilitation building of the University Hospital, Kuala Lumpur. Administratively it comes under the Department of Psychological Medicine, University of Malaya. The staff of the centre consists of a consultant psychiatrists, one lecturer, a medical officer, two nurses, a psychologist and an occupational therapist, a psychiatric social worker and an attendant. Except for the nurses and attendant, the rest of the staff have clinical and academic responsibilities in the University Hospital.

The therapeutic milieu included psychotherapy, both group and individual, a work programme, group community meetings, staff meetings, special projects, group activities like singing, ball games, swimming and social gatherings. The doctors also prescribe somatic treatment when necessary.

Facilities are available where, when a day care patient requires in-patient treatment he can be admitted to the psychiatric wards of the University Hospital.

Before admission to the Day Centre, the patient is assessed by the lecturer and/or medical officer of the Day Centre, and usually his family is brought into the picture immediately, the programme of the Day Centre explained to them, and their responsibility discussed.

The goals for each patient, and his progress, are discussed during staff meetings held once weekly. In addition, after each group psychotherapy session, a post-group discussion is held by the staff members. Once every two weeks, all the patients are discussed with the consultant psychiatrist.

Some Problems and their Management

Difficulty in getting suitable patients:

The Day Care Centre has been in existence now for 1½ years (at the time of writing). To date, the patients treated at the Centre totalled 75. The patients' characteristics are:

Diagnosis	*No. of Patients*
Schizophrenia	35
Depression	20
Personality Disorder	9
Obsessive compulsive neurosis	4
OrganicBrain Disease	3
Organic Brain Disease	3
Mental Subnormality	1
Adolescent adjustment reaction	3
Total	75

It is relevant here to discuss the admission policy of the Day Centre and the criteria of suitability of day care patients. Broadly speaking, the aims of admission are:–

1. To provide an alternative to in-patient treatment for
   (a) patients who would otherwise need to enter hospital, thus maintaining daily contact with home and other interests.
   (b) patients already in hospital curtailing their stay, and providing "partial hospitalization" prior to their discharge back into the community.
2. To provide concentrated outpatient treatment for certain patients for whom in-patient treatment is inadvisable, but for whom treatment at out-patient clinic is too brief and infrequent.

The criteria of suitability are:

1. The patient should be able to travel to the Day Centre without special arrangement, alone, or accompanied by relatives.
2. The patient should not be too ill i.e. too psychotic, disturbed, or too weak physically.
3. There should be positive indication for treatment and/or rehabilitation. The Centre does not function as a custodial centre simply to keep chornic patients occupied.
4. The patient should not live too far away.
5. He should be able to converse in English.
6. Relatives should be willing and dependable.

These criteria have not been too rigidly enforced, especially when the case for attendance seemed particularly strong.

Why, then is there difficulty in getting patients?

A major factor is that doctors do not refer enough patients to the Centre. There may be several reasons for this. It may be that they are unaware of the existance of the Day Centre, (this applies especially to general practitioners). It may be that, although they are aware of its existance, they are not clear about its functions or not convinced that it serves a useful purpose. It is our opinion that psychiatrists are not making full use of the Centre. It is noteworthy that those doctors working in the Centre refer far more cases than do the others, having come to consider all their in-patients and out-patients as potential candidates. This point was previously made in the original account of the Bethlem and Maudsley Day Hospitals (Harris, 1957). Other factors include patients who are otherwise suitable for attendance at the Centre, but who live too far away, or patients not conversant enough in English for group psychotherapy. Finance does not seem to be much of a problem; there are occasional patients who require financial help in the form of bus fares, but they soon earn enough from projects to pay their way.

This problem of shortage of suitable patients may be alleviated by bringing to the attention of more doctors, the existence and functions of the Day Centre; this may be done by publications in local journals, by the activities of the local Mental Health Society, and by correspondence with the egneral practitioners.

The Suicidal Patient

In a Centre such as this, the staff is always on the look-out for the suicidal potential in the patient. Unlike the ward milieu, where the patient may find some difficulty in attempting suicide and the staff being aware of it, here in the Day Centre there are relatively fewer restrictions, and more opportunities. The staff made it a point to encourage the depressed patient to talk about any suicidal ideation he had, either in the group setting or individually. If the patient is felt by the staff to be a suicidal risk, he is immediately admitted to the ward. There had been four such patients at the time of writing. We have had one patient, a schizophrenic who successfully committed suicide while attending the Centre, by jumping from the 13th floor of the hospital building during lunch break. We have had to guard against the natural inclination to 'tighten' up the Centre, and increase the restrictions on the patients subsequent on such an incident; we are aware that to do so may destroy the therapeutic milieu we are trying to create.

The Acting Out, Disruptive Patient

This type of patient will be a problem in any setting, and is so in the Day Centre. We have had three such patients so far. One was a schizophrenic male, with marked sociopathic traits, who would concentrate on the female patients, make advances with a sexual overtone to them; he would find out where they lived, and visit them uninvited. When rejected by them, he would speak disparagingly about them to the others, and set out to irritate them in petty ways. The second patient was an obsessive-compulsive girl, aged 28, who had very low self-esteem, and who unconsciously set out to frustrate and quarrel with every body, so that she was rejected by them; thus confirming her view that she was bad – this being her repetition compulsion. The third patient was a juvenile delinquent who lied, bullied the patients, and acted out a lot. With such patients, limit-setting must be clear and unambiguous. All forms of physical assault on another patient or staff is forbidden, and this fact is made clear to the patient at the onset. Any infringement of this rule means expulsion from the Centre.

Emphasis is placed on using the group setting as the main therapeutic agent. Any socially unacceptable act or misbehaviour by a patient is brought into the open, and discussed in the group. The group members decide what should be the appropriate behaviour, and what punishment, if any, should be imposed. Reward, in the form of praise, social approval, etc. is not forgotten. The patients' responsibilities in the Day Centre are also discussed e.g. carrying out roster duties like washing up after lunch. Beahviour modification using the group as the main medium has been fairly effective, but one does not forget the premise that, if a patient is too disruptive in the setting of the Day Centre, he will have to be discharged.

Problem of Dependency, Institutionalization

The finding that some 10 patients grew to be dependent to a somewhat pathological degree on the Centre proved as a surprise. One would have expected otherwise, as the patient returns home to his family daily, and remains in contact with the community outside. The majority of these patients who showed pathological dependency ties with the Centre are those with passive-dependent personality disorders; there were also a few schizophrenics. Usually each of them forms an attachment to a staff member or another patient and then placidly and contentedly attended Day Centre day in and out. Dependency problems are frequently discussed in group meetings, and patients are encouraged to talk about their fears of abandonment and of rejection; these patients are gradually weaned from the Centre, and their attendance is tailed off gradually. Some patients showed an exacerbation of their symptoms when told of their coming discharge, and may enlist the aid of their family to plead with the doctors for an extension of stay. Others, in anger, stopped coming before the required date of discharge; efforts are always made to ask them to return for discussion of their feelings in the group setting. Where indicated, some patients are followed up by one of the doctors working in the Day Centre but as a routine they are followed up by the referring doctor.

Family Involvement

Perhaps more than with in-patients, the family is encouraged to be involved in the management of day patients. As the outset, during the assessment of suitability of the patient for Day Centre attendance, the doctor interviews the family, either the spouse, parents, or other responsible relatives. An assessment is made of the family interactions, strength or weaknesses, and any pathology in the family. The line of management of the patient was explained to family members, and their role was emphasised. We have come against some resistance from family members about getting involved in patient management. Sometimes the resistance is outright and overt e.g. the father refusing to accept that the patient is sick; often it is covert, and acts as deterrent to the patient's progress. Family therapy is often an integral part of many patients' management, and many relapses of schizophrenic patients can be attributed to family pathology.

In the setting of the Day Centre, the family acts as a valuable source of information on patient's progress and behaviour at home, and when there is a discrepancy between his behaviour in the centre and at home, this looked into. Regular classes for overprotective mothers of patients have been held and these have proved to be beneficial, both to the mothers and to the patients.

Discussion

There is a paucity of articles in the literature on clinical problems of the Day Hospital or Centre. On the other hand, there is a plethora of reports about the activities of this or that day hospital, with the emphasis usually on the good work being done, and the advantages of the Day Hospital over in-patient service hospitals.

One of the few articles specifically describing problems in the Day Hospital is the one by Chasin (1967), who wrote about the day hospital of the Massachusetts Mental Health Centre in North America. He listed as problems the difficulty in evaluating the day-patient without the continuous observation possible in the ward, the need to maintain limits, and the suicidal patient. While an American Day Hospital is not strictly comparable to a Malaysian one, still it is apparent that some of the problems are similar viz the suicidal patient, and the need to set limits. Unlike the American study, we do not find any difficulty in evaluating the patients and this must be attributed to the close contact we maintain with the patient's family.

The Ross Clinic day hospital, Aberdeen, Scotland, suffered at times from attempts to contain and treat a preponderance of patients with personality and character disorders, whose aggressiveness and acting out tendencies submerged the more positive attitudes of other patients and occupied a great deal of staff time and energy (Morrice, 1973).

Chasin also pointed out that day hospitalization can be a very agreeable arrangementfor the relatives and patients; the patient may use the Day Centre as a way of passing the time, an excuse for not working, or to get away from the family. For the family, the Day Centre may be a "baby-sitter", there is less guilt aroused in the relatives as compared with the patient being committed to a mental institution. This we have found to be true in some patients, and we have tried to minimize it by definite goal-setting for each patient, with definite time limit in which to achieve the goal.

Finally, the difficulty we experience here in getting suitable patients does not appear to occur in the American study.

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Oral Carcinoma in the Chinese Female

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Summary

ORAL CANCER appears to be the second commonest histologically confirmed malignant tumour in West Malaysia. The Chinese female has the lowest incidence of oral carcinoma (4.1%). The authors report on 36 Chinese female patients. The M:F ratio was 3.5:1. The peak incidence was between 50-69 years. The tongue (33.3%), buccal mucosa (22.9%), gingiva (14.6%) and palate (12.5%) were involved in descending order of frequency. In the tongue the anterior two-third was more commonly involved and the margins and dorsum were the commonest sites. Oral carcinoma presented clinically as: (1) an ulcer (2) an exophytic growth and (3) a swelling. It would appear desirable to consider carcinoma in the differential diagnosis of abscesses of the maxillary sulcus region in adults. Grade I carcinoma fromed 60.0%, Grade II 25.7% and Grade III 14.3%. A comparison is made with oral cancer studies in China, Finland, United States, South Africa and Australia.

Introduction

West Malaysia has a multiracial population of 9.4 million people. The Chinese female forms 17.7% and the Chinese male 18.5% of the total population (Chander, 1972).

Oral cancer appears to be the second commonest histologically confirmed malignant tumour in West Malaysia. The Chinese female has the lowest frequency of oral cancer as a per cent of all cancers (Fig. 1), (Ungku Omar-Ahmad and Ramanathan, 1968).

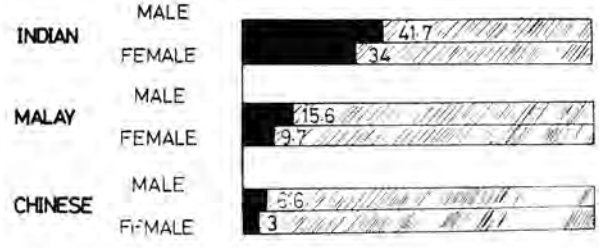

Fig. 1

Frequency of oral cancer as a per cent of all cancers by race and sex in West Malaysia, 1961-63 (after Ungku Omar-Ahmad and Ramanathan, 1968).

Between 1967-72, the Division of Oral Medicine and Oral Pathology, Institute for Medical Research, Kuala Lumpur reported in all 1031 histologically confirmed squamous cell carcinoma cases. Of these 31.3% occurred in the Indian male, 30.8% in the Indian female, 10.7% in the Malay female, 9.3% in the Malay male, 13.8% in the Chinese male and 4.1% in the Chinese female. The buccal mucosa (43.2%), tongue (15.1%), gingiva (14.2%), palate (13.1%), lips (6.4%) and floor of the mouth (3.8%) were involved in descending order of frequency.

Ramanathan and colleagues (In Press, a) have explained the lowest incidence of oral carcinoma in the Chinese female as being due to the least frequency of oral habits in them. Moreover even in those who have oral habits, generally the daily intensity and duration of habit is comparatively minimal.

There seems to be a void in the information on oral carcinoma in the Chinese in the English language medical literature. Studies of oral cancer in the Chinese and comparative studies with the other racial groups in Malaysia as well as with oral cancer groups in other parts of the world would be valuable.

Material and Methods

This study was based on the records of the Division of Oral Medicine and Oral Pathology, Institute for Medical Research, Kuala Lumpur and for the years 1967-72. Only histologically confirmed squamous cell carcinoma cases and patients reported for the first time were included in this study. In all 36 Chinese female patients were reported. For the anatomical charting of oral carcinoma the topographical classification of Roed-Petersen and Renstrup (1969) dividing the oral mucosa into 41 well-defined regions was used (Fig. 2). For purposes of histological grading, the WHO Histological Typing of Oral and Oropharyngeal Tumours was used (Wahi *et al*, 1971).

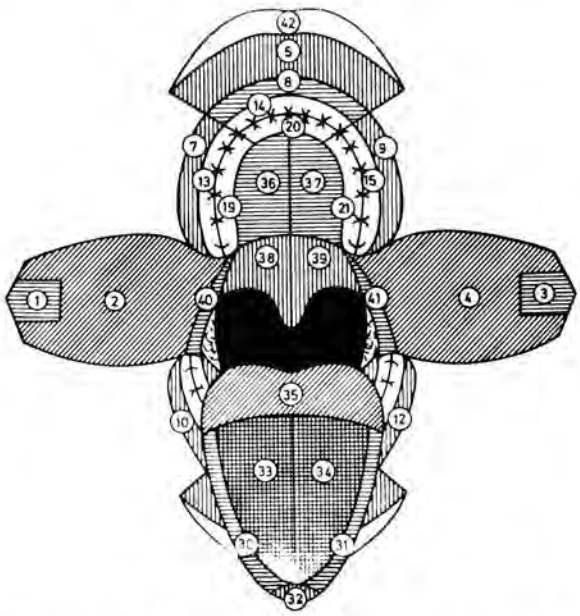

Fig. 2
Topography of the oral mucosa dividing it into 41 well defined regions (after Roed-Petersen and Renstrup, 1969).

Findings

Sex Ratio

Between 1967-72 oral carcinoma was reported in 127 Chinese males (Ramanathan and Lakshimi, In Press, b) thus giving a male: female ratio of 3.5:1.

Age Distribution

The youngest patient was 30 years old and the oldest patient was 88 years. For the group the average age was 61.9 years and the median age was 61.0 years. The peak incidence was between 50-69 years (Table 1).

Table 1

Distribution by Age Groups of 35 Chinese Female Cancer Patients

Age in years	No. of patients	%
0 – 29	0	0
30 – 39	1	2.9
40 – 49	3	8.6
50 – 59	12	34.3
60 – 69	10	28.5
70 – 79	6	17.1
80 – 89	3	8.6
TOTAL	35*	100.0%

*the age of one patient was unknown.

Anatomical Sites

The tongue (33.3%) was the commonest site of involvement (Table 2). The upper half of the mouth was more commonly involved than the lower half. The right and left halves of the mouth were about equally affected.

Clinical Features

In descending order of frequency the clinical presentations were (1) an ulcer with raised indurated margins (45.7%); (2) an exophytic growth (34.3%); (3) a swelling (17.1%) and (4) schirrous infiltration (2.9%). Carcinoma presented as an ulcer most commonly on the tongue followed on the buccal mucosa whereas it presented as an exophytic growth most commonly on the buccal mucosa followed on the tongue. Carcinoma presented as a swelling most commonly in the maxillary buccal sulcus. The only case of carcinoma which presented as a schirrous infiltration involved the tongue.

Symptoms

Sixteen patients complained of an ulcer, 12 of a growth, 8 of pain, 7 of a swelling, 4 of bleeding, 1 of difficulty of speech, 1 of a white patch and another patient of a red raw patch.

Table 2
Distribution of Oral Cancer by Anatomical Site in 36 Chinese Females

Anatomical site		Total	%
Tongue			
Margin —	left	4	
	right	2	
Dorsum —	left	4	33.3
	right	3	
	NOS	1	
Base		1	
NOS		1	
Buccal mucosa			
	left	6	
	right	5	22.9
Alveolar Process			
Upper —	left	4	
	anterior	0	
	right	2	
Lower —	left	0	14.6
	anterior	0	
	right	1	
Hard Palate			
	left	1	
	right	4	12.5
	Palate NOS	1	
Buccal groove			
Upper —	right	1	
Lower —	left	2	8.3
	right	1	
Lips			
Upper		2	
Lower		1	6.3
Floor of mouth			
	right	1	2.1
Total		48*	100.0

*Oral cancer extended to more than one site in some patients.

NOS = Not otherwise specified.

Duration

Table 3 shows the duration of signs and symptoms at the time of diagnosis. In 43.8% of patients the duration was less than three months, in 31.2% of patients the duration was between three months and one year and in 25.0% of patients the duration was over one year.

Table 3
Duration of Signs and Symptoms in 32* Chinese Female Cancer Patients

Duration	No. of patients	%
<3/12	14	43.8
3/12 — 6/12	6	18.7
6/12 — 1 yr.	4	12.5
1 yr. — 2 yrs.	5	15.6
>2 yrs.	3	9.4
TOTAL	32*	100.0%

*For 4 patients this information was inadequate.

Histological Grading of Carcinoma

The histological grading of carcinoma is shown in Table 4. Sixty percent of cases had Grade I, 25.7% had Grade II and 14.3% had Grade III carcinoma.

Table 4
Histological Grading of Squamous Cell Carcinoma in 35 Chinese Female Cancer Patients

Histological grading	Total No. of cases	%
Grade I	21	60.0
Grade II	9	25.7
Grade III	5	14.3
TOTAL	35*	100.0%

*In one patient the biopsied tissue was inadequate for histological grading.

Discussion

The relative frequency of oral cancer as a per cent of all cancers was 3% for the Chinese female and 6.6% for the Chinese male (Fig. 1). Reviewing the six most frequent carcinomas in different parts of China, Hu and Yang (1959) found that oral carcinoma ranked sixth in relative frequency for males (2.5%) and was unplaced for females in Peking; fourth for both males (6.4%) and females (4.4%) in the Second Medical College in Shanghai; fifth for males (8.3%) and unplaced for females in Fukien; and was unplaced for both males and females in Tientsin, Tsinan, Canton, Kwangsi and Sian.

The comparative figures from the Shanghai First Medical College were 5.3% for the male and 1.5% for the female (Anon, 1959). In Finland oral cancer in the female formed 2.3% of all cancers in 1953 and 2.2% in 1961. The relative figures for the Finnish male were 5.8% in 1953 and 5.3% in 1961 (Sainio and Calonius, 1967).

Oral cancer occurred 3.5 times more often in the Malaysian Chinese male than in the female. The Shanghai First Medical College data gave a male : female (M : F) ratio of 1.9 : 1. In Finland oral cancer occurred 2.7 times more often in the male than in the female. Chierici and colleagues (1968) recorded the M : F incidence for their oral cancer patients in the United States as 4 : 1 for the years 1941-64 and for the more recent period of 1955-64 the ratio was slightly less than 3 : 1. Comparing these two respective periods the percentage of women smokers increased from 54% to 75% thus accounting for the increasing ratio of F : M oral cancer patients.

The M : F ratio for the South African whites was 3.7 : 1 and for the South African negroes it was 6.4 : 1 (Shear, 1970). In Australia oral cancer occurred 3.7 times more often in the white male than in the female (Tan, 1969). The Chinese do not chew betel-quid. The predominance of male

oral cancer patients is similar to other non-betel-quid chewing population groups.

The peak incidence for the Chinese female was between 50-69 years (62.8%). The majority of patients (88.5%) were between 40-79 years. Three percent were younger than 40 years and 8% were older than 79 years. The peak incidence for the South African white males and females and for the negro males was in the sixth decade. The majority of patients (88%) were between 40-80 years. Six percent were younger than 40 years and 5% were older than 80 years.

In Australians the peak incidence of oral cancer was between 60-69 years for males (25.5%) and for females the peak incidence was in the seventh (24.2%) and eighth decades (24.8%) of life. About 80% of the patients were between the ages of 40-80 years. Only 11.8% of the patients were below 40 years and 8.4% above 80 years. In Finland the peak incidence was between 70-80 years for both sexes.

The tongue (33.3%) was the commonest site of involvement in the Chinese female. The buccal mucosa (22.9%), gingiva and alveolar process (14.6%) and palate (12.5%) were involved in descending order of frequency. In the tongue the anterior two-third was more commonly involved than the posterior one-third and the margins and dorsum of the tongue were the commonest sites of malignancy.

In both the South African white female and negro female the tongue was the commonest site of involvement. Whereas in the South African white male the lips, floor of the mouth and tongue were involved in descending order of frequency. The site most often involved in the South African negro male was the tongue followed by the floor of mouth and gingiva.

In Chierici and colleagues (1968) American study the tongue (42%) and floor of mouth (20%) were the commonest sites of involvement in the female. In the male however the lips (33%), tongue (27%) and floor of the mouth (13%) were involved in descending order of frequency.

In Australians the lips (62.1%), tongue (12.3%), floor of the mouth (5.7%), gingiva (3.7%) and palate (3.1%) were involved in descending order of frequency.

In Finland the lips and tongue were the commonest sites. The contribution of lip cancer to all male oral cancer cases in 1953 and 1961 was 58.5% and 64.9%. The female had much lower relative lip cancer frequencies namely 14.6% and 13.5% in 1953 and 1961. Both sexes presented higher lip cancer frequency among rural than urban population. The high incidence of lower lip cancer in the white male has been attributed to prolong exposure to actinic rays of the sun. Such exposure is an occupational hazard of farmers. In contrast lip cancer was the second lowest site (6.3%) in the Chinese female. Of all oral cancers, carcinoma of the tongue accounted for 7.3% and 5.1% in the Finnish male and 12.6% and 9.9% in the female in 1953 and 1961 respectively.

In two Chinese female patients where cancer presented as a swelling, a provisional clinical diagnosis of alveolar abscess of the maxillary molar sulcus region was made. It would therefore appear desirable to consider oral carcinoma in the differential diagnosis of maxillary molar sulcus swellings in adults. It is also probable for some of the carcinomas presenting as buccal sulcus and palatal swellings to have originated from the maxillary antrum.

Acknowledgement

We wish to thank the Editor, Medical Journal of Malaysia for the use of Fig. 1 and the Editor, Acta Odontologica Scandinavica for the use of Fig. 2.

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Chronic Ectopic Pregnancy – A Challenge in Diagnosis

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Introduction:

TO MOST DOCTORS the mention of an ectopic pregnancy conjures up visions of a very pale and severely shocked patient in pain being wheeled into the casualty. This classical and acute picture of a ruptured ectopic pregnancy, presenting a straightforward diagnosis is however not common, though it receives the most attention. The majority of ectopics present in a far less dramatic fashion. An analysis of the cases of ectopic pregnancy seen at this hospital during 1972 showed that in fact 66% presented as chronic cases. Further the symptoms may be so varied and present in such a quiet way that the diagnosis is often missed. It becomes therefore a real challenge for the doctor to make a correct diagnosis.

In this paper a number of cases of chronic ectopic pregnancy are presented to show the varied symptomatology.

Case Reports:

Case 1: C.A.N. female Chinese 41 years presented with vomiting and mucous diarrhoea for three days and was admitted as a case of gastroenteritis. She had no history of amenorrhoea but two days previously when her period was due she had started to bleed, and this was assumed to be a normal period. On examination she was not in shock but a little pale. There was some tenderness over the abdomen though very slight and no rebound tenderness was present. On vaginal examination the typical "prune juice" bleeding was seen and tenderness was present in the left lateral fornix. At laparotomy a leaking left tubal pregnancy with a small haematocele in the Pouch of Doughlas was seen. The gastrointestinal symptoms were due to irritation of the rectum by the haematocele.

Case 2: A.B.K. female Malay 32 years presented with severe abdominal pain and retention of urine for one day. Three days prior to this she had been seen at the casulty department of another hospital with retention of urine and was catheterised and sent home. She gave a definite history of fainting when she had the abdominal pain. No amenorrhoea or vaginal bleeding was present. On examination she was not in shock and her general condition was satisfactory. The bladder was grossly distended and 800 ml of urine was obtained by catheter. A tender soft mass was present in the pelvis and the pregnancy test was negative. At laparotomy a large pelvic haematocele was seen with a leaking tubal pregnancy. The cause of the retention of urine was due to pressure from the haematocele on the urethra.

Case 3: Y.H.M. 30 years Chinese female was admitted as a twisted ovarian cyst. She gave a history of bleeding per vaginum for 3 weeks since the start of her period, and left sided colicky abdominal pain. On specific questioning there was a history of fainting. On examination she was in very good condition, with mild tenderness on the left side of the abdomen. The vaginal bleeding was however typical – prune juice in colour. On pelvic examination a small tender mass was present in the left adnexa. Pregnancy test was negative. At laparotomy a partially extruded left tubal pregnancy with an intact sac was seen.

Case 4: Z.M.L. 30 years Malay female was admitted with abdominal pain for three weeks. She had missed her periods for two months and this was followed by bleeding and pain. She was treated as a septic abortion at another hospital and following a D & C the bleeding had stopped but the pain had persisted. Direct questioning elicited the fact that she had felt like fainting on a number of occasions. On examination her condition was satisfactory and the abdomen was soft. A firm mass about the size of a 14 week pregnancy was present and on vaginal examination this mass was tender. At operation an old ruptured ectopic pregnancy with a haematocele surrounded by dense adhesions was found.

Case 5: C.H.F. 36 years Chinese female presented with severe right hypocondrial pain radiating to the back. She had fainted initially but subsequently had no further attacks. She was admitted with an initial diagnosis of biliary colic. Urine examination showed the presence of bilirubin. Pregnancy test was negative. There was no vaginal bleeding and the period was delayed by six days. On examination her condition was good and abdominal and pelvic examination elicited hardly any tenderness from the patient. However during pelvic examination the patient said that she felt like fainting. In view of the characteristic history a laparotomy was done and a leaking right tubal pregnancy was found. The tracking of blood under the right diaphragm explains the cause of the patient's symptoms.

Discussion:

As can be seen from the above case histories, the symptoms of chronic ectopic pregnancy may be so varied that confusion occurs with a variety of other abdominal conditions e.g. gastroenteritis (Case 1), retention of urine (Case 2), ovarian cyst (Case 3), septic abortion (Case 4), and biliary colic (Case 5). Diagnosis can therefore be elusive.

In considering the symptoms, the only constant and by far the most important one is *abdominal pain.* This pain is almost always associated with *fainting.* In fact fainting is the second most important symptom of ectopic pregnancy. Any female patient in the reproductive age group who presents with a combination of these two symptoms should be strongly suspected of having an ectopic pregnancy irrespective of any other contradictory symptoms or signs.

The other symptoms namely amenorrhoea and vaginal bleeding are so variable and inconstant, that no certain reliance should be placed on them. In many cases amenorrhoea and vaginal bleeding are absent. However if vaginal bleeding does occur, the colour is so characterestic – "prune juice" like – that one can even make, on occasions, a spot diagnosis of ectopic pregnancy. Another important feature of this bleeding is that it is *persistent* and continues without stopping even if a D & C is done.

Physical Signs:

The only reliable physical sign is pelvic tenderness on vaginal examination. However, physical signs can be most inconspicuous even in a patient who has a fair quantity of blood in the peritoneal cavity. The author has been impressed by the fact that particularly in young healthy patients, abdominal tenderness, rebound tenderness, and tenderness on vaginal examination can be completely absent even when subsequently at laparotomy it was shown that there was a good amount of blood in the pelvic cavity. This is particularly noticeable in Chinese patients. Negative physical signs should not therefore be allowed to overrule the characterestic symptoms. In this one agrees entirely with Jeffcoate's (1967) contention that 'diagnosis of an ectopic pregnancy rests almost entirely on the history and physical signs are of secondary importance'. The more thoroughly one goes into the history, keeping in mind the ever possibility of an ectopic in any woman of child bearing age, the less one is likely to miss the diagnosis.

Special Investigations:

Pregnancy Test: The results of pregnancy testing are so variable in ectopic pregnancy, that as an aid to diagnosis it is practically worthless. The result of the test seems to depend very little on the state of the ectopic pregnancy and even in an unruptured case quite often the test is negative.

Examination under Anaesthesia: Since on physical examination the all important sign is pelvic tenderness and examination under anaesthesia completely obscures it, one can only condemn this procedure as useless. Further it may be positively dangerous as bleeding may be provoked as a result of the examination.

Posterior Colpotomy: Although this procedure is very popular in certain countries, it is unreliable. In any case of pelvic congestion e.g. infection, blood may be drawn and conversely even in the presence of a clotted haematocele one may get negative findings.

From the above it can be seen that the less one depends on the accessory aids, the better it is, in arriving at a correct diagnosis.

Aetiology:

Although most text books emphasise the importance of tubal disease and blockage as being the chief cause of ectopic tubal pregnancy, one is impressed by the completely normal looking tubes of many cases of ectopic pregnancy at operation. Although tubal disease is certainly a factor, it has perhaps been over emphasised.

A condition which has received little attention is transmigration of the ovum. An ovum discharged from one ovary may become fertilised in the peritoneal cavity and migrate across the pelvis to enter the other tube on the opposite side. By this time the ovum is overdeveloped and has acquired a trophoblastic shell which encourages it to implant in the tube, and so a tubal pregnancy results. Transmigration can be presumed to be the cause if the corpus luteum is in the ovary on the opposite side to that of the tubal pregnancy. To test this hypothesis the corpus luteum was specifically looked for during laparotomy. In 24 cases so observed, the results were as follows:–

Corpus luteum on the same side as the tubal pregnancy – 10

Corpus luteum on the opposite side to the tubal pregnancy – 14(58%)

In all these cases there was no evidence of any pelvic infection and the tubes appeared perfectly normal. Therefore in a significant proportion of ectopic pregnancy – 58% in the above series – the cause is most likely due to transmigration of the ovum and not to any defect or blockage of the tube.

Conclusion:

Chronic ectopic pregnancy, presenting as it does a very quiet and varied clinical picture, can be most difficult to diagnose. Diagnosis is aided by paying the most careful attention to the history. Physical signs are of secondary importance only. The so-called special investigations are more often a hindrance in arriving at a correct diagnosis. Transmigration of the ovum seems to be a significant factor in the causation of an ectopic pregnancy.

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Mucocele of the Appendix

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MUCOCELE OF the appendix is that condition where the appendix contains a jelly-like material, pseudo-mucin (Johnston, 1954). It was first described by Rokitansky in 1842. This was followed by the description by Virchow in 1863 of a case. It is a relatively uncommon condition and Woodruff and McDonald (1940) reported that it occurred in 0.3 per cent of appendicectomies over a period of 24 years at the Mayo Clinic in the United States of America. Wesser and Edelman (1961) calculated that there have been more than 600 cases of mucocele of the appendix reported in the literature. Its incidence varies from 0.1 to 0.3 per cent of all appendicectomies (D'Annreuther, 1936; Mayo and Fauster, 1932; Weaver, 1937).

Case Reports

Case 1

A 33 year old Malay man was admitted to the District Hospital, Telok Anson, Perak, complaining of vomiting and constipation for 3 days. He had noticed a swelling in the abdomen for the last 2 years and this followed an attack of acute pain in the right iliac fossa. On examination he was looking ill and had a pulse of 90 per minute, blood pressure 140/70 mm.. Hg. His temperature was 100 degrees Farenheit. The abdomen was distended and the bowel sounds markedly hyperactive. There was a tense tender swelling 2 inches to the right of and below the umbilicus. A diagnosis of bowel obstruction due to a strangulated Spigelian hernia was made. Four hours after admission, the patient was operated upon by the author. It was found that the swelling was due to a mucocele of the appendix. The fundus of the appendix had become attached to the abdominal wall and had ruptured so that a mucoid substance lay immediately beneath the skin. The appendix was fifteen centimetres long and five centimetres wide and was very thin-walled. Inside the appendix was a colourless mucinous material. A fine probe could not be passed from the lumen of the appendix into the lumen of the caecum. The other intra-abdominal organs were normal. Appendicectomy was done and the patient made an uneventful recovery post-operatively. The histological study of the appendix wall revealed features of chronic inflammation.

Case 2

A 28 year old Malay man was admitted to the General Hospital, Kuala Lumpur on 26.11.72 for an interval appendicectomy. He had previously suffered from an appendicular abscess for which drainage was performed on 24.10.72. Appendicectomy was done on 27.11.72 and at operation a mucocele of the appendix was found. There were plentiful adhesions around and involving the appendix.

Discussion

Animal experiments, mainly in rabbits, have shown that three factors are involved in the development of a mucocele of the appendix, namely, obstruction of the lumen of the appendix, continued secretory activity of the appendiceal mucosa and sterility of the contents of the appendix (Cheng, 1949; Grodinsky and Rubnitz, 1941). The usual cause of obstruction is inflammatory stricture (Chan, 1965). Other rarer causes include neoplasms of the appendix, faecal concretion, multiple polyposis,

natural diverticula of the appendix, implants of endometriosis with stricture and neoplasms of the caecum (Hilsabeck et al, 1952; Muir, 1931; Shemilt, 1949; Topping, 1937). Wangensteen (1937) suggested the possibility of functional obstruction due to a sphincter mechanism at the appendix base since he found resistance to the flow into the caecum of fluids injected into an appendicostomy.

Clinically, mucocele of the appendix can present in four ways (Wesser and Edelman, 1961). Firstly, most cases present as acute appendicitis. Secondly, many cases are associated with chronic abdominal pain and a palpable mass. In the third group, there are no symptoms and the condition is discovered on routine physical examination or at autopsy. Finally, there is a fourth group of cases which present with bizarre or complicated courses, such as "appendiceal abscess", mucous fistula after surgery, right iliac fossa pain with intestinal obstruction or diarrhoea due to pseudomyxoma peritonei. The author's first case belongs to this fourth group. Other complications include volvulus of the appendix (Chan, 1965), diverticulosis of the appendix and ileo-caecal intussussception (Adelman and Teplich, 1955; Ward-McQuaid, 1949; Watkins, 1963).

Pseudomyxoma peritonei is the most important complication of mucocele of the appendix and is characterised by the presence of masses of colloid in the peritoneal cavity. The colloid lies either free or enclosed in membranous adhesions. It is identical in composition with the contents of the mucocele. It may be widespread in the peritoneal cavity or localised to the region of the appendix. It appears that the initial cause of pseudomyxoma peritonei is perforation of an appendix distended with a mucocele, usually through a diverticulum of the organ. However, it is not certain how the large quantities of pseudomucin which are present in pseudomyxoma peritonei arise. Three theories have been postulated, namely:—

1. The peritoneal pseudomucin results from the continued discharge of this material from a perforation of the mucocele. Against this theory is the fact that pseudomyxoma peritonei may recur after appendicectomy and finally lead to the patient's death (Johnston, 1954).
2. The presence of pseudo-mucin in the peritoneal cavity stimulates the serosal cells of the peritoneum to secrete an identical substance. Trotter (1910) believed that the cells lining the peritoneum could become columnar by metaplasia but he thought that their reaction was that of a foreign-body peritonitis and limited to the formation of enclosing adhesions.
3. The most likely theory is that mucus-secreting cells escape into the peritoneal cavity through the perforation in the appendix. Upon becoming implanted on the peritoneal surface, these cells continue to secrete pseudo-mucin. Although such cells are difficult to demonstrate histologically in the peritoneal pseudo-mucin, the theory is supported by the work of Grodinsky and Rubnitz (1941). They injected the contents of mucoceles into the peritoneal cavities of animals and produced progressive pseudomyxoma peritonei. However, if the contents of the mucocele were first passed through a Seitz filter to remove the pseudo-mucin secreting cells, pseudomyxoma peritonei did not develop.

Woodruff and McDonald (1940) studied 146 cases of mucoceles of the appendix and divided them into two groups. In the smaller group, the mucosa of the appendix is hyperplastic due to papillae covered with large columnar cells containing hyperchromatic nuclei. This is regarded as a Grade 1 adeno-carcinoma and perforation of the appendix in such cases leads to the dissemination of malignant cells in the peritoneal cavity and a diffuse progressive pseudo-myxoma peritonei. In the larger group of cases, the appendiceal mucosa consists of a single layer of columnar cells. Rupture of such a mucocele leads to the localised variety of pseudo-myxoma peritonei which does not recur after appendicectomy.

Pesudo-myxoma peritonei may also follow rupture of a pseudomucinous cyst of the ovary. In the female patient, there may be present a concomitant pseudo-mucinous cyst of the ovary and for this reason the ovaries should always be examined when operating upon a mucocele of the appendix in a woman. Eden (1912) described a patient in whom an appendix mucocele was found two years after an operation for a ruptured pseudo-mucinous cyst of the ovary. Bailey (1916) and Ries (1924) reported patients with concomitant ovarian pseudo-mucinous cyst and mucocele of the appendix. These patients also developed pseudomyxoma peritonei. These concomitant ovarian and appendiceal lesions are usually complicated by pseudomyxoma peritonei (Johnston, 1954) and it is possible that one lesion results from trans-coelomic implantation of mucus-secreting cells released by perforation of the other lesion, although it is not clear why ovary and appendix are alone selectively involved. Willis (1952) states that the probable sequence of events is rupture of a primary ovarian pseudo-mucinous cyst which causes colloid and cell spread in the subserous tissues and finally involves the appendix leading to a mucocele of the appendix. In the case reported by Hentz

(1932), both the appendix and ovary were involved but there was no pseudo-myxoma peritonei. He suggested that the pseudomucin-producing cells passed from the ovary to the appendix by lymphatic channels.

The material in a mucocele of the appendix is pseudo-mucin which is a jelly-like gluco-protein distinguishable from mucin by reduction tests and by staining with muci-carmine (Johnston, 1954). Its presence may be due to abnormal secretion by the mucosa or, since all grades of staining and reduction reactions occur, the change from mucin to pseudomucin may be a gradual extracellular one. In mucoceles present for a long time, the pseudomucin may become inspissated and calcification of this may lead to the formation of a large stone in the appendix (Bunch, 1945).

The treatment of mucocele of the appendix is appendicectomy. During the operation in a female patient, both ovaries should be inspected for a concomitant pseudomucinous cyst of the ovary and oophorectomy done if necessary. When pseudomyxoma peritonei is present, as much of the pseudomucinous material is removed as is possible. When this complication is present, Byron et al (1966) recommend that the peritoneal cavity be also irrigated with mechlorethamine (Nitrogen mustard) whilst Johnston (1954) advises post-operative radiotherapy to the abdomen. The irradiation destroys the mucus-secreting cells in the peritoneal cavity. It is not advisable to drain the peritoneal cavity as there is then a tendency to secondary infection.

Summary

Two personal cases of mucocele of the appendix seen and treated by the author are presented. The incidence and aetiology of the condition is discussed. The most important complication is pseudomyxoma peritonei. Treatment of the mucocele is by appendicectomy and the pseudomyxoma peritonei is treated by intraperitoneal mechlorethamine, manual evacuation and post-operative radiotherapy. The four types of presentation of appendiceal mucocele are also discussed.

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Rapid Intravenous Induction Followed by Self-Applied Cricoid Pressure and Rapid Intubation

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Summary

A COMBINATION OF methods is described for rapid and safe intubation and is suitable for the anaesthetist working alone or without competent help. It is for the prevention of regurgitation during induction of anesthesia by a provision for rapid induction followed by self-applied cricoid pressure during the dangerous phase of 'going-under' up to the time just prior to laryngoscopy. Rapid laryngoscopy and intubation follows in the safe period. The author finds it suitable for use in obstetric anaesthesia and in other patients predisposed to regurgitation.

The factors predisposing to regurgitation are well described (Dinnick, 1967). These include food and fluid in the stomach or a distended stomach (Robson, 1959); incompetent cardia (e.g. hiatus hernia, Dinnick, 1961); presence of a gastric tube; intermittent positive pressure ventilation (a potent factor); raised intra-abdominal pressure such as during suxamethonium fasciculations; lowered intra-oesophageal pressure such as active respiration during induction and respiratory obstruction (O'Mullane, 1954); cough, and straining (Marchand, 1957) and hiccoughing; relaxation of the cricopharyngeus muscle; light general anaesthesia; and hypotension which may provoke vomiting in twilight states.

Thus the patient, for emergency anaesthesia, unlikely to regurgitate is one who is well preoxygenated, rapidly and safely induced and rapidly and completely paralysed in the horizontal position and neck flexed.

The technique described is suitable for the emergency anaesthetist working alone or without the assistance of a competent nurse or technician, a situation sometimes happening at night and weekends; and in district hospitals.

Details of Methods

The patient, preferably premedicated with an antiemetic, e.g. hyoscine 0.3 mg is placed on the tilting operation table (Wylie, 1956, Steel, 1961). Normally other patients are often anaesthetized on the trolley in the Induction Room. Anti-emetics also reduce post-operative sickness (Riding, 1963).

The stomach and oesophagus may be, if deemed necessary, be decompressed or emptied by passage of a No. 10 oesophageal tube, or by inducing rapid gastric emptying by use of metoclopramide (Maxolon; in obstetric anaesthesia, McGarry, 1971) in the absence of an acute abdomen or bowel obstruction. The gastric tube is removed (and re-inserted later) because its presence tends to trip the integrity of the cardiac sphincter and interferes with cricoid compression (Sellick, 1961).

The patient is checked for any possibility of difficult intubation, which may be present especially in the obstetric patient, who may also have a functional hiatus hernia (Dinnick, 1961, 1967). Equipment for management of failed intubation (bougie, stylets, etc) should always be ready.

Preoxygenation

This is an integral part of this technique. Preoxygenation by the patient herself holding the mask or by a harness (later removed) for 5 minutes, which

is also the time spent in checking and getting anaesthetic equipment ready and setting up a free flowing drip, with intravenous placement of plastic cannula under local analgesia.

Complete denitrogenation results in an alveolar po2 of about 673 mmHg, arterial po2 of 640 mmHg and 100% arterial saturation. It obviates the need for intermittent positive pressure ventilation for at least one minute; and reduces the hazard of an episode of hypoxia.

Preoxygenation for 2 minutes may not be sufficient in the presence of lung diseases, leaks around the mask etc.

The suction apparatus, preferably high flow suction is checked.

Position of the Patient for Intubation

The patient lies supine in a horizontal position most suitable for intubation, that is, with the neck flexed and head extended and steadied on a head ring.

In Sellick's manoeuvre (Sellick, 1961), the patient is placed in the tonsillectomy position with the head and neck down and extended to stretch the oesophagus and to minimise its lateral displacement; at the same time assist the flow of regurgitated fluid away from the larynx should it occur. But this position is not ideal for easy laryngoscopy and rapid intubation.

In the horizontal position, extension at the atlanto-occipital joint creates a small pocket or reservoir in the posterior part of the oro-pharynx, laryngo-pharynx and post-nasal space, in which any regurgitated material collects after the self-applied cricoid pressure is lifted (Figure II).

In the horizontal position, the long axis of the trachea and larynx is inclined at an angle of 25° – 30° downwards and backwards; and the upper third of oesophagus and crico-pharyngeus 20 – 25°. A head down slope of more than 30° is necessary for gravity to protect the laryngeal aditus. Laryngoscopy and rapid intubation may be difficult in this steeply inclined position for the unfamiliar anesthetist.

A method of intravenous induction for rapid intubation: The intravenous agent, such as for Caesarean section, is methohexitone (1 – 1.5 mg/kg) while thiopentone (3 – 4 mg/kg) is for other patients. Intravenous titration of the sleep dose is not done.

Half the amount of methohexitone (for example, total dose of 70 – 100 mg) premixed with 0.6 mg atropine is drawn up in a 10 ml syringe, while the remaining half dose is mixed with 75 to 100 mg of suxamethonium (freshly prepared), in another 10 ml syringe.

The first half of the barbiturate is rapidly given through the rubber injector of the tubing to give a bolus effect and flushed; immediately the premixed methohexitone-suxamethonium mixture follows

Fig. I

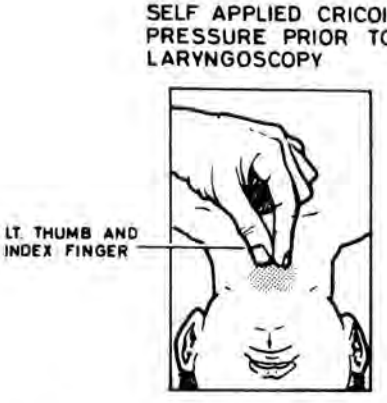


Fig. II

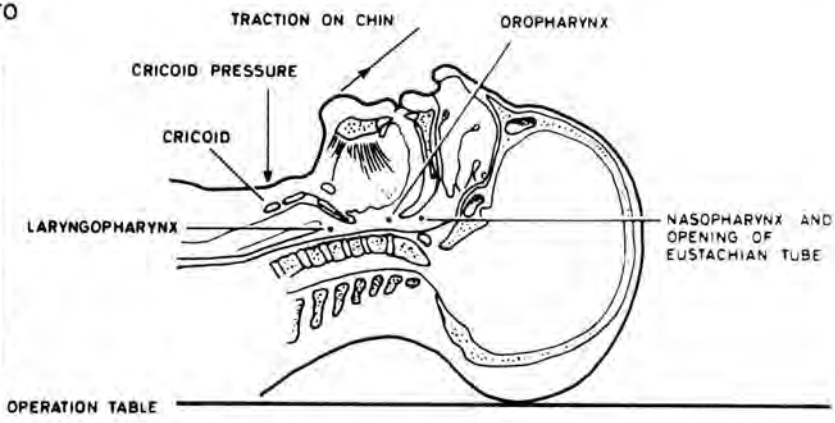
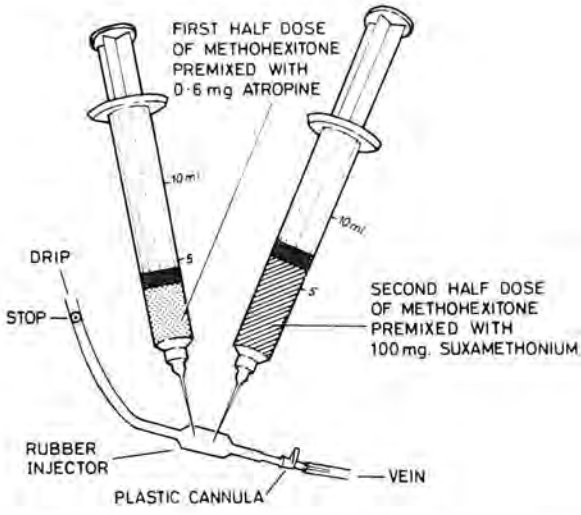


Fig. II

A SAGITTAL SECTION THROUGH THE HEAD AND NECK TO SHOW THE SUBDIVISIONS OF THE PHARYNX. POSITION SUITABLE FOR EASY INTUBATION, SELF APPLIED CRICOID PRESSURE AND CHIN TRACTION.

(Figure IIIa). The dose of suxamethonium is large to avoid the danger of a partial neuromuscular blockade. The disadvantages of I/V methohexitone are hiccoughing and hypotension (though the hypotensive index is less than that of thiopentone). Note that injections are given rapidly without fear of affecting the foetus in obstetric anaesthesia; too slow the mother may not become unconscious and yet paralysed.

Fig. III a



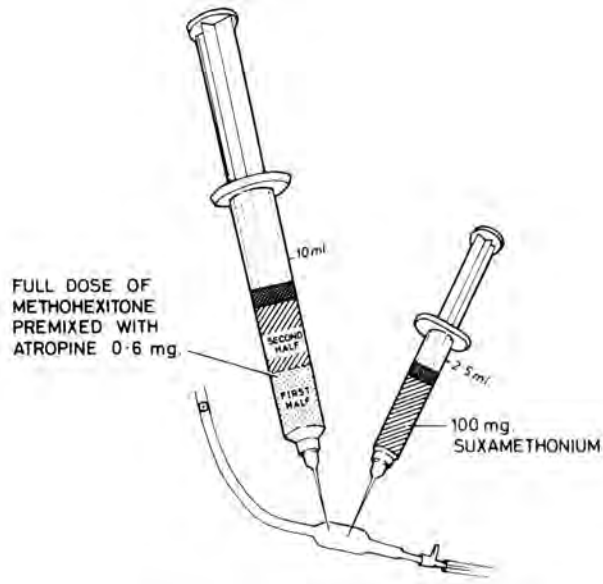
METHOD OF RAPID INTRAVENOUS INDUCTION

Alternatively (Figure IIIb) thiopentone or methohexitone premixed with 0.6 mg atropine is drawn up in a 10 ml syringe and suxamethonium 75 to 100 mg in a 2.5 ml syringe. Half the barbiturate is given and drip flushed; immediately the remaining half is injected simultaneously with the suxamethonium to get a premixed effect. The drugs are flushed into the venous circulation by the drip full on to produce a "crash" or "short gun" induction.

The initial half of the barbiturate will tend to minimize the chance of the patient being aware of the suxamethonium fasciculations (Khawaja, 1971 a, b) whether they be pleasant or unpleasant. The occurrence of scoline pains is a price to pay for producing rapid and profound relaxation. This method of injection has the effect of a premixed barbiturate-suxamethonium mixture, which has been established to produce conditions for rapid intubation (Khawaja, 1971a, b).

In the conventional method, suxamethonium is injected after the barbiturate in which complete relaxation comes only after 45 – 65 secs. The high

Fig. III b



ALTERNATIVE METHOD OF INJECTION

risk period is about 45 secs stretching from the 20th second (loss of consciousness) to the 65th second; and will be much longer if the needle comes out of the vein during the change over of syringes.

With the author's method, the period between loss of consciousness and total paralysis is shortened to about 20 to 25 seconds from about the 20th-25th second to the 40th or 45th second.

Hypotension (in short-gun or crash-induction, Bonica 1967) is uncommon except in the presence of hypovolaemia; and supine hypotensive syndrome of late pregnancy (Scott, 1968), latent or overt, which can be obviated by the left lateral tilt top table technique. The hypertensive response to intubation is a feature of methohexitone-suxamethonium intubation sequence.

Method of Self-applied Cricoid Pressure prior to Laryngoscopy.

After the completion of the injections, the anaesthetist commences to apply increasing (moderate and then firm) pressure on the cricoid which has been previously identified and marked or ringed with a ball-point. At this time, the patient is just becoming unconscious if it is less than 20 seconds after injection. He uses the left thumb and index

finger, whilst his right hand applies traction on the chin in an upward and cephalic direction to tauten the oesophagus, and to avoid fumbling with the cricoid cartilage (Fig. I, II, Fig IV).

Fig. IV

Cricoid pressure manoeuvre can withstand reflux pressures of up to 100 cm H20 (Sellick, 1961). Once the fasciculations are over and profound relaxation achieved in about 40 – 45 seconds, the anesthetist abandons the cricoid pressure, and commences the conventional laryngoscopy and endotracheal intubation.

It is probable that the mean intra-gastric pressure, normally 7 cm H_2O (in elective surgical patients, Spence 1967) or twice that in pregnancy, would have returned to normal after an initial rise, even to more than 20 cm H_2O, as a result of suxamethonium fasciculations (Anderson 1962; Roe 1962). The cardia is probably competent when the intragastric pressure does not exceed 20 cm H_2O. With coughing and straining it can reach in excess of 60 cm H_2O (Spence 1967).

Regurgitation is very unlikely during laryngoscopy in the completely paralysed and flaccid patient, since the normal cardiac sphincter is unaffected by general anaesthesia, relaxants or autonomic drugs, (O'Mullane, 1954).

If regurgitation occurs, reliance is based on tipping and efficient suction of the pharynx. Avoid intermittent positive pressure ventilation as this is a sure way to pump regurgitated material into the trachea, and to churn up more vomitus in your way.

This technique of rapid intubation to seal off the airway may be further assisted by use of a pre- and over-inflated balloon of the cuff of the endotracheal tube.

Discussion

By combination of a method of achieving a short injection-intubation time with self-applied cricoid pressure up to the time of laryngoscopy, the hazard of regurgitation and aspiration of vomitus is very distant.

In Sellick's method (Sellick, 1961), cricoid pressure must be exerted by a technician, who must be, albeit easily, taught or has previous experience. Pressure may be applied, though gently, even before onset of unconsciousness. The method allows intermittent positive pressure ventilation through a mask or mouth to mouth. Also posterior displacement of the larynx facilitates, sometimes, intubation. It is contra-indicated in active vomiting such as in the conscious or semi conscious patient.

The author's method relies mainly on preoperative preparation; use of I/M hyoscine as a premedicant; and I/V premixed atropine as an anti-emetic and antisialagogue and to doubly strengthen the cardiac sphincter to withstand pressure from the gastric aspect (Clark, 1962) but does not offer resistance to pressure from above such as ventilation prior to intubation; generous preoxygenation and non-ventilation; a method of rapid intravenous induction akin to premixed barbiturate-suxamethonium technique; self-applied cricoid pressure just prior to or from the onset of unconsciousness till laryngoscopy; laryngoscopy and intubation in the easy position.

The patient can still regurgitate during the short period of laryngoscopy when cricoid pressure has to be lifted. Here the anaesthetist need to perform lightning intubation.

In Sellick's series (Sellick, 1961), release of cricoid pressure after intubation was followed promptly by gastric reflux of gastro-oesophageal contents in 3 cases out of 26 high risk cases.

It has been stated that there is no fool-proof method of prevention of regurgitation and the subsequent aspiration of vomitus into the respiratory tree (Mendelson's or acid-aspiration syndrome, Mendelson, 1946). The ideal anaesthetic for operative obstetrics does not exist (Utting and Gray, 1968). The watch word is great care, competence in preventing regurgitation and commonsense in management should it occur. The anesthetist, often working alone, should develop and use a technique that he is most familar with in a difficult situation.

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Congenital Diaphragmatic Hernia: A Case Report

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The true incidence of Congenital Diaphragmatic Hernia is difficult to be certain about. Publications based on hospital admissions (Gross, 1953; Bonham Carter et al, 1962; Rickam and Johnstone, 1970) seem to indicate an incidence of about 1 in 12,000 live births. According to Butler and Claireanx (1962) the true incidence is in the region of 1 in 1,120 still births and 1 in 4,000 live births. The British Perinatal Mortality Survey (Butler and Claireanx, 1962) showed that this malformation was present in 2,200 of all births and that it comprised 8% of all major fatal congenital anomalies; and also that many of the perinatal deaths with diaphragmatic hernias were grossly premature. It is, therefore, probable that majority of these cases do not get admitted to the neonatal surgical wards for repair.

We have had only one admission during the last 2 years and 10 months and we wish to report our case.

Case Report

Soon after birth, a normally born infant weighing 7lbs was seen to become cynosed on crying. Except for some respiratory rales on the left side of the chest no other abnormalities were detected by the doctor who examined the child first. Nursing the child in an incubator with 30 per cent oxygen did not prove the colour and the condition gradually deteriorated. Every attempt to suck its feeds brought on the cynosis and the frequency of such attacks increased. On examination, we found a fully grown, cynosed and breathless infant. There was minimal expansion of the left side of the chest and auscultation revealed marked intestinal gurgling of the same side. Except for the shifting of the heart to the right, no organic lesion of the heart were detected. A radiograph of the chest confirmed a left sided diaphragmatic hernia (No:1).

Fig. 1
Pre-operative X'ray.

This was an emergency of the first order. An endotracheal tube was inserted and lungs inflated by gentle positive pressure with oxygen. The stomach was frequently aspirated through a nasogastric tube. After wrapping the infant well, the case was transfered to the operation theatre, maintaining the positive pressure ventilation during transport.

The operation theatre had been prepared in advance to receive the infant. Only the air circulation without the air conditioning had been

maintained for sometime. The infant was placed on hot water bottles, and covered with sterile cotton, exposing only the area for the surgical procedure. General Anaesthesia mainly consisted of a combination of muscle relaxation with intermittent suxamethonium and positive pressure ventilation with 50 : 50 mixture of oxygen and nitrous oxide. After a preceding dose of 0.06 mg of atropine sulphate, an initial dose of 0.3 mg of suxamethonium was given intravenously to obtain muscle relaxation. Subsequently, incremental doses of 0.1 mg of suxamethonium was administered whenever relaxation was required. A 10% dextrose drip was set up, and a three way tap interposed between the scalp vein needle and the drip facilitated rapid replacement of lost blood. The pulse rate, peripheral circulatory status and temperature were monitored through out the procedure. The replacement of lost blood was based mainly on subjective estimation in correlation with the circulatory status. Thoracotomy performed through the eighth left intercostal space revealed complete absence of diaphragm, with loops of small intestine and transverse colon filling the space.

The small amount of lung tissue present was resistant to forced inflation and, was probably, hypoplastic. The repair of the defect was achieved by plicating the peritoneum from the posterior to the anterior end and the thoracotomy was closed, leaving a drain. The recovery from anaesthesia was uneventful with the infant maintaining good colour.

Post operatively the infant was nursed in an incubator for two weeks. Clinically, the air entry on the left side gradually improved. Radiograph of the chest (No: 2) taken immediately after the operation showed that the repair had been successful. There was a left sided pneumothorax and minimal return of the mediastinum to normal position. On the tenth post operative day the infant developed breathlessness and radiograph of the chest (No: 3)

Fig. 3
On The Tenth Post-operative Day.

showed gas shadows which seemed to suggest a tension pneumothorax on the left side with marked shift of mediastinum. At a second thoractomy performed under general anaesthesia to exclude the possibility of recurrence we found pockets of pus filling the cavity. The repair was intact and was difficult to be certain whether the lung had expanded or not. Post operatively the infant continued to improve and since discharge on the 28th post-operative day has been followed up periodically. Radiograph of the chest (No: 4) taken two months

Fig. 2
Immediate Post-operative X'ray.

Fig. 4
At The Second Month.

after the surgery shows fully expanded lung on the affected side and the heart in the normal position. By the end of seventh month the child had grown both physically and mentally but the radiograph of the chest (No: 5) showed a gas shadow with shift

Figure 5
At The Seventh Month.

of heart to the opposite side suggestive of a recurrence. We were unable to confirm the diagnosis by screening using contrast medium for the child had died two weeks after the last radiograph had been taken.

Discussion

The most commonly encountered type of abnormality is the hernia through the Foramen of Bochdalek (Rickham and Johnstone, 1970; Bonham Carter et al, 1962). The other types of abnormalities include the absence of diaphragm on one side, and hernias through the Foramen of Morgagni and Para oesophageal openings.

In the newborn the onset of respiratory difficulties at birth is determined by the size of the hernia and the degree of dysfunction of the lungs and nearly always presents as an acute emergency. In contrast, in most of the older children the symptoms and signs are usually gradual in onset and may be referred to the pulmonary, alimentary, or cardiovascular system (Bonham Carter et al, 1962). The moment the diagnois is made nasogastric aspiration must be started to prevent further distension of stomach and intestines, and consequent shift of mediastinum. Positive pressure ventilation through an endotracheal tube must be instituted immediately, taking care not to employ high pressures. If the infant does not respond to these resuscitative measures, tension pheumothorax or mediastinal emphysema must be suspected and appropriate treatment given. The administration of oxygen through a close fitting mask or through an intragastric catheter must be avoided at all cost. It is important that the anaesthetist accompany the infant from the ward to the operation theatre in order to ensure adequate ventilation.

A naked infant ventilated with dry gases in a cold operation theatre rapidly looses body temperature (Cecil Gray and Nunn, 1971). Simple measures like wrapping the exposed areas in sterile cotton and using hot water bottles will have to be resorted to if modern facilities are lacking. New born infants are far less tolerant to blood loss and great care, therefore, must be exercised in assessing the loss and replacing it. In the absence of calorimetric method, subjective estimation of blood loss and the clinical status of the cardiovascular system of the infant will have to be relied upon. It is important to warm the blood before transfusion in order to avoid the complications of generalised hypothermia. Many methods are used in sophisticated centres, but we depend entirely on the heat exchange obtained by immersing the bottle in a waterbath, the temperature of which is kept at 40°C. The importance of prevention of hypoglycaemia in the new born infants, particularly in those suffering from respiratory difficulties, cannot be over emphasised (Cornblath and Reisner, 1966; Cornblath et al, 1966). It is our practice to use 10% dextrose solution pre and post operatively. The problems of post-operative ventilation and lack of expert nursing care can be so acute as to preclude the use of non-depolarising drugs for muscle relaxation in the new born infants, and employ instead, alternative techniques of general anaesthesia.

Older infants of adequate size with few serious associated abnormalities seem to survive better following operation. Gross (1964) reported that the survival rate of children operated upon for diaphragmatic hernia at Boston Childrens' Hospital have fallen drastically, because much younger infants with a much poorer survival rate are now admitted. The survival rate following operation was 100 per cent in infants over 24 hours of age, but it fell to 47 per cent in infant under 24 hours of age. When we saw the infant it was already 16 hours of age and was operated upon within an hour of diagnosis.

At the conclusion of the operation it was impossible to expand the small lung on the affected side, and consequently such an infant was left with a pheumothorax post-operatively (X'ray No: 2). In the course of succeeding days the lung on the affected side had expanded fully (X'ray No: 4), which may be taken as evidence that there was compression atelectasis of the lung rather than true hypoplasia (Bonham Cartel, 1962).

Conclusion

A case of Congenital Diaphragmatic Hernia is described and the relevant literature reviewed. Majority of the infants with this abnormality are either stillborn or die within a few minutes or hours of birth. The presenting symptoms are dyspneoa and cynosis. Control of ventilation and surgical repair of the defect must be undertaken as an emergency procedure. The age of the infant, absence of associated abnormalities, knowledge of pathophysiological processes and meticulours attention to detail are the criteria for the success of neonatal anaesthesia and surgery. The need for close collaboration between those involved in the care of these infants is vital.

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The Pattern of Bacteriological Cultures in a State Laboratory*

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THE PERAK BRANCH OF the Institute for Medical Research (I.M.R.) at Ipoh serves as the Government Clinical Laboratory for all the 13 hospitals in the State of Perak. About a third of the specimens come from the Ipoh General Hospital, about 2 miles away, and the rest from other hospitals in the State, stretching from Parit Buntar in the north to Tanjong Malim in the south, about eighty miles away. I.M.R. Ipoh is also the only place in Perak where bacteriological cultures are done for the hospitals in the State.

The purpose of this paper is to survey the pattern of bacteriological isolates, the sensitivity pattern of the various pathogens and to identify the problems involved in running a bacteriological service for the State with hospitals upon to 80 miles away.

Material and Methods

Information of the various cultures done in 1970 were gathered from the records. Specimens for culture from the various hospitals were received by ambulance, taxi, rail or through the post with considerable delay in some cases.

Urine specimens were sent in sterile plain bottles and a semi-quantitative count (1) of the bacteria content was done using a standard loop delivering approximately 0.004 ml. urine and the growth obtained assessed as to its significance ($>$ 400 colonies) in conjunction with the smear and clinical findings. Swabs were sent in Stuart's transport medium. Blood for culture were sent in liquoid broth, those of suspected typhoid cases in bile salt medium which were kept for 48 hours before innoculation into blood agar and Desocycholate agar (DCA) respectively. Stools of gastroenteritis and suspected typhoid cases were conveyed in selenite encrichment medium and incubated for 24 hours before innoculation into DCA. Stools of "infants" (children below 2 years old) were also innoculated into Blood Agar and Robertson's cooked meat medium besides DCA. Identification of pathogens were by techniques similar to those recommended by Stokes (2). Antibiotic sensitivity was done on lightly stroked plates of Oxoid diagnostic sensitivity test agar using single antibiotic discs. For M. tuberculosis drug sensitivity testing was by the dilution method using H 37 RV as the control organism.

Results

Of the total 11,411 cultures done on various types of specimens, 1,543 or 13.5% were positive for a potential pathogen (see Table 1). Blood and Stool cultures accounted for about 50% of all cultures done but only for about 18% of positive isolations. On the other hand Urine, Pus and Swabs accounted for only 25% of all the cultures done but for 71% of all positive isolates.

Urine Cultures

1,393 cultures (12.2% of all cultures) were done on urine of which 477 (34.2%) were positive (Table 1) or 30.9% of all positive isolates. Of the 916 "negative" urine cultures 309 (22%) were contaminated specimens. From the records, there

*This paper was presented in part at the 7th Malaysia-Singapore Congress of Medicine in Kuala Lumpur on August 1972.

was no significant difference in the pattern of cultures among the various races and between the sexes or in the number of contaminated specimens between males and females. Coliforms were the most frequently isolated organism constituting 62% (297 of 477 positive cultures) of the urine isolates, followed by Staph. aureus (12%), Proteus (8%) and Pseudomonas (7%).

The sensitivity pattern of the various pathogens is shown by Table II. Nearly all of the organisms isolated were sensitive to Gentamycin (Garamycin).

Table I
Distribution of Cultures (1970)

Specimens	Total Number	% Total	Positive Cultures Number	% Specimens	% Positives	Negative Cultures Number	% Specimens	% Negatives
Urine	1393	12.2	477	34.2	30.9	916	65.8	9.3
Pus & Swabs	1471	12.9	620	42.1	40.2	851	57.9	8.6
Throat Swabs & Sputum	1672	14.7	67	4.0	4.4	1506	96.0	16.2
M. tuberculosis	693	6.0	91	13.1	5.9	602	86.9	6.1
Blood	2716	23.8	133	4.9	8.6	2583	95.1	26.2
Stools	3004	26.3	141	4	9.1	2873	95.3	29.1
C.S.F.	462	4.1	14	3.0	0.9	448	97.0	4.5
Total	11411	100%	1543	—	100%	9878	—	100%
% Total	100%	—	13.5%	—	—	86.5%	—	—

Table II
Sensitivity Patterns of 477 Urine Isolates

Antibacterial Drugs	Percentage Sensitive Coliforms (297)	Proteus (39)	Pseudomonas (32)	Staphylococcus (59)	Streptococcus (5)
Penicillin	—	—	—	9	25
Erythromycin	—	—	—	98	75
Cloxacillin	—	—	—	83	60
Ampicillin	56	87	3	88	100
Chloramphenicol	57	69	3	86	60
Streptomycin	42	51	15	59	25
Tetracycline	31	0	3	36	60
Nitrofurantoin	28	3	0	—	—
Sulphatriad	3	0	3	10	0
Cephaloridine	71	72	6	98	100
Septrin	68	46	—	93	—
Neomycin	85	92	81	—	—
Kanamycin	59	88	12	—	—
Polymyxin B	87	15	100	—	—
Gentamycin	100	100	97	100	—
Carbenicillin	—	—	100	—	—

The majority of Coliforms isolated were also sensitive to Polymyxin and Neomycin; Proteus to Neomycin and Kanamycin; Pseudomonas to Polymyxin and Carbenicillin (Pyopen); Staphylococcus to Erythromycin and Cephaloridine (Ceporan) and Streptococcus to Ampicillin (Penbritin) and Cephaloridine. The majority of organisms were resistant to Sulphatriad; Staphylococcus and Streptococcus were resistant also to Penicillin; Coliforms, Proteus and Pseudomonas to Tetracycline and Nitrofurantoin (Furadantin).

Pus and Swab Cultures

This constituted 12.9% of all cultures done (Table I). Of the total 1,471 examinations carried out, 620 (42.1%) were positive; this formed 30.2% of all positive cultures. 52% of pus specimens, 50% ear swabs, 24% vaginal swabs, 17% nasal swabs, 10% eye swabs and 8.3% unbilical swabs were positive. Of the 620 positive isolates, 499 (81%) were from pus specimens. The 851 "negative" cultures included 69 isolates of Staph. albus which were considered as commensuals. Staph. aureus was the most often isolated pathogen constituting 45.5% of all cultures followed by Coliforms (25%), Pseudomonas (14%) and Proteus (13%). Staph. aureus was also the main pathogen isolated from pus specimens and eye swabs.

Table III shows the sensitivty pattern of the isolates. The majority of organisms were again sensitive to Gentamycin and the gram-negative bacilli also to Neomycin. The majority of Coliforms isolated were in addition sensitive to Polymyxin and Kanamycin; Proteus to Septrin (Bactrim), Kanamycin, Cephaloridine and Ampicillin; Pseudomonas to Polymyxin and Carbenicillin; Staphylococcus to Erythromycin, Cephaloridine and Septrin; and Streptococcus to Erythromycin, Chloramphenicol, Penicillin and Tetracycline. The majority of organisms were resistant to Sulphatriad and the gram-negative bacilli also to Tetracycline. The majority of Staphylococcus were penicillin resistant and Pseudomonas were usually resistant to all antibiotics tested except Carbenicillin, Gentamycin, Polymyxin and Neomyxin.

Throat Swabs and Sputum Cultures

1,672 cultures (14.7% of the total cultures done) were performed, of which 67 (4%) were positive for a potential pathogen. 5.6% of throat swabs

Table III

Sensitivity Patterns of 620 Pus and Swabs Isolates

Antibacterial Drugs	Percentage Sensitive				
	Coliforms (153)	Proteus (79)	Pseudomonas (85)	Staphylococcus (282)	Streptococcus (21)
Penicillin	—	—	—	6	86
Erythromycin	—	—	—	98	95
Cloxacillin	—	—	—	96	—
Ampicillin	74	19	2	71	—
Chloramphenicol	60	84	6	89	95
Streptomycin	65	75	29	68	—
Tetracycline	48	6	5	66	86
Sulphatriad	10	0	0	7	—
Cephaloridine	59	89	4	99	—
Septrin	84	95	2	98	—
Neomycin	94	95	94	—	—
Kanamycin	89	86	6	—	—
Polymyxin B	97	11	94	—	—
Gentamycin	99	100	98	100	100
Carbenicillin	—	—	100	—	—

and 13% of sputum grew an organism, the majority being gram-negative bacilli. One case of diphtheria was positive out of 989 cultures done. No Pneumococcus nor Haemophilus was siolated.

All the Staphylococci isolated were resistant to Penicillin and Tetracycline and the majority to Sulphatriad; all were sensitive to Ampicillin Erythromycin, Chloramphenicol, Gentamycin, Cloxacillin and Cephaloridine. All the Streptococci were sensitive to Tetracycline, Erythromycin, Ampicillin and Chloramphenicol. The Pseudomonas were all sensitive to Neomycin, Polymyxin, Carbenicillin and Gentamycin, and the Coliforms to Gentamycin and Polyxin.

Cultures for M. tuberculosis

693 cultures (6% of all cultures) were done, of which 91 (13.1%) were positive. Specimens were of various types, the majority (49%) were sputum, followed by Cerebro-spinal fluid (17%), body fluids (12%), urine (9%), gastric lavage (4%) and pus (4%). Of the 91 positive cultures, most (89%) were sputum cultures. Positive cultures were also obtained from pus (4 cases), C.S.F., body fluids and curettings (2 cases each). 15 Guinea-pig innoculations were also performed, of which 2 were positive (1 each from curettings and knee tissue). 10% of the 602 negative cultures was positive on smear examination, nearly all being sputum specimens. 29% of positive cultures were negative on smear examination, the majority again being sputum specimens. All the positive cultures of C.S.F., pus, body fluids, and curettings were negative on smear examination.

73 cultures were tested for sensitivity against Para-Aminosalicylic Acid, Isoniazid and Streptomycin. There were no growth in 6 cases. The majority (about 69%) were sensitive to the three primary drugs.

Blood Cultures

There were 2,716 blood cultures (23.8% of all cultures done) and 133 (4.9%) were positive. Of the 2,716 cultures, 88% were clot and blood cultures for Salmonella organisms. 5.7% (28 out of 449 cultures) of blood cultures and 2.9% (55 out of 1,945 cultures) of clot cultures for Salmonella were positive. Of the 322 blood cultures, 50 (16%) were positive; the majority of organisms isolated being Staph. aureus or Coliforms. Staph, albus was isolated in 22 instances and these were regarded as contaminants.

All the organisms isolated were sensitive to Gentamycin. All the Staph. aureus were also sensitive to Cephaloridine, Cloxacillin and Septrin but resistant to Penicillin and Sulphatriad. The majority of Staphylococcus were sensitive to Chloramphenicol, Erythromycin and Ampicillin. One case of Streptococcus was resistant to Penicillin and Sulphatriad but sensitive to all the other antibiotics tested. The majority of Coliforms were sensitive to Neomycin and Polymyxin.

Stools Culture

3,004 cultures (26.3% of all cultures done) of stools were performed, of which 141 (4.7%) were positive. Of 750 cultures of "infant" stools (up to 2 years of age), 108 (14.4%) were positive; the majority (96%) being Staph. aureus or pathogenic E. coli in about equal proportions. 54 cases of pathogenic E. coli were isolated, of which 24 (44.4%) were of serological type 0128/B12, 11(20.4%) type 026/B6, 6(11%) type 0125/B15, 4 type 055/B12 and 3 each of types 0126/B16 and 0127/B8. In 467 cultures of gastro-enteritis cases above 2 years, 7 instances of Shigella organisms were isolated. Of 566 requests for Salmonella isolations, 26 (4.6%) were positive. 1,221 cultures of stools were done on pilgrims going to Mecca and all were negative for V. cholera.

The antibiotic sensitivity of 50 cases of Staph. aureus from "infant" stools were tested and the sensitivity pattern was similar to that of Staph. aureus isolated from pus specimens.

C.S.F. Cultures

14 positive isolations (3%) were obtained from a total of 462 cultures done. There were 7 cases of H influenzae, 5 of Pneumococci, 2 of M. tuberculosis and a case of Torulosis.

Frequency of Organisms Isolated

Of the total 1,543 positive cultures, Coliforms were the most commonly isolated, accounting for 569 isolates (36.9%), the majority coming from urine, pus and swabs specimens. Staphylococcus were the next most frequently isolated, comprising 424 isolates (27.5%), mainly from pus and swabs specimens. Pseudomonas was isolated 129 times (8.4%) from urine, pus, swabs and sputum specimens. There were 118 isolates (7.6%) of Proteus from urine, pus and swabs specimens. There were 109 isolations (7.1%) of Salmonella typhi from blood and stools, of which blood specimens accounted for 76% of positive isolates of Salmonella. M. tuberculosis isolates accounted for 6% (93 cases) of all positive cultures.

Discussion

The pattern of bacteriological cultures and isolates are for 1970 for I.M.R. Ipoh. The pattern will be different for different years as requests for

cultures change and techniques of isolation and identification are improved and as difficulties are identified and overcome. The pattern is also unique for I.M.R. Ipoh and is not comparable to a Hospital Laboratory where the laboratory is within the Hospital itself. Ipoh General Hospital is two miles away and bacteriological specimens come from as far as 80 miles away, sometimes involving a delay of up to 24 or even 48 hours. Nevertheless the isolation rate of 13.5% is comparable to that in a General Hospital laboratory in Adelaide (3) where the isolation rate was about 10%.

Blood and Stools specimens accounted for half of all specimens examined (5,720 specimens out of the total 11,411) but for only 18% of positive isolates. This is largely due to the fact that the majority of blood cultures (70%) done were clot cultures for Salmonella organisms from blood specimens sent for the Widal and Weil-Felix test, and that 40% of the stools specimens were from Mecca pilgrims for the screening of V. cholera. On the other hand urine, pus and swabs specimens formed only 25% of all specimens examined but accounted for 71% of pathogens isolated. This is also the pattern in the hospital mentioned in Adelaide (3) where urinary tract and "localised infections" comprised 68% of all isolates. In I.M.R. Ipoh Coliforms formed the majority (62%) of organisms isolated from urine specimens and Staph. aureus formed 46% of positive isolates from pus and swabs specimens. Coliforms and Staph, aureus are the common pathogens in urinary tract infections and localised infections respecitvely, and as they are also easily cultured from the specimens; urine being a good culture medium itself, account for the majority of pathogens isolated. Of the total 1,543 positive cultures from all types of specimens, E. coli formed 37% and S. aureus 28% of all pathogens isolated.

22% (309 out of 1,393) of all ruine cultures were contaminated. This rather high rate of contamination is partly explained by the delay of urine specimens in reaching I.M.R. Ipoh especially when the specimens are from outstation. Contaminated specimens usually yield a mixed growth. In cases of comtamination in which Coliforms predominate and the growth is profuse, extra care has to be taken in interpreting the results, as the long hours of delay enable the Coliforms to multiply several generations to give a "significant growth". Here, the presence of pus cells, the clinical history and repeated positive cultures must be taken into account. A common cause of contamination in urine is the insufficient care taken in its collection. A urine culture is ordered by the ward doctor who usually leaves it to the Staff Nurse to collect the urine who in turn may leave it to the Assistant Nurse or Attendant who makes the patient collect the urine himself without the help of specific instructions on the proper way of doing it.

44% of urine cultures did not yield any growth. In some of these the clinical picture was that of urinary tract infection, with pus cells in the urine. Such cases might have been treated with antibiotics. Often no information is given regarding this. The role of growth inhibitors in urine e.g. vegetable anti-bacterials like paciferrins, leaves and tubers of Arum species and tumeric spices (4) has to be considered as these are consumed by our local population.

Isolations from throat swabs and sputum were not satisfactory. Partly to circumvent the problem of drying and delay in the transportation, swabs were transported in Stuart's transport medium. We have since dispensed with the transport medium and swabs are now conveyed to I.M.R. Ipoh as such. The medium may itself disperse and dilute whatever organisms that may have been present on the swabs in the first place. The presence of detergents on inadequately washed rubber bunds of the screw caps of bottles, the inadequate surface area for culture of Diphtheria organisms on Loeffler's medium in Bijou bottles, the death of organisms due to delay in the transportation of specimens, the chemotheraphy that has already been administered, and improper bacteriological techniques are some of the problems that have been identified, which have contributed to the rather poor results. However, it is also interesting to note that the Hospital in Adelaide had only about 17% positive isolations from sputum specimens and that 31% were Gram-negative organisms (3).

The pattern of M. tuberculosis culture was interesting in that 10% of negative cultures had positive smears. The possibilities of this are non-viable M. tuberculosis present in the specimens, contamination, and acid-fast bacilli other than M. tuberculosis from e.g. the tap. 29% of positive cultures were at first seen to be negative on smear examination. This may be explained by inadequate smear examination or inadequate or non-representative material examined. The moral of this discrepancy would be to submit specimens for culture even though these specimens are microscopically negative. Repeated microscopic examinations should also be the rule.

Of the pathogenic E. coli that were isolated from stools of children up to 2 years old, serotype 0128/B12 was the commonest (44%) followed by 026/B6 (20%). Stools of adults were not tested for pathogenic E. coli. However a recent report

has implicated that certain strains of E. coli e.g. 015: H11 not previously recognised as enteropathogenic can cause acute diarrhoea and that a previously unrecognised serotype 0148:K:H28 is responsible for "travellers' diarrhoea" (5). These serotypes are different from that which cause diarrhoea in infants.

The sensitivity pattern of Urine, Pus and Swabs isolates are as shown in Tables II and III. In general, most organisms isolated were sensitive to Gentamycin and the gram-negative bacilli also to Neomycin. Pseudomonas were usually only sensitive to Polymyxin, Carbenicillin, Gentamycin and Neomycin and resistant to other antibiotics. Most pathogens were resistant to Sulphatriad, Staphylococcus to Penicillin, and the gram-negative bacilli to Tetracycline. Sulphonamide sensitivity testing is affected by "inhibitors" present in many laboratory media unless neutralised by lsyed horse blood (6). Oxoid Diagnostic Sensitivity Test Agar, which is used in I.M.R. Ipoh, does not contain inhibitors of Sulphonamides and other antibiotics.

As the frequency of organisms isolated depends on the type of specimens examined and as different organisms vary in their sensitivity to different antibiotics, it is essential that the causative pathogen be isolated, identified and its sensitivity determined. The principles of rational chemotherapy are adequately discussed in Garrod's book on Antibiotic and Chemotherapy (&). Suffice to say that when specimens e.g. urine, pus, ear and vaginal swabs are known to yield a variety of organisms, both gram-positive and gram-negative, it is important that culture and sensitivity be done, especially when infection by Pseudomonas is a possibility as they are usually sensitive to only certain antibiotics.

The present situation where I.M.R. Ipoh is the only place in Perak where bacteriological cultures can be done for all the hospitals in the State is naturally not ideal for a good bacteriological service in the State. The incidence of contaminated specimens and the frequency of isolates can be improved with hospital laboratories doing their own bacteriological cultures and where there is minimum delay in culturing the specimens obtained. The situation can be further improved with the services of a Bacteriologist in the State and with "refresher courses" for the Laboratory Technologists concerned.

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The Laboratory Diagnosis of Venereal Diseases*
I. Serological tests for syphilis

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EXAMINATION OF sera for the evidence of syphilitic infection forms a large part of the work of most routine serology laboratories.

For instance, in the serology division of the Institute for Medical Research, Kuala Lumpur, an average of some 30,000 sera are examined annually. Most of these sera are from routine screening of blood donors, expectant mothers and routine medical examinations in addition to patients being investigated after known exposure.

Table I shows the number of serological tests for syphilis done in the Serology Division of the IMR[6]

Table 1

Tests	Year		
	1970	1971	1972
Kahn	24,614	26,023	10,993
Wasserman	23,603	25,649	30,480
VDRL	—	—	19,487
FTA	396	106	968

The most direct and early evidence of syphilitic infection is of course to demonstrate the presence of *Treponema pallidum* in the primary chancre in the mucous lesions of secondary syphilis. This is done by means of dark field microscopy[13] which requires the procedure to be performed at the patient's side and requires trained personnel who are able to recognize *T. pallidum* and to differentiate it from other commensal treponemas. Because of this and because the chances of finding treponemes are only during limited periods in the natural history of the disease one usually has to depend on the indirect evidence provided by serological examination.

Serological tests for syphilis

Serological tests for syphilis have evolved rapidly since they were first introduced and today the clinician is faced with a large gamut of tests to choose from. It is the purpose of this paper to review the current tests available, their interpretation and to make recommendations on a uniform testing system for this country.

All serological tests for syphilis can be divided broadly into either non-treponemal or treponemal.

Non-treponemal tests for syphilis are non specific tests that detect the presence of an antibody "reagin" that is found in the sera of patients suffering from syphilis and related treponematosis and from a multitude of other unrelated diseases like the collagen diseases, malaria, leprosy, infectious mononucleosis, certain viral infections, 10,5,3 some cases of pregnancy and even in blood donors after repeated donations.[4] Reagin is found in the gamma globulin fraction of serum but its exact nature is unknown. Reactive results in cases other than syphilis are referred to as biological false positive

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reactions and may be termed as either acute or chronic depending on whether the reaction persists for longer than six months.3

Treponemal tests on the other hands, detect the presence of treponemal antibodies and can be considered specific for syphilis and related treponematosis. It must be mentioned that there is no test at the moment that can differentiate syphilis from yaws, pinta and bejel which are the other treponeme caused diseases. One may wonder why, in the presence of treponemal tests, is there a need for non treponemal tests to be performed. The reasons are that treponemal tests are expensive, technically more difficult to perform, requiring specialised personnel and equipment and are usually only available in very specialised laboratories. Furthermore treponemal tests merely give information on the serological status of the patient indicating either present or past infection. The state of activity of the disease will not be known since treponemal tests remain reactive for long periods (sometimes for life) and usually do not show any change following treatment. Non-treponemal tests, on the other hand, are relatively cheap, easier to perform and allow quantitation. Titres will usually drop after successful treatment and hence they will be useful in following response to therapy.

It is the current practice therefore to use non treponemal tests as routine screening tests and to follow response to treatment. Treponemal tests are reserved for confirmation – to be performed at the special request of the clinician. They are of great value in distinguishing syphilitic reactions from biological false positive reactions in non treponemal tests and to aid in establishing a diagnosis of syphilis in a patient with clinical or epidemiological evidence of syphilis who shows non reactive non-treponemal tests.14

Non-treponemal tests

The following non-treponemal tests are available:

(1) The Kahn test
(2) VDRL test
(3) Complement fixation test (Wasserman)
(4) Rapid reagin tests
(5) Automated reagin tests

Present day non-treponemal tests do not use the crude lipoidal antigen (from beef heart) that is used in the Kahn Test. Tests like the VDRL utilise a purified preparation consisting of cardiolipin, lecithin and cholesterol, allowing for better control on sensitivity, specificity and reproducibility.

The Centre for Communicable Disease Control (C.D.C.) in Atlanta, Georgia, who in conjunction with WHO run an international proficiency testing programme for syphilis serology, recommend that only one cardiolopin test be done routinely. They recommend the VDRL as it is cheap, easily standardised, reproducible and easy to perform. There is no point in performing more than one cardiolipin test as no additional information can be gathered and in fact conflicting results may further confuse the clinician.

The VDRL flocculation test takes preference over the complement fixation tests because the latter, while requiring more reagents, more manipulation and more time is harder to standardise and is considered to be less sensitive.

The principle to remember is that it is better to perform a single test well than several tests poorly.14

The Rapid reagin tests are so called because they were originally designed to serve as a screening procedure for large groups of persons and could also be employed as a field test in mass surveys. The rapid plasma reagin and the RPR (teardrop) card test can be used for this purpose and while they may pick up many false positives, this is not really a disadvantage as all positive cases can then be subjected to the more standardised laboratory tests. A recent improvement on these tests, the RPR (circle) card test has the advantage that it has about the same sensitivity as the VDRL test and also allows for quantitation.

For laboratories performing a large volume of serological tests a suitable innovation is the automated reagin test which utilises the continuous flow antoanalyser system.8,9.

Treponemal tests

The treponemal tests utilise a specific antigen – either the pathogenic *Treponema pallidum* itself or a fraction of the non pathogenic Reiter treponeme. The tests now available are:–

(1) Treponema immobilisation test (TPI)
(2) Fluorescent treponemal antibody test (FTA)
(3) FTA – ABS
(4) Reiter protein complement fixation test
(5) *Treponema pallidum* haemagglutination test
(6) Microhaemagglutination test for *Treponema pallidum*
(7) Automated FTA – ABS

The Reiter protein complement is a modification of the cardiolipin complement fixation test except that a fraction of the non pathogenic Reiter treponeme is used as the antigen. It is more specific than the cardiolipin tests but less specific and less sensitive than the TPI or FTA tests which are described below.

The TPI (Treponema Pallidum Immobilisation Test), once considered the standard by which all serological test for syphilis are assessed employs living treponemes that have been grown in rabbit testicular tissue and extracted in survival medium. This test is expensive, time consuming, technically difficult and requires an elaborate system of controls. Standardisation of the test is difficult and this test is only performed in a few research laboratories.

The FTA – ABS test has now virtually taken over as the standard from the TPI as it has been found to be just as specific while being more sensitive (95% as compared to 89% in a study).2 The FTA – ABS test (introduced in 1964) is a modification of the earlier FTA where the antigen (cell components of *T. pallidum*-Nichol's strain) is absorbed with sorbent (an extract of Reiter treponeme cultures) to remove group specific antigens for *Treponema pallidum*.

The FTA, FTA-200 and FTA-ABS employ the indirect fluorescent antibody technique.

Recently the *T. pallidum* haemagglutination test was developed and has been assessed and some studies showed it to be just as specific and sensitive as the FTA-ABS.12 The TPHA test employs a haemagglutination reaction using *T.pallidum* (Nichol's strain) sensitised erythrocytes. The TPHA however appears to have a slightly lower positivity rate in early (primary) syphilis. The TPHA test is simpler and cheaper than the FTA-ABS and recently, a quantitative microhaemagglutination assay for *T. pallidum* has been introduced7 and shows great promise of being introduced as a test more practicable for routine use than the FTA-ABS. However, like the FTA-ABS, the haemagglutination tests have not proved useful in following the efficacy of treatment.

Automation has also been introduced in the treponemal tests and tests available are the Automated fluorescent treponemal test (AFTA)11 and the Quantitative Automated Micro-haemagglutination Assay for antibodies to *Treponema pallidum*.

The serological course of syphilis14

The primary chancre usually appears about three weeks after infection. The cardiolipin tests and the FTA-ABS become reactive about the forth to the sixth week. The TPI becomes reactive a bit later in the primary stage.

In secondary syphilis all serological tests are positive.

In late and latent syphilis it must be noted that in about a third of the cases the cardiolipin tests may be non-reactive, and the only means of laboratory detection may be the treponemal tests.

Of all tests assessed so far, the FTA-ABS appears to be the most sensitive test in primary syphilis, is fully reactive in secondary syphilis and maintains its high level of reactivity through latent and late syphilis.

Let us examine the effect of treatment on the serological course of syphilis.

If treatment is given before the primary chancre appears or before the cardiolipin tests become positive it is likely that the cardiolipin tests will remain non-reactive.

If treatment is given in the early stage after the cardiolipin test have become reactive it will take about six months before these tests become non-reactive. If treatment takes place in secondary syphilis reversion to non-reactivity may take between 12-18 months. If treatment is given very late the cardiolipin tests may persists for life.

As far as the treponemal tests are concerned reversion to non-reactivity will only occur if treatment is given very early in the disease. Otherwise it is very likely that these tests will remain reactive for life.

Recommendations

The serological tests for syphilis have been reviewed.

One flocculation test should be used for routine testing. At the moment, the VDRL test appears to be the most reliable and it should be adopted. Most laboratories doing serological tests can be easily equipped and staff trained so as to perform this test satisfactorily. All other non-treponemal tests should be discontinued.

All reactive sera should have a quantitative VDRL test done. A reactive result should be assessed in the light of clinical and epidemiological findings. If these do not support a diagnosis of syphilis, the test should be repeated at regular weekly intervals to establish the presence of a static or rising titre.

Verification may then be sought in doubtful and inconclusive cases by doing the FTA-ABS test. If this is positive it shows the presence of treponemal antibodies, indicating past or present infection.

Summary

The serological tests for detection of syphilis that are currently available have been reviewed. It is suggested that laboratories in this country utilise one non-treponemal test, the V.D.R.L. as a screening test and the FTA-ABS test as a confirmatory procedure.

Acknowledgements

I would like to thank Dr. R. Bhagwan Singh, the Director of the Institute for Medical Research for his advice, encouragement and permission to publish this paper, and Miss A. Selvarani for typing the manuscript.

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*Erythrocyte Transketolase Activity and Anaemia

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THE ENZYME transketolase in the haemolysate of red blood cells is associated with the glucose oxidative pathway and requires the co-enzyme thiamine pyrophoshate for its function. In thiamine deficiency, the activity of transketolase is depressed but the addition of the co-enzyme thiamine pyrophosphate, in vitro, produces a stimulatory effect on the transketolase activity. This effect (TPP effect) has therefore been widely used for the assessment of thiamine nutrition and we have previously reported on the thiamine status of Malaysian healthy adults, pregnant women (Chong & Ho, 1970) and the Orang Asli (Burns-Cox, Chong et al 1972) by the application of the above method.

In a study on the Orang Asli and those of a group of children with heavy trichuris infections conducted during 1968-1969, we noted amongst other things, an inverse relation between their haematocrit values and erythrocyte transketolase activity ($r = -0.51$; $p < 0.001$) — (Fig. 1). Subsequently, we came across three reports describing this phenomenon (Wells, 1968, Schouten et al. 1971 and Wells et al. 1972).

We therefore felt the need for further study and have since examined the red cell transketolase of 49 patients admitted to hospital for investigation of anemia. We have found a similar inverse relationship between their transketolase activity and haematocrit ($r = -0.38$; $p < 0.01$) and between the former and haemoglobin concentration ($r = -0.33$; $p < 0.02$), thus confirming our earlier observation (Figs. 2 & 3).

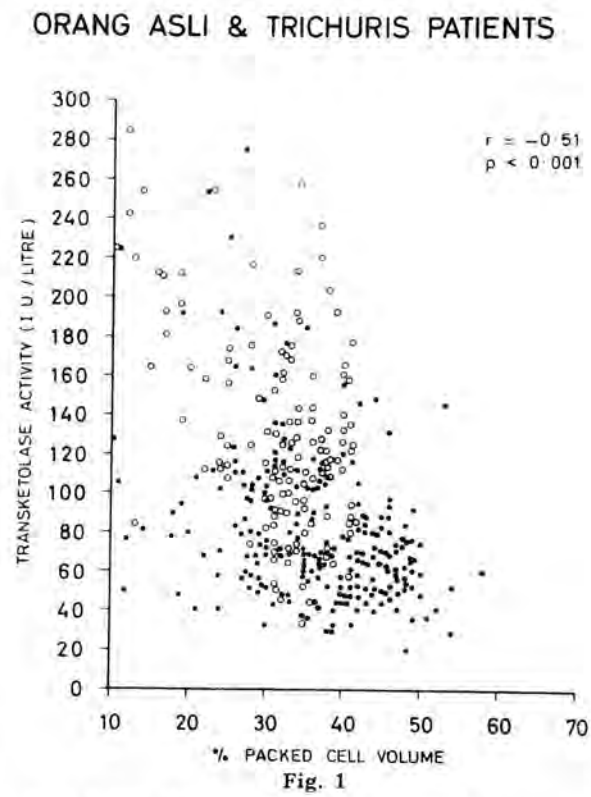

Fig. 1

The mean transketolase activity of the patients was 83 ± 42 I.U./litre (mean p.c.v. = 25%; mean Hb. = 7.5 g%), compared to a mean of 50 ± 11 I.U./

*Read by the senior author at an "International Symposium on Malnutrition and Functions of Blood Cells", 28-29 November, Kyoto, Japan, 1972.

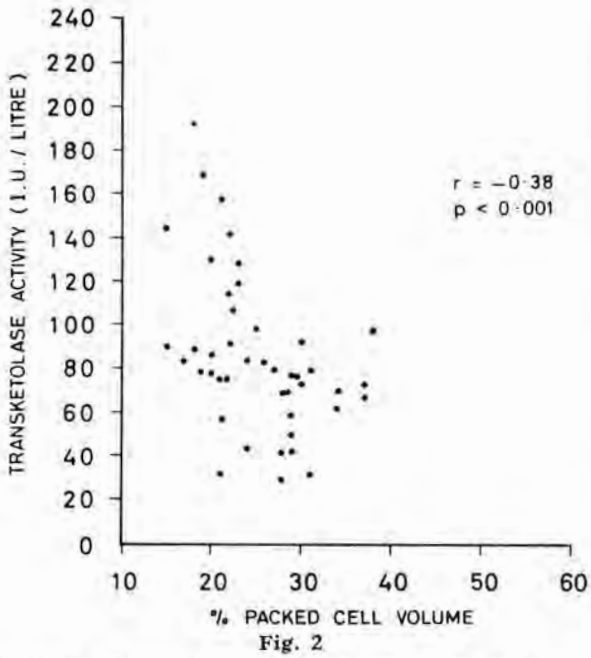

Fig. 2

litre in 37 healthly control subjects whose red cell transketolase was determined at the same time (mean p.c.v. = 46%; mean Hb. = 15.1 g%). The difference between their transketolase activities was statistically significant ($t = 2.85$; $p < 0.01$). But no such difference was found between their thiamine pyrophosphate effect ($t = 1.16$; not significant).

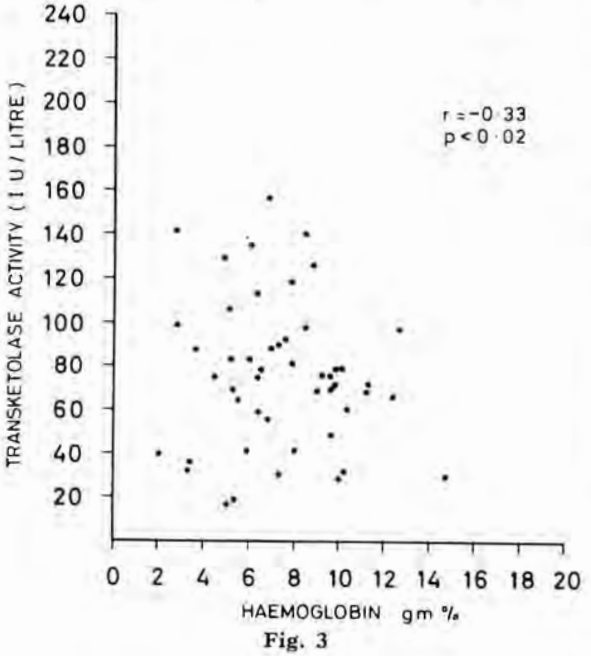

Fig. 3

The mean transketolase activity of 16 patients in whom reticulocytosis was present (reticulocyte counts greater than 2.5%) was 88 I.U./litre which was higher than the overall mean of 83 I.U./litre observed for all patients.

When the transketolase activities of these patients and control subjects were plotted against their reticulocyte counts, a significant positive correlation was obtained ($r = 0.44$; $p < 0.001$) — (Fig. 4).

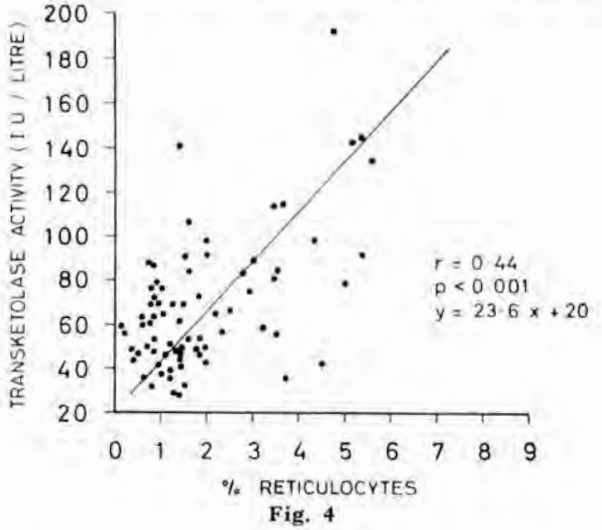

Fig. 4

Our observation is therefore in agreement with the current knowledge concerning the increased activity of several red blood cell enzymes, including transketolase, in the presence of a young red blood cell population.

We would like to stress that this observation in no way invalidates the usefulness of this test for assessing thiamine status since the increased transketolase activity was not related to the stimulatory effect of added thiamine pyrophosphate (TPP effect).

Acknowledgements

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A Practical Scheme for the Estimation of Serum Total Protein and Albumin

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Summary

THE BROMOCRESOL GREEN (BCG) dye-binding method for serum albumin was found to be rapid and convenient. This method compares well with the electrophoresis method ($r = 0.91$) and the salt fractionation method ($r = 0.96$). A simplified scheme is proposed which allows for the rapid measurement of both albumin (BCG method) and total protein (Biuret method) together. This scheme is ideal for a busy clinical laboratory which has to cope with a large routine workload by manual methods.

Introduction

The measurement of serum total protein is usually carried out by the simple and popular Biuret method. Following this, serum albumin measurement is then undertaken by the salt fractionation method in which the globulins are precipitated by a sulphate-sulphite mixture and the albumin in solution quantitated by the Biuret method. This salt fractionation procedure for albumin is somewhat tedious and the method is prone to errors.

Recently Doumas *et al.* (1971) and Miyada *et al.* (1972) have perfected a specific dye binding technique for the quantitation of albumin using bromocresol green (BCG). We have evaluated the method of Doumas *et al.* and found it to be simple and reliable. We now propose a practical scheme whereby the new BCG method is combined with the Biuret method so that the measurement of serum albumin and total protein may be carried out together rapidly and accurately by the busy hospital laboratory.

Materials and Method

Re agents

1. *Biuret re agent*
   Dissolve 9 g of sodium potassium tartrate in 500 ml of 0.2 M sodium hydroxide. Add 3 g of copper sulphate ($CuSo_4.5H_2O$) and dissolve by stirring, then add 5 g of potassium iodide and make up the volume to 1 litre with 0.2 M sodium hydroxide.
2. *Succinate buffer, 0.1 M, pH 4.2*
   Dissolve 11.9 g of succinic acid in about 800 ml of water, adjust the pH to 4.2 with 2.0 M sodium hydroxide (about 35 ml) and dilute to 1 litre with water. Store at 4°C.
3. *Stock bromocresol green solution*
   Dissolve 419 mg of bromocresol green (from BDH, England or E. Merck, Germany) in 5 ml of 0.2 M sodium hydroxide in a 1 litre volumetric flask. Dilute to volume with water and store at 4°C.
4. *Working dye solution*
   Dilute 250 ml of the stock BCG solution with 750 ml of the 0.1 M succinate buffer. Add 4.0 ml of 30% Brij-35 (from Sigma Chemical Co. USA) and mix. Store at 4°C.
5. *Total protein and albumin standard.*
   The same standard is used for both total protein and albumin. The standard can be (1) commercial control serum, (2) commercial standard bovine serum albumin solution, (3) pooled serum, calibrated by the Micro-Kjeldahl method or against commercial control serum.

Method

Set up two test tubes, the first tube to be used for total protein and the second for albumin. Pipette 3.9 ml water into first tube, followed by 0.1 ml of of serum. Mix. Transfer 0.5 ml of the diluted serum into the second test tube. Also set up the standard and blank tubes similarly.

Total protein

Add 3.0 ml Biuret reagent to the first set of tubes. Mix and incubate at 37°C for 10 min. Read the absorbance on the EEL Colorimeter using the green filter (OGR 1) or on a Spectrophotometer at 540 nm, setting zero absorbance with the blank.

$$\text{Total protein (g/100 ml)} = \frac{\text{Test absorbance}}{\text{Standard absorbance}} \times \text{Concentration of standard}$$

Albumin

Add 6.0 ml of working BCG dye solution to the second set of tubes. Mix, leave at room temperature for 10 min and then read the absorbance on the EEL Colorimeter with the red filter (Ilford 607) or at 628 nm, using the blank for zero absorbance.

$$\text{Albumin} = \frac{\text{Test absorbance}}{\text{Standard absorbance}} \times \text{Concentration of standard}$$

Results

An albumin standard curve was plotted to establish the linearity of the BCG-albumin complex with respect to albumin concentration (Fig. 1).

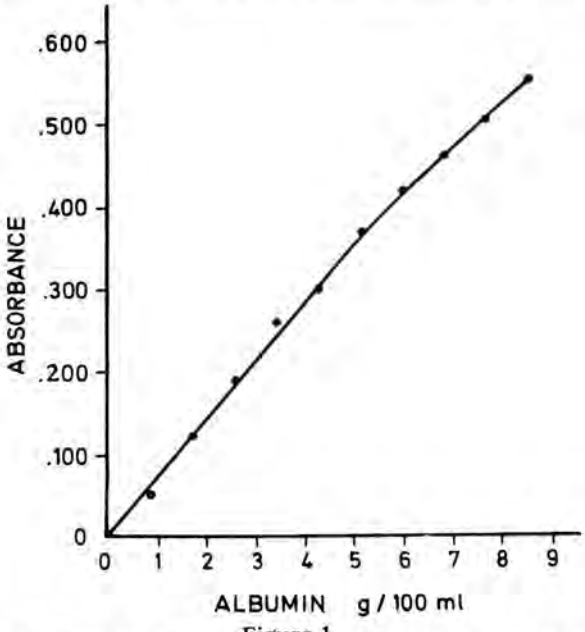

Figure 1
The absorbance-concentration relationship of the BCG method on the EEL Colorimeter.

Absorbance was read on the EEL Colorimeter and on the Coleman Junior IIA Spectrophotometer. On the EEL Colorimeter the Beer's Law holds good up to 5 g/100 ml, while the Coleman Junior gives linear absorbance up to 8 g/100 ml.

The albumin values obtained by the BCG method was compared with values obtained by electrophoresis of serum protein according to the Shandon System (Shandon Monograph on Electrophoresis using cellulose acetate membrane) and with values obtained by the sulphate-sulphite salt fractionation method (as described in Varley, 1967). The results are summarised in Table 1.

Table 1
Comparison of albumin values by 3 different methods.

	Albumin (g/100 ml)		
	BCG	Electro-phoresis	Sulphate-sulphite
Range found	1.1 – 4.5	0.8 – 4.4	0.8 – 4.2
Mean value	2.9	3.0	2.8
No. of samples	29	29	29

The correlation between the BCG and the electrophoresis method (Fig. 2) and between BCG and the sulphate-sulphite method (Fig. 3) is good.

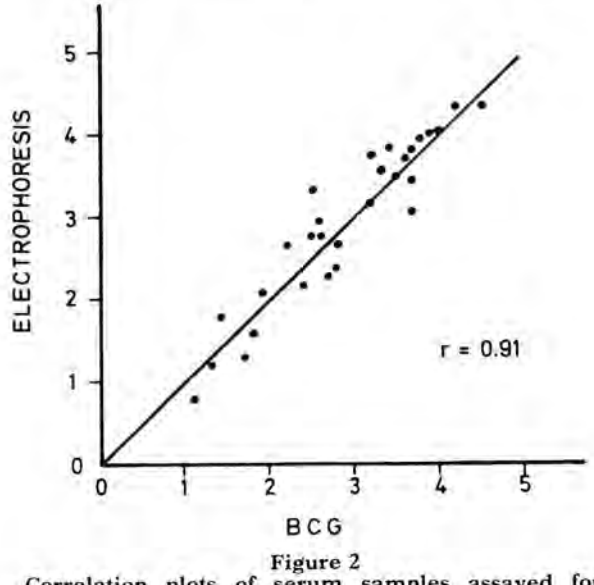

Figure 2
Correlation plots of serum samples assayed for albumin, in g/100 ml, by the Electrophoresis and and BCG methods.

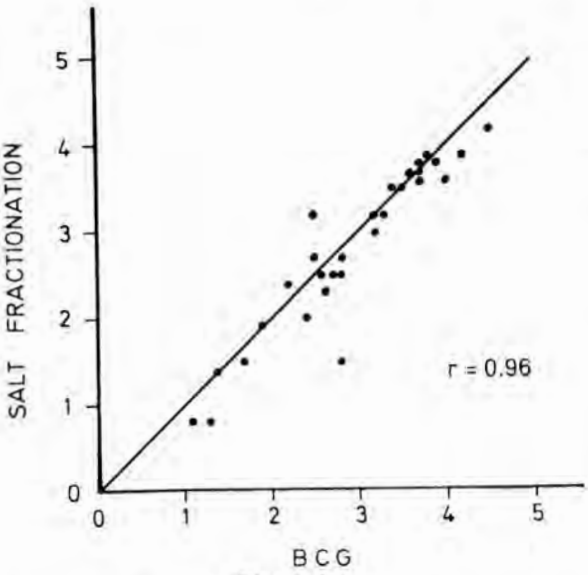

Figure 3
Correlation plots of serum samples assayed for albumin, in g/100 ml, by the Salt Fractionation and BCG methods.

The between-batch precision of the BCG method was established using a commercial control serum and a pooled serum as shown in Table 2.

Table 2
Precision studies on the BCG method.

	Hyland control serum (3.8 g/100 ml)[a]	Pooled serum
Mean value	3.6	3.7
Standard deviation	0.13	0.14
Coefficient of variation[b]	3.6 %	3.8 %
No. of determinations	20	20

[a] Value obtained by salt fractionation.
[b] Coefficient of variation, CV = SD/Mean

Discussion

Quality of BCG

Depending on the make of BCG, we encountered some problems with the dye-albumin complex. Initially we used BCG from May and Baker (supplied by the Government Medical Store) and found that the absorbance of the dye-albumin complex did not pass through the origin, although it gave a linear relationship with increasing albumin concentration. We subsequently used the BCG from BDH and Merck and found both suitable but Merck's was better.

Buffer pH

The recommended buffer pH is 4.2. We have tried out the dye solution buffered at 4.0 and 4.4 and found the results to be similar. The blank absorbance increases with the pH but the absorbance of the dye-albumin complex is highest at pH 4.2.

Albumin standard

The use of a commercially prepared control serum or a standard Bovine Serum Albumin solution (Metrix, Armour Pharmaceutical Co., Chicago, Illinois 60690) has been found to be convenient. To economise and facilitate measurement we recommend dilution of the reconstituted control serum or the standard BSA solution with 0.05 g% sodium azide solution. The control serum is diluted forty-times while the Metrix standard BSA solution (about 6.5 g/100 ml) is diluted eighty-times. Colour development is carried out with 0.5 ml and 3.5 ml solutions using the BCG and Biuret reagents respectively. Working standard solutions thus prepared should be stored in the refrigerator.

The working standard solution from the control serum will have both albumin and total protein values within the working ranges. The working BSA solution is suitable as an albumin standard, but low for total protein.

Crystalline BSA (obtained from Sigma Chemical Co.) may be used as standard but the powder must first be dried according to Doumas *et al.* (1971), otherwise the uncertain moisture in the powder gives an unreliable standard solution.

We have used the BCG manual method for albumin measurement in our laboratory satisfactorily. When establishing this test a standard curve should be done to show linear relationship between colour development and albumin concentration. This will serve to check the buffer, the BCG dye and the colorimeter.

Conclusion

We have found the BCG dye-binding method for serum albumin estimation to be simpler, faster and cheaper than the traditional methods of electrophoresis and salt fractionation, without any loss in accuracy. We have no doubt it will gradually replace the latter two methods. Our proposed scheme will help the busy clinical laboratory cope with the ever increasing requests for serum total protein and albumin/globulin ratio.

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Dystocia Caused by Congenital Hydronephrosis

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CONGENITAL MALFORMATIONS are not uncommon. Malpas (1937) gave the incidence as 21 per 1000 births. Most cases deliver spontaneously but some major malformations may cause dystocia. The incidence of major malformations with dystocia is 0.75 per 1,000 total births (Monks, 1969). Hence obstetricians seldom encounter this complication, but when they are faced with such an obstetric emergency they have to act adeptly. We report here a rare cause of dystocia caused by congenital hydronephrosis.

Case Report

The patient, an Indian woman aged 33 years, was admitted on 9th November 1970 at 36 weeks gestation. She had 5 previous full-term normal deliveries. On admission her blood pressure was 150/100 and she had gross oedema. The uterus was full-term size with hydramnios. X-ray abdomen was not helpful because of the hydramnios and marked oedema of the anterior abdominal wall. Labour was induced because of the pre-eclampsia. At full cervical dilatation there was no descent of the presenting part (breech) into the pelvis; hence caesarean section was performed.

At operation the breech was in the pelvic brim. The grossly distended abdomen was obstructed at the level of the pelvic brim. A fresh stillborn infant weighing 2,200 gm. was delivered. It had multiple external congenital abnormalities and a grossly distended abdomen.

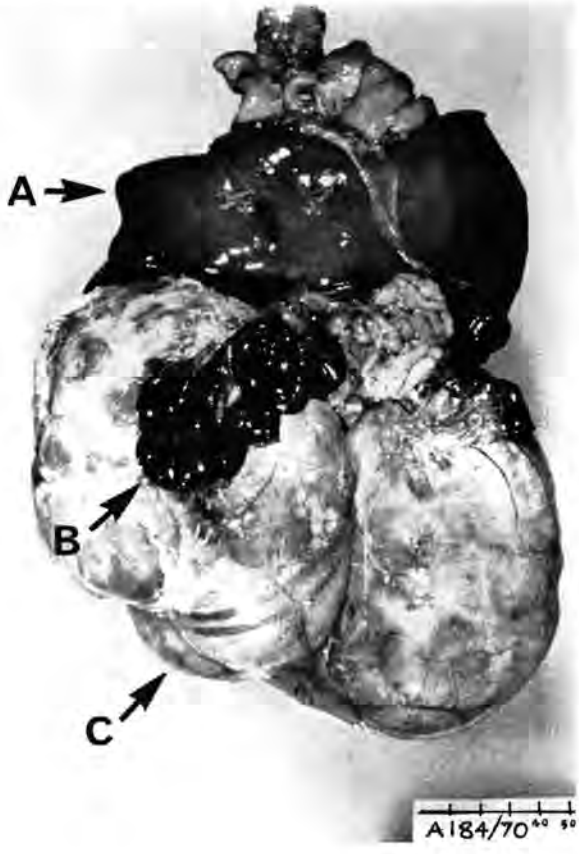
Post-operatively, the mother's condition was satisfactory. When discharged on 20th November 1970 her oedema had almost completely subsided and her blood pressure had returned to normal.

Postmortem examination on the foetus was carried out. This showed no congenital abnormalities of the respiratory system. Both lungs were collapsed. The heart was normal in appearance. The abdomen was distended with ascitis. The stomach showed a small diverticulum arising from the fundus but there was no abnormality seen in the diaphragm. The intestines were malrotated and displaced forwards and upwards by a large, oval retroperitoneal, cystic mass measuring 11.0 x 19.0 cm. arising in the right renal fossa and extending across the midline, anterior to the inferior vena cava. Dissection of the mass revealed that it was a right hydronephrotic kidney with hydroureter. The cortex and medulla were atrophic and represented as a convex body on the right margin of the cystic mass. The surface of the mass was traversed by numerous small arteries and veins (See Fig. 1). It contained approximately 100 ml. of urine and the distended calyces gave it a loculated appearance. The hydroureter terminated 2.0 cm. above the bladder, the remaining distal portion of the ureter was represented by a somewhat flattened pinkish white band. At the junction of the hydroureter and the band, a valve-like fold of ureteral mucosa was seen obstructing the lumen. No twists or kinks of the ureter were present and no aberrant renal vessel was found. The left kidney and ureter showed no abnormality and communicated with a normal bladder.

Discussion

It is rare for major foetal malformations to cause dystocia because they are often associated with premature labour (Claye, 1963). If the condition is diagnosed early induction of labour is

recommended, but usually this complication is unsuspected until it is found impossible to deliver the shoulders, the abdomen or the breech. Foetal abdominal swellings are seldom diagnosed before dystocia occurs but x-rays may show the "Buddha attitude" of the foetus. Such foetal abdominal swellings may be caused by abdominal neoplasms, distended bladder, ascitis, and congenital cystic kidneys (Barr and MacVicar, 1956). It is rare for such conditions to cause dystocia unless the abdomen is grossly distended or there is associated ascites as in the case described. Clark and Gipson (1948) described a case in which after delivery of the head they had difficulty in delivering the large abdomen with bilateral polycystic kidneys causing dystocia.



Congenital hydronephrosis may be due to congenital ureteral stricture, valves, twists or kinks. The pathologic changes proximal to the obstruction depend on the degree and duration the obstruction has been present. The atrophic right kidney and the large hydronephrosis and hydroureter suggest that urinary flow was impeded relatively early in the foetus and the obstruction was of a severe degree. At autopsy, a valve-like fold of ureteral mucosa was found to obstruct the ureteral ulmen. Such folds of redundant mucosa have been demonstrated in the foetal ureter, usually in the lower third (Culp, 1967). They are a rare cause of hydronephrosis.

Foetal dystocia may be managed by vaginal destructive operations or caesarean section. chassar Moir (1964) wondered if destructive operations are justified in modern obstetrics, with the relative inexperience of obstetricians in these dangerous operations compared to the relative safety of caesarean sections. However, if the major foetal malformation causing dystocia is incompatible with life, destructive operations still have a place in developing countries provided they are done by experienced obstetricians without endagering the life of the mother.

Summary

A rare case of congenital hydronephrosis with ascitis causing dystocia is reported. The literature and the management of congenital malformations causing dystocia is reviewed.

Acknowledgement

We thank Miss P.K. Lee for secretarial assistance and Professor T.A. Sinnathuray for permission to publish this case report.

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Termination of Pregnancy by Single Large Dose Injection of Prostaglandins E_2 and F_2 Transcervically into the Extra-Amniotic Space

by Allan Y. H. Ng
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Summary

26 PATIENTS WITH gestations between 8 and 20 weeks were selected for termination of pregnancy by injection of large single doses of Prostaglandins E_2 and F_2 into the extra-amniotic space.

PGE_2 was used in 22 cases; 17 aborted. Of the 5 failures, 4 were not given larger doses because of the severity of side-effects (severe vomiting, headaches, rigors with high pyrexia and acute bronchospasm).

PGF_2 was used in 4 cases. 3 aborted after the 3rd dose of 20 mg. 1 case failed to abort after the third dose of 20 mg. Side-effects were noted in 3 cases.

All the abortions were incomplete.

Introduction

The use of intermittent small doses of prostaglandins E_2 and F_2 injected through a catheter inserted into the extra-amniotic space between the fetal membranes and uterine wall to terminate early pregnancies has been reported by Embrey and Hiller[1]. While this method appears to be quite successful, it has the disadvantages of a high risk of infection because of the length of time the catheter remains within the uterus[2], the tediousness of repeated injections, and the possibility of the catheter slipping out of the uterus.

In an attempt to overcome these disadvantages, single large doses of PGE_2 or PGF_2 were used in first and second trimester pregnancies.

Materials and Method:

Twenty-six patients, whose pregnancies ranged from 8 weeks gestation to 20 weeks and whose requests for termination of pregnancy were approved by the Pregnancy Termination Board of the Ministry of Health, Singapore, were selected for the trial in the University Department of Kandang Kerbau Hospital in 1972. All the patients were fit and had no evidence of renal, cardiovascular or hepatic disease. Under aseptic conditions, with the patient in the lithotomy position, a small polyethylene catheter or Ryles tube was then passed into the extra-amniotic space through the cervical os, to a depth of about 6 to 16 cm depending on the uterine size. The aim was to place the tip of the catheter at the uterine fundus. Aspiration was performed prior to the instillation of prostaglandins to prevent accidental intravenous injection.

The prostaglandins (dissolved in 0.5 ml of absolute alcohol and diluted with 4.5 ml of sterile water) was injected slowly into the extra-amniotic space, followed by 250 mg of Ampicillin dissolved in 2.5 c.c. water. The catheter or Ryles tube was then removed and any side effects were noted. The patient was kept under close observation. Hourly pulse and blood pressure recordings, 4 hourly temperature charts and fluid balance charts were kept.

Twenty-four hours later the procedure was repeated with double the initial dose of prostaglandins if there were no signs of abortion. After a further 24 hours, if abortion did not occur the procedure was again repeated with an increased dose of prostaglandins. If the patient still had not aborted 24 hours after the third injection, the procedure was recorded as a failure and the pregnancy terminated by other methods. When abortion occurred a curettage of the uterine cavity was performed routinely and the curettings sent for histological report.

Table I

PGE_2

Case No.	Nationality	Age	Parity	Gestation (weeks)	No. 1	Of 2	Injections 3	Result	Last Injection-Abortion Interval	Side-Effects
1	Chinese	42	6	12	2.5 mg			Successful	7½ hrs.	Nil
2	Indian	18	0	14	2.5 mg	5 mg		,,	7 ,,	Pyrexia
3	Malay	18	1	10	2.5 mg			,,	16½ ,,	Nil
4	Chinese	25	2	12	2.5 mg	5 mg		,,	6½ ,,	Pyrexia, Diarrhoea
5	Chinese	39	9	12	2.5 mg	5 mg		,,	6 ,,	Pyrexia, Abd. pain (severe)
6	Chinese	31	5	12	2.5 mg	5 mg		,,	8	Nil
7	Indian	29	4	12	2.5 mg			,,	5	Pyrexia, Severe abd. pain
8	Chinese	28	6	12	2.5 mg			,,	13	Pyrexia, Diarrhoea Bronchospasm
9	Malay	26	3	10	2.5 mg			,,	19	Nil
10	Indian	37	5	14	2.5 mg			,,	3	Nil
11	Chinese	26	4	14	2.5 mg	5 mg	10 mg	,,	28	Nil
12	Chinese	33	4	14	2.5 mg			,,	7	Abd. pains (severe)
13	Chinese	26	5	10	2.5 mg			,,	21	Nausea, vomiting
14	Chinese	28	6	12	2.5 mg			,,	13	Pyrexia diarrhoea Bronchospasm
15	Chinese	36	7	14	2.5 mg			,,	5	Nil
16	Malay	25	4	8	2.5 mg			,,	20	Nil
17	Chinese	32	2	12	2.5 mg			,,	5	Nil
18	Chinese	32	5	10	2.5 mg			Abandoned	—	Pyrexia, severe abd. pain
19	Chinese	36	9	16	2.5 mg	5 mg		Abandoned	—	Nausea, copious Vomiting
20	Malay	22	3	20	2.5 mg	5 mg		Abandoned	—	Nausea, vomiting headaches, rigors, pyrexia.
21	Indian	32	3	14	2.5 mg	5 mg		Abandoned	—	Vomiting, diarrhoea Abdo. paints.
22	Chinese	31	3	14	2.5 mg	5 mg	10 mg	Failed	—	Nil

1st Injection 2.5 mg
2nd Injection 5 mg
3rd Injection 10 mg

PGE_2 was used in 22 cases. 17 aborted. Of these 4 cases required 5 mg. and 1 case 10 mg. Of the 5 failures, larger doses were not given in 4 because of the severity side effects. 1 case failed to abort despite the 3rd dose of 10 mg.

Side-effects occurred in 12 out of 22 cases. These consisted of Pyrexia (transient up to 102°F all subsided with 24 hours without any treatment other than the initial Ampicillin given together with the Prostagladins), nausea, vomiting, diarrhoea, throbbing headaches, severe lower abdominal pains which ceased on abortion, and acute, severe bronchospasm which occurred in 2 cases. (Aminophylline was given in both to relieve the bronchospasm).

All the abortions were incomplete.

Conclusion:

Although 77% of the cases aborted, the high incidence of side-effects and the fact that all the abortions were incomplete, make this method of administration of Prostagladins unsafe unless a new generation of prostaglandins with fewer side-effects is used.

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Table II

PGF_2

Case No.	Nationality	Age	Pzrity	Gestation (weeks)	No. 1	Of 2	Injections 3	Result	Last Injection-Abortion Interval	Sice Effects
1	Malay	30	3	4	5	10	20 mg.	Successful	4 hrs.	Pyrexia, nausea, vomiting mild dyspnoea (lasted w minutes)
2	Chinese	39	2	10	5	10	20 mg.	Successful	4 hrs.	Vomiting
3	Chinese	40	8	14	5	10	20 mg.	Successful	16	Nil
4	Chinese	36	2	14	5	10	20 mg.	Failed	—	Vomiting, Diarrhoea, Mild Dyspnoea (subsided after 3 min.)

1st injection 5 mg.
2nd injection 10 mg.
3rd injection 20 mg.

PGF was used in 4 cases of which 3 aborted after the third dose of 20 mg.
Side-effects occurred in 3 cases and were severe.
All the abortions were incomplete.

The Tampered Implant

Intra-medullary nailing of the Femur for fracture of the shaft-unusual difficulty in extraction: Case report.

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THE USE OF a clover leaf Kuntschner Nail I (1958) for the internal fixation of fracture of the shaft of a long bone isa well established technique. The intra-medullary nail finds its maximum use in dealing with fractures of the shaft of Femur. From the extensive writings of Kuntschner and others in this field, it would appear that the operation by the open method is very much standardised. Any difference, if at all, is in the different ways individual surgeons measure the exact length required of the K-nail. Several nails of varying length and diameter are usually kept on the instrument table. Only one, of appropriate length and diameter is used. Occasionally a transverse bar is used either at the upper or lower end to prevent ratation of the fracture.

Recently a patient was seen at the University Hospital, in whom, in order to fix a fracture of the shaft of Femur, *two half nails* (Figure I) were used.

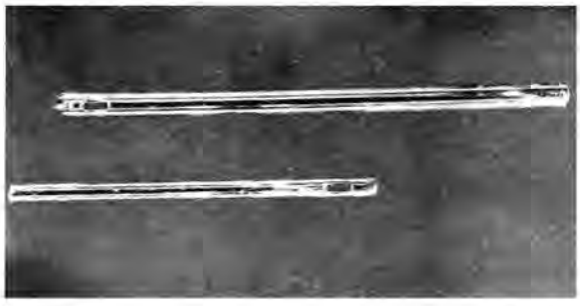

Fig. 1
The two 'half nails' that were removed from the Femur. Note the corroded metal at the sawn off ends. Both 'eye-lets' were buried in bone.

This was at another centre and three years before the present admission. The author had the unpleasant and tedious task of removing the nails, because of symptoms produced by 'metal reaction' on the bone.

Case Report

Patient A. M. a 30 year old Malay male presented with a history of chronic discharging sinus in the back of the right lower thigh for six months. Three years ago he had sustained a fracture of the right Femur. He had two operations for this, the second one apparently to cut off a 'protruding nail'.

On examination, his general condition was satisfactory. There was a low-grade fever. All systems were normal. There were two operation scars on his right thigh – one over the Greater trochanter and a second larger one on the antero-lateral aspect of the right thigh. At the lower part of the back of the thigh, was a discharging sinus. The discharge was thin and watery, and was sterile on bacterial cultures. The surrounding tissues were indurated and painful.

Radiological examination of the right thigh showed (Fig. 2) a satisfactorily united fracture of the shaft of Femur. The intramedullary nial was visualised but its outline was not clear. The upper thire of the nail appeared smaller in diameter than the rest of the nail. Though the radiological picture looked deceptively like a single nail, a correct appreciation of the presence of two nails was made preoperatively. The bone around the lower end of the nail showed 'reaction' to metal and a possible focus of osteomyelitis.

Fig. 2

X'Ray of the Right Femur showing the intramedullary nails. Note the translucent area of bone at the lower end of the nail, due to metal reaction.

Fig. 3

Post-operative X'Rays of the Femur, showing the area of bone removed to extract the nail.

At operation, the upper end of the nail was first exposed. There was no 'eye' to be seen and a tentative pull did not budge the nail. With a view to pushing the nail out from below, the lower part of the Femur was exposed and a roof of bone, measuring 4 centimetres in length and 2 centimetres in breadth was removed from the lateral surface. There was escape of a thin yellow fluid but no pus. With the lower end of the nail exposed, it was impossible to hammer this up. Exhausted, I decided to give a good pull to the upper end of the nail by a wrench. Quite unexpectedly, a nail measuring about 14 centimetres in length and 6 millimetres in diameter came out. The eye-let of this nail was at the lower end! The other nail was then gently coaxed up by blows with a mallet over a transverse rod and removed through the upper end with some difficulty. This measured 19 centimetres in length and 9 millimetres in diameter. The bone cavity which was exposed in the window was scraped clean and the wound closed with a Redivac drain in situ. The sinus at the back of the thigh was excised. (Figure 3).

Inspection of the nails (Figure 1) showed that both had been sawn off, at approximately their middle. It appeared that the sawn off lower end had set up electrolytic changes in the adjacent bone resulting in osteolysis of the bone and sinus formation. Swabs taken from the cavity of the bone and the sinus tract did not grow any organisms.

Discussion:

There are occasions when two nails may be required, especially when the medullary cavity is spacious and the nails of the necessary diameter are not available. In such a case, two clover leaf nails devetailed to each other are used without cutting them. A search of the literature did not reveal the use of two 'half nails'. It should be pointed out that tampering with implants such as bending or cutting, produces a focus of electrolytic activity. This causes the adjacent bone to necrose and set up inflammatory changes in the surrounding tissues, requiring the removal of the implant. Metallic implants that are available now are certainly of very superior quality and for all practical purposes are inert and can be left in situ indefinitely. When multiple implants are used such as plates and screws or nails, care must be taken to see that both metals are the same quality. Preferably they should be from the same manufacturers and if possible the same batch of production.

There is one consolation in the present case, namely, the two 'half nails' did achieve their intended purpose – the fracture had soundly united.

Summary

A report of an usual case of Intramedullary nailing of the Femur is presented. Special attention has been drawn to the incidence of electrolytic changes in tampered implants, and the difficulties of a second operation, if the implants require to be removed. More care should be exercised in the technique of implant surgery.

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A Comparison of Trimethoprim-Sulphamethoxazole and Penicillin/Streptomycin in the Treatment of Gynaecological Infections

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Summary

A CONTROLLED TRIAL OF the use of trimethoprim-sulphamethoxazole and penicillin and streptomycin in gynaecological infections was undertaken. One hundred and fifty five patients were treated in two randomly selected groups. Clinical responses were much better with trimethoprim-sulphamethoxazole in similar type of gynaecological infections. Significant responses were seen with septic abortions and post-operative gynaecological infections. ($p > 0.02 < 0.05$). For all groups, good responses were obtainable in 70 per cent of cases treated with trimethoprim-sulphamethoxazole and 50 per cent of cases treated with penicillin and streptomycin. The bacteriological studies correlated well with the clinical response. The invitro sensitivity was not significantly different. ($p > 0.8 < 0.9$). The side effects were minimal with both drug combinations.

Introduction

Trimethoprim-sulphamethoxazole has been reported in the treatment of various infections. Results have been generally favourable notably in the treatment of urinary tract infections (Brumfitt et al, 1969; Cox et al, 1969; Lao et al, 1971), gonorrhoea (Csonka and Knight, 1967; Lao et al, 1971) and acute gynaecological infections (Chong and Lean, 1970). We have previously reported on a clinical and bacteriological study of the use of trimethoprim-sulphamethoxazole in obstetrical and gynaecological infections (Ng et al, 1973) .

Of importance in the use of trimethoprim-sulphamethoxazole in gynaecological infections is whether it is better than previously commonly used drugs or drug combinations. This is with special reference to the use of penicillin/streptomycin combinations which have been very commonly used in the treatment of acute gynaecological infections. This paper presents the results of a clinical trial comparing the use of trimethoprim-sulphamethoxazole and penicillin and streptomycin in the treatment of acute gynaecological infections (excluding urinary tract infecitons).

Materials

One hundred and fifty five cases of gynaecological infections as seen in the gynaecological ward of the University Hospital, University of Malaya Medical Centre, were included in this study. The cases included the common infections seen in the gynaecological wards, namely acute pelvic inflammatory diseases, septic abortions and post-operative infections. We have specifically excluded urinary tract infections, there being obvious difficulty in comparison of effects and responses, as penicillin and streptomycin have minimal clinical effect on urinary tract infections.

Diagnosis was chiefly based on clinical and laboratory findings. Laboratory investigations done, both as a method of diagnosis and as a method of assessing treatment, were total white and differential counts, microscopic examination and culture of urine, and culture of cervical and high vaginal swabs, and of pus from sites of infection when indicated.

Patients were randomly selected and treated with trimethoprim-sulphamethoxazole. A course of treatment consisted of 2 drapsules twice a day for five days given orally. The remaining patients patients were treated with intramuscular injections of procaine penicillin and streptomycin. Penicillin

was prescribed as procaine penicillin 1 mega by intramuscular injection and streptomycin was given as 1 gram. by intra-muscular injection daily.

Daily assessment of the patient was made. Improvement was based on disappearance of pyrexia, lowering of the pulse rate to normal and disappearance of pain and tenderness. Possible side effects were specifically asked and looked for.

Responses were divided into 3 categories namley good, moderate and poor. Cases in which symptoms and signs of infection disappeared rapidly, that is, within 48 hours were considered to have responded favourably. In cases where symptoms and signs disappeared much more gradually, that is more than 48 hours but less than 96 hours, the response was considered as moderate. In cases where the condition of the patient remained the same or deteriorated, the response was considered to be poor.

Results

Table I(a)
Use of Trimethoprim-Sulphamethoxazole

Clinical Conditions	No. of Cases	Response		
		Good	Moderate	Poor
*Pelvic Inflammatory Disease	18	12	4	2
+Septic Abortions	40	31	7	2
Post-operative ≠Infections:	17	10	6	1
(a) Cellulitis	16	10	5	1
(b) Peritonitis	1	0	1	0
Total	75	53	17	5

* $p > 0.3 < 0.5$
\+ $p > 0.02 < 0.05$
≠ $p > 0.02 < 0.05$

Table 1(b)
Use of Penicillin and Streptomycin Combinations

Clinical Conditions	No. of Cases	Response		
		Good	Moderate	Poor
*Pelvic Inflammatory Disease	25	15	3	6
+Septic Abortions	40	20	16	4
Post-operative ≠Infections:	15	4	5	6
(a) Cellulitis	14	4	4	6
(b) Wound Infection	1	0	1	0
Total	80	40	24	16

* $p > 0.3 < 0.5$
\+ $p > 0.02 < 0.05$
≠ $p > 0.02 < 0.05$

Comments on the Results

From a comparison of the results so obtained, the combination of trimethoprim-sulphamethoxazole seemed to be more effective than parenteral penicillin and streptomycin. There was a good response in 70 per cent of cases when trimethoprim-sulphamethoxazole was prescribed [Table I(a)]. Good response was only seen in 50 per cent of cases which were treated with penicillin and streptomycin [Table I(b)].

The responses were significantly different in those patients treated with trimethoprim-sulphamethoxazole and those treated with penicillin and streptomycin. The results were significantly better when trimethoprim-sulphamethoxazole was used in the treatment of septic abortions and post-operative infections and pyrexia, when compared with penicillin and streptomycin under similar conditions [Table I(a) and I(b)].

Bacteriology

Out of the 155 patients, culture of organisms could only be obtainable from 102 i.e. 67 per cent. Out of the organisms cultured, 78 were considered pathogenic or possibly pathogenic. The sensitivity of these organisms were tested in vitro against both drug combinations.

Table II

Sensitivity of Organisms to Penicillin/Streptomycin Compared to Trimethoprim-Sulphamethoxazole in Patients Treated with Trimethoprim-Sulphamethoxazole

Organisms	No. Isolated	Sensitive to	
		Penicillin/ Streptomycin	Trimethoprim-Sulphamethoxazole
E. Coli	11	2	9
Staph. Pyogenes	9	5	8
Coliform Organisms	5	0	5
Proteus	3	0	3
Klebsiella Aerogenes	3	1	2
Pseudomonas	1	0	0
Strept. Faecalis	2	2	2
Haemolytic Strept.	3	3	3
Anerobic Strept.	2	2	2

Table III
Sensitivity of Organisms to Penicillin/Streptomycin Compared to Trimethoprim-Sulphamethoxazole in Patients Treated with Penicillin/Streptomycin

Organisms	No. Isolated	Sensitive to	
		Penicillin/ Strep-tomycin	Trime-thorpim-Sulphame-thoxazole
E. Coli	7	2	7
Staph. Pyogenes	8	4	8
Coliform Organisms	2	0	2
Klebsiella Aerogenes	3	1	3
Pseudomonas	4	3	0
Non-Haemolytic Strept.	2	2	2
Haemolytic Strept.	5	5	2
Anaerobic Strept.	2	2	2
Para Colon	6	4	6

As can be seen, the bacteria cultured were similar for both groups. More organisms cultured from both groups were sensitive to trimethoprim-sulphamethoxazole than were to penicillin and streptomycin. Out of the 78 pathogenic organisms 84.6 per cent (66) were sensitive to trimethoprim-sulphamethoxazole, and only 49.7 per cent (38) were sensitive to penicillin and streptomycin.

42.5 per cent (34) of these micro-organisms were sensitive to trimethoprim-sulphamethoxazole but not sensitive to penicillin and streptomycin.

7.8 per cent (6) of these micro-organisms were sensitive to penicillin and streptomycin but not sensitive to trimethoprim-sulphamethoxazole.

7.8 per cent (6) of these micro-organisms were not sensitive to both drugs.

All 5 cases of Pseudomonas cultured were insensitive to trimethoprim-sulphamethoxazole.

Table IV
Comparison of Sensitivity of Organisms to Drugs in In-Vitro Tests

Drugs		Total	Penicilin & Streptomycin	
			Sensitive	Resistant
		78	38	40
Trimethoprim-Sulpha-methoxazole	Sensitive	66	32	34
	Resistant	12	6	6

$p < 0.8 < 0.9$

A statistical analysis however showed that these findings were not significant.

Side-Effects

There were 2 cases of nausea and one with skin rash in those patients treated with trimethoprim-sulphamethoxazole.

Of those patients treated with penicillin and streptomycin, one developed a rash, probably urticarial in nature. Of particular interest in any comparison of usage, is that there were 3 patients who were supposed to have treatment with penicillin and streptomycin but were not so treated because of history and signs of allergic reactions. They were left out of the study.

Conclusion

It would seem that trimethoprim-sulphamethoxazole is more useful in the treatment of gynaecological infections than the combination of penicillin and streptomycin. This was significant for cases of septic abortions and post-operative infections.

In vitro bacteriological investigation showed that a greater proportion of organisms isolated from gynaecological infections would respond to trimethoprim-sulphamethoxazole.

The side effects were minimal with both drug combinations.

Acknowledgements

We thank Mr. A.E. Long of Roche, Malaysia for supply of Bactrim, Professor Donald Chan for arranging this trial, Miss P.K. Lee for secretarial assistance, and Professor T.A. Sinnathuray for permission to publish the results.

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Do-it-yourself Slides for Projection: An easy way

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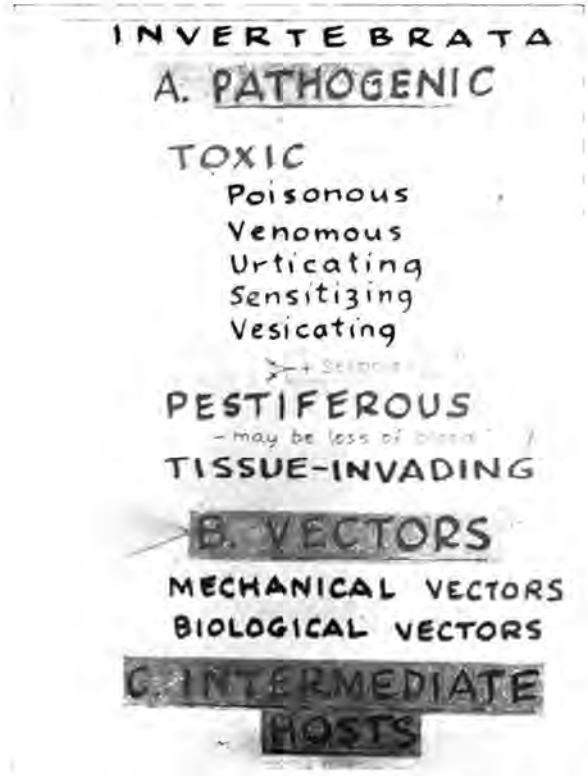
EFFECTIVE SLIDES for projection during lecturing or delivering papers can be made by using coloured felt-tip pens (heavy type) for the lettering and drawing, together with soft pencil or ink to add variety, on stout paper. These can then be photographed with colour film. Take the meter reading directly from the white paper and divide the exposure index of the film by 5 (High Speed Ektachrome should thus be used as if ASA 32). Colour film may be used for wholly black-and-white figures, but it is as well to take full advantage of the colour. It is often convenient to take the material outdoors for photographing.

A lightly pencilled frame of 12 x 8 inches is a useful size, but this may be altered by drawing a diagonal and fitting a convenient frame in the same proportions of a 35 mm negative. Letters and drawings should fill the pencilled frame, but allow a margin of more than 1/2 inch all around when photographing to compensate for the encroachment of the card frame in which the slides will be bound. Freehand lettering is effective but may be greatly improved if a soft pencil is used with a stencil as a guide. A moderately complex diagram with lettering, in several colours, can be completed in 20 minutes.

Charts from published works may be redrawn, usually to great advantage. Photograph the originals on black-and-white film, bind the negatives as slides (unless you use an enlarger, which is even easier), mark the necessary points in pencil on the 12 x 8 inch frame by projecting the negative, and fill in heavily with colour. At the same time, such charts may be edited to suit the talk, and parts of the caption may be transferred to the figure itself.

Aim at using *large* lettering — at least $\frac{3}{4}$ to $1\frac{1}{2}$ inches high with heavy felt pen in a 12 x 8 inch frame — so that most of the available space is filled with bold lettering and heavy lines. One advantage of this method is that the felt pens facilitate easy reading from the back of a hall. Another advantage is that use of a variety of colours makes it much easier for the audience to follow complicated charts — or any charts. Also, the slides are attractive to the eye.

Intermingling usual colour slides of scenes, patients, etc. with black-on-white charts requires constant readjustment of the eye after the glare of the charts. It is better to use heavy felt pens for the black-on-white charts and to photograph these with contrasty film given contrasty development. The *negatives* can be used effectively for direct projection of white on black; but it is nevertheless better to intermingle slides prepared as here described.



One type of slide that is very useful for keeping the audience informed while the subject is changed is a set of headings, perhaps in more than one colour. Shown repeatedly, each time with a moving arrow indicating a different line, it gives the audience an overview of the subject. Quick glances at such slides help to simplify a complex talk.

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Myocardial Infarction in Pregnancy
Case Report and Brief Review

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Kuala Lumpur,
Malaysia.

A 40 YEARS OLD Chinese lady, gravida nine, para eight, suffered two episodes of myocardial infarction in pregnancy, one at eight weeks and the other at seventeen weeks of gestation. She survived both episodes to give birth to a healthy male infant at terms. Despite medical advice and contraception, she became pregnant again two years later. This time the patient agreed to termination and an abdominal hysterotomy with tubal ligation was performed at 14 weeks gestation.

Case Report

K.Y., a 40 years old Chinese lady, gravida nine, para eight, was admitted to the University Hospital on 6th March 1968 with the diagnosis of recurrent myocardial infarction in pregnancy. Her last menstrual period was on the 7th of November 1967. On 2nd January 1968, at eight weeks gestation, she suddenly experienced a severe epigastric pain which radiated to the root of her neck. This was associated with cold sweat and dyspnoea. Soon after, she collapsed and was admitted to the Assunta Hospital where she was warded for fifty days. The pain subsided slowly after three days of injections and medications. One week after discharge, she again had severe epigastric pain, now associated with palpitations. The epigastric pain was aggravated by activity and relieved by rest. There was no orthopnoea, paroxysmal nocturnal dyspnoea or ankle oedema. She was admitted to the University Hospital on 6th March 1968, at seventeen weeks of gestation.

On examination, her blood pressure was 100/70 mm Hg. and her pulse was 120 per minute with extrasystoles. The jugular venous pressure was not raised and there was no ankle oedema. The apex beat was 12 cm from the mid-sternal line outside the mid-clavicular line in the 5th intercostal space. There were no thrills and the heart sounds were normal. There were no heart murmurs. The uterus was enlarged to eighteen weeks gestational size. Electrocardiagram showed Q waves with raised S-T segments and inverted T waves in the chest leads best seen in V3 and V4, indicating acute anterior myocardial infarction. Chest X-ray showed an increased transverse diameter of the heart with prominence of the left ventrivular segment consistent with left chamber enlargement; but on fluroscopy after delivery, showed no aneurysm. Serum glutamic oxalacetic transaminase (SGOT) was normal (10 IU/1) and so were her haemoglobin, white cell count, blood urea and electrolytes. The Kahn and Wasserman tests were negative. The serum cholesterol was 302 mg per cent and the erythrocyte sedimentation rate was 27 mm per hour. She was treated by bed rest, sedated with phenobarbitone and the pain relieved by injection pethidine, codeine phosphate tablets and glycerine trinitirte. No anticoagulants were given. She made an unevenful recovery and was discharged forty days after admission to be followed up in the antenatal clinic. Her pregnancy progressed uneventfully and her cardiac status remained satisfactory.

At the 29th week of her pregnancy, she was readmitted for bed rest. On 2nd June 1968, four days after admission, she developed severe retrosternal pain radiating to the back of her chest. An electrocardiogram showed further elevation of the S-T segments in leads I, AVL and V2 to V5 suggesting further ischaemic episode. She was again

treated with analgesics, sedation, bed rest and glycerine trinitirte. She improved and on the 1st of July 1968, she discharged herself against medical advice.

On 7th August 1968, she went into spontaneous labour and was admitted to the labour ward. The first stage of labour which lasted a total of eleven hours was uneventful. She had a spontaneous delivery to a live male infant weighing 2640 grammes after a very short second stage of seven minutes. Throughout labour, her heart was well compensated and she suffered no ischaemic episodes. No oxytocics was given and the blood loss was minimal. The puerperium was uneventful and she was discharged fourteen days after delivery. She was advised sterilization but she refused.

At the post-natal follow up, an intra-uterine contraceptive device was inserted. She was followed up in the cardiac clinic and remained well. However, she removed the contraceptive device and became pregnant again. In view of her previous myocardial infarction and her present cardiae status, her pregnancy was terminated by abdominal hysterotomy and tubal ligation on 14th December 1970 at 14 weeks gestation. She has since remained well.

Discussion

So far, there are forty-five reported cases of myocardial infarction in pregnancy and labour confirmed by electrocardiagram or enzyme studies (Hussaini 1971). Myocardial infarction is rare in women of the child-bearing age (Weinreb, German & Rosenberg 1957; Oliver 1970), since this condition occurs among elderly women. Also, circulating oestrogens in the pre-menopausal women is protective against atherosclerotic changes (Eilert 1949; Barr 1953). On the other hand, the total cholesterol increases and its distribution changes in normal pregnancy to resemble that found in patients with ischaemic heart disease; more cholesterol being attached to the p lipoprotein (Oliver & Boyd 1955). This is inspite of the greatly increased amounts of circulating oestrogens in pregnancy.

The diagnosis of myocardial infarction in pregnancy presents a clinical and electrocardiagraphic difficulty, since upper abdominal pain, flatulence and chest pain are common in normal pregnancy. Those symptoms may mask ischaemic heart disease and electrocardiographic diagnosis of the condition has to be corelated with the clinical picture (Fletcher 1967). In the later months of pregnancy, the QRS axis may rotate leftwards owing to the elevation of the diaphragm and a deep Q wave deflection may appear in lead III. Similarly, active pulmonary embolism may produce abnormal Q wave deflection, especially in lead III and S-T segment and T wave changes which may mimic postero-diaphragmatic infarction.

Management consists essentially of supportive treatment to prevent cardiac decompensation, suppressing the thrombo-embolic tendency which is considerable during pregnancy and management of the pregnancy itself. The patient should be adequately sedated and potent analygesics given. These drugs will help to reduce the shock. Angina can be treated with glycerine trinitrite and cardiac failure by digitalisation. In the presence of shock, congestive cardiac failure, embolism or recurrent myocardial infarction, anticoagulants should be employed. This is even more so in the pregnant patient because of venous stasis in the lower limbs and the pelvis and the increased thrombo embolic tendency in pregnancy (British Medical Journal 1970).

Subsequent management of the pregnancy depends on the cardiac status. If failure and angina persists, it appears that termination of the pregnancy is of remarkable therapeutic value (Hussaini 1971). Of forty-six patients with myocardial infarction in pregnancy and labour, thirteen died and of these, eleven were cases of myocardial infarction occuring at or after thirty two weeks of gestation. The other two occured at five and six months respectively and died soon after the episode. It would seem that myocardial infarction in the later part of pregnancy carries a far worse prognosis than if it occured in early prgnancy. All patients who recovered from the initial infarction survived the rest of pregnancy and labour. This may be because in early pregnancy, there is time for the patient to convalesce before being subjected to the strain of labour.

Management of labour depends entirely on the cardiac status and the prospect of a short and easy vaginal delivery. In a multiparous woman in whom reasonably easy vaginal delivery is expected, this is the route of choice. On the other hand, if her cardiac status is decompensated and labour might be expected to be prolonged by say disproportion, then Caeserean section is prefered. The anaesthetic risks involved and the danger of hypotension should be weighed against the hazards of permitting a patient who has just suffered a myocardial infarction to labour relentlessly. Of nine cases who underwent Caeserean section, one died. She had a myocardial infarction near term (Lynge 1961). Ergometrine should not be given routinely in the third stage in patients who have recently suffered a myocardial infarction. The ergot group of drugs has long been known to cause generalized arterial and coronary vasoconstriction. Stein and Weinstein

(1950) concluded that Ergometrine B.P. in doses of 0.2 – 0.6 mg had a direct tonic effect on the coronary vasculature and Canning (1969) attributed a case of myocardial infarction immediately after delivery, to the administration of Syntometrine (ergometrine 0.5 mg; Pitocin 5 i.u.) at the time of delivery.

In the post-partum period, early mobilization is preferred. If this is not possible due to her cardiac status, one should consider anticoagulant therapy. The patient should be advised against further pregnancy and sterilization offered.

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Book Reviews

HEALTH SERVICE PROSPECTS — Edited by I. Douglas Wilson and Gordon McLachlan. Publ. by The Lancet and the Nuffield Provincial Hospitals Trust Lond. 1973. p.p.346; $6.

THIS IS an international survey covering eleven countries from China and Japan in the East to Cuba and USA in the West. The conditions in each of these countries are described by a national of the country, who writes from long and expert first-hand knowledge and observation. The book brings out clearly the great differences that exist in the organisation and ideology of the health services in these countries. At one end is the predominantly free-enterprise approach of the United States and at the other is the emphasis on State Health Service represented by the United Kingdom. The developing countries are marshalling their limited resources against environmental hazards at the same time trying to keep pace with the expensive technology of modern medicine. The more developed countries without the closely knit family ties have to contend with the care and maintenance of aging populations. However rich, these countries cannot meet the soaring cost of the maintanence of health and treatment of illnesses, and the trend is towards more efficient management and economical use of resources.

This is a book that should be in the hands of not only medical and health administrators but also of politicians, sociologists, planners and doctors.

ADVANCES IN MOLECULAR GENETICS — Edited by W. Hayes British Medical Bull. Vol. 29 No. 3. 1973 Publ. by The British Council, 65 Davies Street, London, WIY 2AA.

THIS IS a symposium designed to illustrate the most important steps forward in knowledge and techniques in this rapidly expanding field of molecular genetics. The fifteen papers cover various aspects of chromosomes, particularly that of replication, the nature and behaviour of RNA, and phage, cytoplasmic, viral and behavioural genetics. This will be of interest, not only to those working directly in the field of molecular genetics, but also the biochemists, microbiologists and cancer research workers.

CHEMOTHERAPY OF MALARIA AND RESISTANCE to ANTIMALARIALS — WHO Tech. Rpt. Series No. 529 pp. 120. Geneva.

THE PROVISION OF effective chemoprophylaxis and treatment of malaria is still a major problem in tropical countries. The present report is concerned specifically with (1) the important role that 4-aminoquinolines may still play in the prevention and treatment of malaria, (2) improved techniques for evaluating the response of malaria parasites to drugs, (3) a critical appraisal of the present geographical distribution of resistance to the 4-aminoquinolines, (4) a review of promising new antimalarial drugs currently under evaluation and (5) the need for continuing effort in the field of malaria chemotherapy.

This report contains the collective views of a WHO international scientific group of experts on the chemotherapy of malaria and resistance to antimalarials which met in October, 1972.