time towards activities which are in themselves rewarding, enjoyable, and satisfying. Our policy chimes in with the way people naturally feel about sport and games[3 17] (Table IV).

But people cannot play games and go in for physical recreation unless there is a place where they can do so. Therefore, in pressing for a more realistic and appropriate level of recreational provision (as we do in *Provision for Sport*[18] and *Sport in the Seventies*,[19] and now in our "Sport for All" campaign) we can claim that we are not only abiding faithfully by our avowed goal but also doing what may in the long run—when an exercise and health relationship is definitely established—prove to be of service to the nation's physical and mental wellbeing. Sport is to be seen not simply as part of a fully rounded life but as an *essential* part and should not be treated as a residual element when it comes to spending of Government or local authority funds.

What kind of facilities make sense? There are now 50 indoor sports centres built and 100 more in construction.[20 21] Such sports centres have proved an outstanding success and are clearly major costs in sporting provision of the future. They make sense in a country with uncertain weather and long dark winter evenings. Any properly managed centre is full all day and every evening, used for activities like badminton, squash, handball, gymnastics, judo, dancing, even theatricals, not to speak of restaurant and crèche. The recreational facilities for new schools can be designed for community use too, extra money for capital and running costs coming from the local authority. This makes sound social as well as financial sense. I can foresee a time when sports facilities, squash courts, recreation rooms, and swimming pools will become a mandatory and integral part of every major new building, whether it be hotel, factory, flat, or office block—as usual and necessary as modern plumbing.

As doctors we are in danger of being cast in the bleak role of saying "no" to so many things—eating, smoking, drinking, drugs, and now even to too many babies. Somehow our cumulative advice is deadening, giving people a negative view of health. Instead could we not say a massive "yes" to innocent, wholehearted recreational pursuits, so giving a considered, buoyant, positive view of health? Over a century ago Sir Edwin Chadwick, whose memory we honour today, fought to improve the water supply, drainage, and cleansing of our great cities. Now that these and so many other health battles have been won can we not join the new planning battle of the next decade for realistic community recreational provision in order to, as Åstrand[13] said, "add life to years, not just years to life"?

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Hospital Topics

Follow-up of Hydatidiform Mole by Radioimmunoassay of Human Chorionic Gonadotrophin

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British Medical Journal, 1972, **4**, 715–719

Summary

An improved method for the follow-up of patients delivered of a hydatidiform mole using radioimmunoassay of human chorionic gonadotrophin is employed to ensure adequate sensitivity. Four illustrative case histories are described. Their HCG findings are presented to show that this is the principal basis on which decisions should be made.

There are three aspects to the work of the laboratory. The technical work of the assay, the clerical effort of patient follow-up, and the clinical interpretation of results. The laboratory keeps a close check on follow-up (one of its most important functions) and receives specimens direct from patients. Overall control of all three aspects is by a clinician. It has been found useful to organize a special clinic for these patients to be seen. In this region it has been possible for this to be run by the same clinician.

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Introduction

For many years gynaecologists have been taught that patients recently delivered of a hydatidiform mole should be "followed" for a period of two years lest a choriocarcinoma develop undetected. Traditionally follow-up consisted in clinical examination and "pregnancy" testing every three months. It has recently been appreciated that more frequent follow-up is necessary, particularly in the early months after delivery of a hydatidiform mole.

Many attempts have been made to improve follow-up procedures, yet Bagshawe *et al.* stated recently: "It is apparent from this series that strenous efforts have been made by

clinicians to achieve good follow-up of their patients with mole, but that this is difficult to achieve. Diagnostic delays have resulted from a variety of factors such as patients' failure to keep appointments. They have also resulted from technical failures with pregnancy tests, from the use of particularly insensitive pregnancy tests, from the inadequate sensitivity for this purpose of even the most sensitive pregnancy tests, from the failure of positive reports to reach the attention of the clinician responsible, and from failure to interpret both positive pregnancy tests and radiological evidence of pulmonary metastases as evidence of a potentially fatal process. . . . A few patients said that no arrangements were made for clinical examination or follow-up tests after their moles had been evacuated."[1]

Although it was felt that these features did not apply to this region, an attempt was made in the Eastern Region of Scotland to centralize the control of follow-up of patients who had been recently delivered of a hydatidiform mole.

Clerical Arrangements of Laboratory

Patients who had been delivered of a hydatidiform mole or had been noted to have molar changes in the placenta usually provided a specimen of urine which was sent to the laboratory from the ward or clinic for estimation of chorionic gonadotrophin (HCG). Close contact was maintained with the pathology department through Dr. W. W. Park, reader in pathology at the University of Dundee, and any histological findings suggestive of hydatidiform mole were notified to the assay laboratory.

Patients known to be positive histologically from whom no urine specimen had been received were sought after receiving the permission of the consultant in charge. All cases were recorded by the laboratory and arrangements made for the regular collection of aliquots of 24-hour urine specimens direct from the patient. Subsequent specimens were asked for on a regular basis and any failure in receipt of specimens was actively investigated and the appropriate action taken. It was decided that two years would be the usual follow-up period. Assays were undertaken initially weekly and, if consistently low, then fortnightly and, finally, monthly. The number of assays undertaken and reported on for a case which remained low in titre throughout was about 30. The results were reported to the clinician in charge with a comment on interpretation.

Material and Method

The method was based on the work of Midgley[2] with minor modifications.

Anti-HCG was supplied by Dr. Vernon C. Stevens, Department of Obstetrics and Gynecology, Ohio State University, Columbus, Ohio.

Anti-rabbit Gammaglobulin prepared from donkeys was purchased from Wellcome Laboratories and diluted 1:32 in phosphate-buffered saline.

Labelled HCG.—HCG supplied first by Dr. K. D. Bagshawe, Charing Cross Hospital (Fulham), and later by Dr. Stevens was labelled with ^{131}I and later ^{125}I by the method of Greenwood *et al.*[3] Recently the already labelled HCG has been supplied lyophylized by Dr. Bagshawe.

Standards.—The second International Reference Preparation of HCG was used to prepare a standard curve with which all unknown specimens were compared.

Urine Samples.—Patients were instructed to collect a 24-hour specimen and to measure the quantity. An aliquot was sent to the laboratory and stored at 4°C usually without preservative, though Merthiolate (thiomersal) was used if storage was to be prolonged or for aliquots of specimens submitted by post.

Results

The results were processed direct from the paper tape output of the gamma counter by a programmable desk calculator using a programme[4] which mathematically computes the standard curve and prints the result if it falls within the limits depicted by the dots (Fig. 1). No manual calculations are necessary.

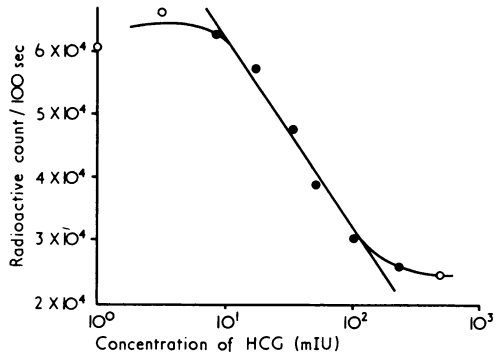

FIG. 1—HCG concentration related to radioactive count. Logarithmic scale on X axis. In the computer programme the values noted with open circles are ignored in calculating the line.

Case 1

The first patient was 34 years old and had three children, the youngest of whom was aged 2. She had had no previous illnesses of note and requested termination and sterilization. On admission to hospital the size of the uterus was compatible with a 14-week pregnancy. Hysterotomy and sterilization were performed through a midline incision, and only at the time of hysterotomy was the molar pregnancy discovered.

Histological examination showed hydatidiform mole with some degree of trophoblastic proliferation. HCG follow-up was arranged (Fig. 2) She regularly attended the special "mole" clinic, and in two months the uterus had involuted completely and her periods had returned to normal. Follow-up continues. This is an example of the hoped for results and is representative of most cases.

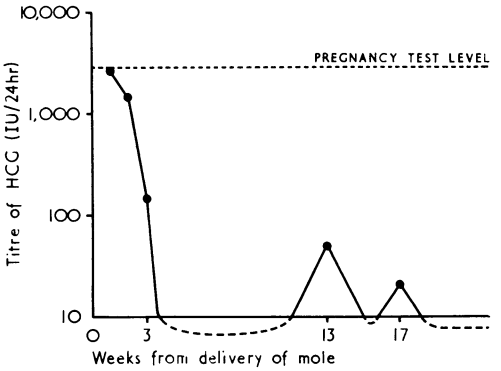

FIG. 2—Case 1. Titres of HCG after delivery of mole. Logarithmic scale on Y axis. LH peaks can be seen.

Case 2

This patient, 28 years old, married, and nulliparous, had had a partial thyroidectomy and appendicectomy in the past. She was referred to the antenatal clinic but was admitted immediately to the gynaecological ward with vaginal bleeding. She had had amenorrhoea for 10 weeks but the size of her uterus agreed with a 14-week pregnancy. No fetal heart sounds could be detected and a pregnancy test was positive in a dilution of 1:100. Hydatidiform mole was the clinical diagnosis and an ultrasonic scan was arranged. The scan was not conclusive but further bleeding occurred and the clinical diagnosis was unchanged. Five days later another scan suggested incomplete abortion with no fetus identifiable, and on the basis of the strongly positive pregnancy test the assay laboratory was informed and HCG follow-up was started. (Fig. 3.)

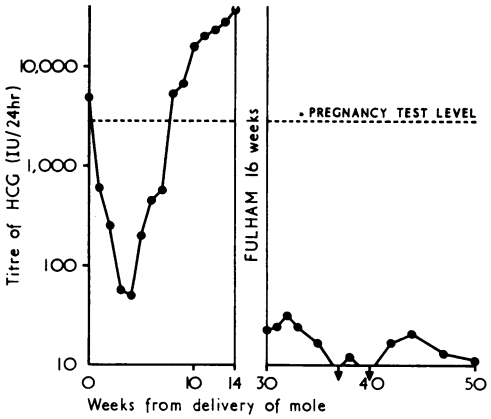

FIG. 3—Case 2. Rise in HCG titre due to presence of chorionic tissue.

Abdominal *x*-ray examination showed no fetal parts and unsuccessful attempts were made to induce labour with oxytocin. She was then taken to the theatre for hysterotomy and a hydatidiform mole was removed. Histologically this was of a moderately hyperplastic type, which was felt to imply a 5% risk of subsequent choriocarcinoma. Chest and skull *x*-ray films were clear. Eight days after hysterotomy she was discharged from the ward for HCG follow-up by the laboratory and clinical follow-up by her own consultant.

Six weeks later she was seen in the outpatient department. A heavy period had occurred some four weeks previously and the uterus was still bulky. The next appointment was arranged for six weeks ahead again, but frequent assays were made of HCG levels, and in view of the titre (Fig. 3) she was admitted to the ward two weeks after this visit. The chest *x*-ray film was still clear and vaginal examination showed a normal sized uterus with non-cystic ovaries. Curettage was performed and the curettings were sent to the pathology laboratory, which reported: "endometrium with decidual changes and chronic endometritis. No villi and no trophoblast seen." In spite of these findings, on the basis of the HCG titre alone arteriography was arranged. This showed a large tumour circulation supplied by the left uterine artery, the appearances consistent with a trophoblast tumour (Fig. 4). Admission to Fulham Hospital was arranged. At the time of writing she was well and radioimmunoassay showed normal levels of luteinizing hormone (LH).

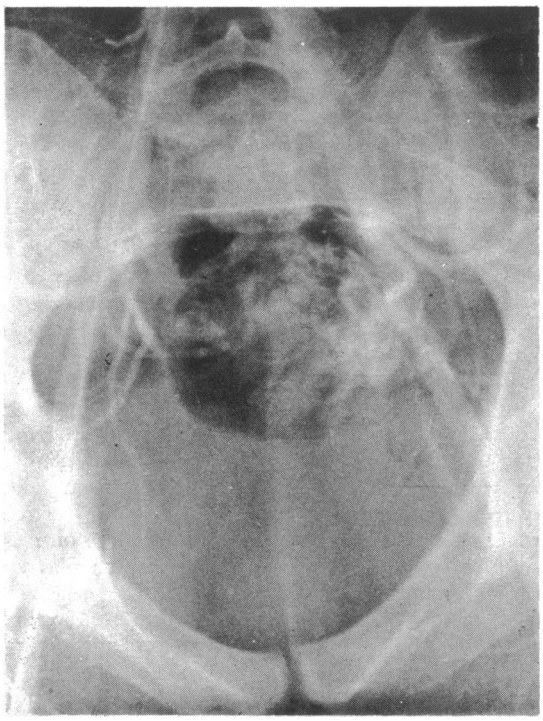

FIG. 4—Case 2. *X*-ray film showing main blood supply by left uterine artery.

Case 3

An 18-year-old single girl with no previous pregnancies had undergone appendicectomy nine months previously. She was complaining of abdominal pain, nausea, and vomiting with irregular periods. The uterus was found to be larger than the period of amenorrhoea suggested, being compatible with about 16 weeks' gestation. No fetal heart could be heard. A pregnancy test was found to be positive at a dilution of 1:300. The clinical impression was of a hydatidiform mole, and an oxytocin infusion was given after which typical vesicles of hydatidiform mole were passed.

She was taken to the theatre shortly afterwards and suction curettage completed the evacuation of the uterus. Palpation of the ovaries suggested the presence of luteal cysts. Subsquent chest *x*-ray examination showed nothing abnormal and HCG follow-up was arranged. Histologically the trophoblastic layer of the hydatidiform mole was proliferative. She was discharged to the mole clinic two days after evacuation and attended regularly. The uterus quickly became well involuted and her periods were re-established. Later, however, a rise in titre was noted (Fig. 5) of the same type as the previous case. On this occasion the uterus had reached eight weeks' size. A scan confirmed the clinical impression that she was pregnant. At the time of writing pregnancy was continuing normally.

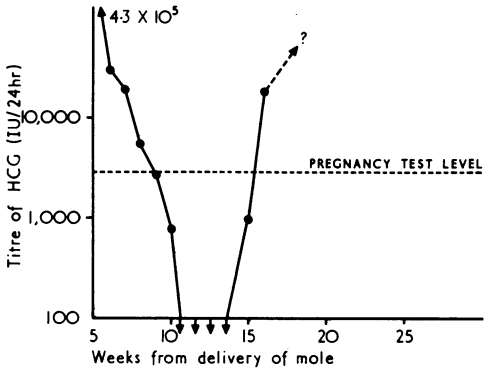

FIG. 5—Case 3. Rise in HCG titre due to pregnancy.

Case 4

The last patient was a 23-year-old para 1 with no previous illnesses of note. She gave a history of having had a normal period 15 weeks before, with some vaginal bleeding six weeks previously, and intermittent bleeding since. The uterine size agreed with the date of last menstrual period and she had had no bleeding since then. She was advised to rest at home and to book at the antenatal clinic at once. She did not do this until another 10 weeks had elapsed, at which time the uterus had reached only 16 weeks' size and no fetal heart could be heard even with ultrasound. Three weeks later ultrasonic scan showed no fetal outline and no fetal heart was heard, and on this basis a tentative diagnosis of incomplete abortion was made. Ultimately she was admitted to the gynaecology ward where a pregnancy test was said to be negative and the external os was found to be open. An attempt was made at evacuation with an oxytocic drip, but using even 1000 units in 500 ml it was not successful. She was taken to the theatre where the uterus was evacuated and molar tissue remnants were obtained. A repeat pregnancy test was positive but negative in a dilution of 1:10. Histological examination showed a largely dead hydatidiform mole, wide areas having no trophoblast, and where there was trophoblast it was very minimally hyperplastic. On the basis of this report HCG follow-up was arranged.

Repeat ultrasonic scan 10 days after evacuation showed areas of hydatidiform mole adherent to the upper part of the uterus and the pregnancy test was still positive. On pelvic examination three weeks after evacuation it was suspected that the bowel was adherent to the top of the uterus. In view of these findings she was returned to the theatre for laparotomy. The terminal ileum and sigmoid colon were densely adherent to the posterior uterine wall, where there was a half-inch (1·3-cm) perforation; wide areas of trophoblastic tumour were visible. Molar tissue

was removed from both bowel and uterus and the uterine defect excised and sutured. Subsequent skull and chest *x*-ray pictures were normal. The pregnancy test was negative. Histologically the material showed omental tissue with occasional degenerate villi and trophoblastic giant cells. The pathologist added his opinion: "I do not regard this as a part of a choriocarcinoma." The HCG radioimmunoassay results are shown in Fig. 6.

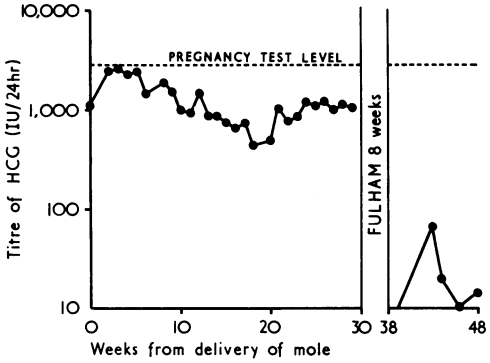

FIG. 6—Case 4. HCG titres after delivery of mole. Though levels were high, for many weeks they were below average "pregnancy test" sensitivity.

She was referred to the mole clinic, and during follow-up the uterus was noted for some time to be bulky, but otherwise no abnormality was detected clinically, her periods becoming, so far as she could tell, normal. Five months after evacuation she had another period, which was normal, and thereafter developed amenorrhoea. Throughout this time the level of HCG assays (Fig. 6) had not been at all reassuring, and again on this basis alone arteriography was arranged (Fig. 7). This showed a large trophoblastic tumour in the pelvis with massive arteriovenous shunt in the ovarian vein region. Once again chest and skull *x*-ray films were clear but nevertheless her admission was arranged to Fulham Hospital for treatment. She made a very satisfactory recovery and subsequent follow-up showed normal levels.

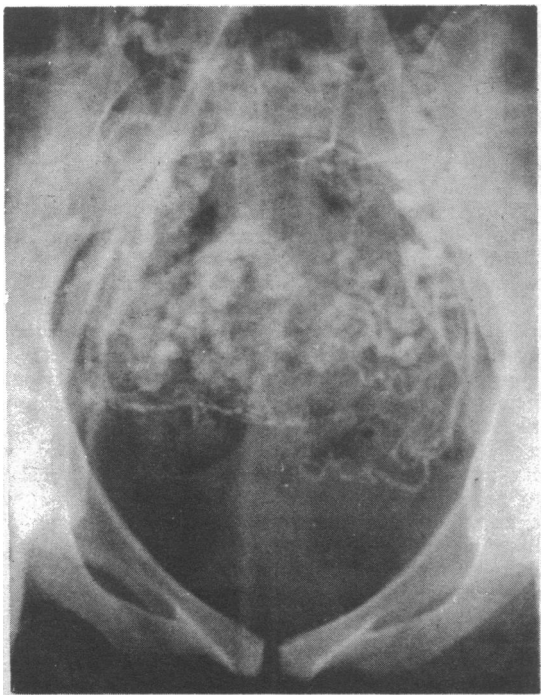

FIG. 7—Case 4. *X*-ray film showing main blood supply by ovarian arteries.

Discussion

Perhaps the most crucial role of the laboratory has been its careful and frequent follow-up. The quotation given above shows this is often neglected. The difficulties encountered and the time required to be sure that all patients are registered, receive appointments and send specimens at the correct time, are contacted when they fail to report or send a specimen, and are traced when they change their address or even when they are admitted to another hospital department should not be underestimated. To do this properly requires great clerical effort and includes enlisting the support of the clinician in charge, the general practitioner, and, on occasion, the health visitor and the executive council. Since this service was instituted only one patient has been lost within the two-years of follow-up, and this was not pressed because she was in the last three-months of the follow-up period.

The follow-up of Case 2 shows how inappropriate and dangerous spaced-out appointments are immediately after delivery of a hydatidiform mole, especially if, as is often the case, HCG testing is also spaced out. The first six months are important, the first three months perhaps crucial, for the detection of trophoblastic growth early enough to ensure cure. In this case after a normal fall in titre the sinister secondary rise (Fig. 3) in HCG was obvious early in the recurrence of the growth.

The second most important aspect of the assay service is its great sensitivity, as Case 1 shows. The assay quite fortuitously picked up two LH peaks four weeks apart, indicating that the patient was then ovulating (Fig. 2). The anti-HCG antibody used in the assay cross-reacts with LH and indeed is used for this purpose in the laboratory and by other workers.[2 5] Case 4 (Fig. 6) shows clearly the practical importance of this sensitivity. Without it the pregnancy test, chest and skull *x*-ray pictures, and histological examination of the curettings would all have encouraged inappropriate complacency throughout the period when, in fact, the patient was and should have been causing active concern.

Case 3 highlights a problem in interpretation of this sinister secondary rise (Fig. 5), which in this case was a result of pregnancy. Contraceptive advice is offered to all patients attending the special follow-up clinic. It has been recommended that use of the pill should be avoided since oestrogens may favour the development of invasive change;[6] this is doubtful, however, and when necessary the pill has been prescribed. In Case 3 the patient admitted afterwards that she wanted a baby and had no intention of following our advice.

Since HCG assay is the method of follow-up and is overwhelmingly more important than (though it does not exclude) clinical follow-up and since efficient collection of further specimens is so central to success, the laboratory should share with the clinic and consultant in charge this responsibility. In this region it has been possible to arrange for a special clinic for postmolar patients, which is run in close collaboration with the laboratory. One can expect virtually to eliminate what can be for the young family a particularly disastrous tragedy—the occasional death after hydatidiform mole. These young women can now have their full health restored including reproductive function if diagnosed in time. The results are often dramatic. Park[7] cited Bagshawe's case of blindness from choriocarcinoma metastases in which after treatment the patient was completely cured and had her sight restored.

Our own experience of a case referred from Africa (not included in this series) diagnosed there after craniotomy after a normal birth is also instructive. The patient was investigated here referred to Fulham Hospital for treatment, and made a complete recovery from her choriocarcinoma but an incomplete recovery from neurosurgery. Such a result is not unique. This case emphasizes another and most important point; at best only half the cases of choriocarcinoma can be diagnosed by postmole follow-up and it requires much effort to achieve this. The other cases occurring after childbirth or abortion must be diagnosed by the watchfulness of gynaecologists, physicians, surgeons, ophthalmologists, neurosurgeons, and others, such is the protean character of choriocarcinoma's symptomatology.

Another, radically different approach to the problem of choriocarcinoma after hydatidiform mole has been by pro-

phylactic chemotherapy to all patients delivered of a mole.[8-11] Many of the series so far reported probably are not large enough to evaluate the efficiency of this procedure,[1] but the dangers to patients of this prophylaxis is considerable and the cost must be much higher than careful follow-up and treatment of only a selected few. Goldstein asked "Is it justifiable to administer chemotherapy to all patients with molar pregnancy when only about 20 per cent of the total number actually develop life-threatening sequelae, particularly when careful gonadotrophin follow-up permits early selection of those patients who are destined to develop trophoblastic neoplasia."[12]

Radioimmunoassay is a comparatively complex technique, but once established many assays are as easily carried out as a few, particularly with automatic data processing. It would be most efficient if a few centres were geared to give such a service and adequate clerical staffing could be supported. In this region the success of such an arrangement has been apparent and strongly supports the comment, "a case can therefore be made for having some form of centralized follow-up service. . . . It could be arranged for patients to be sent instructions and requisites for urine collections from a central laboratory. The patients would post the specimens to the laboratory, which would in turn send the assay result to the referring clinician and inform the patient when to send in the next specimen. Such a service would aim not to replace follow-up arrangements made locally but to provide the clinician responsible for the patient with supplementary information."[1] Even this understates the position. The information derived from the HCG level is not supplementary it is the central pillar of hydatidiform mole follow-up, and it is the clinical follow-up which is supplementary.

It is intended to extend this laboratory service to any clinician anywhere who wishes to make use of it.

Throughout the time the method was being organized Dr. K. D. Bagshawe and his staff were unfailingly helpful, and this has continued. The co-operation of Dr. Vernon C. Stevens, Ohio State University, Columbus, Ohio, and his staff has been invaluable. Thanks are also due to Mrs. R. Booth and Mrs. J. Marnie for their technical and clerical help. Such work is not possible without the co-operation of clinical colleagues, to all of whom I am grateful. Professor J. Walker by his support and helpful advice throughout the development has made the service possible.

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Outside Europe

Concept of a Paediatric Emergency Ward for the Cities of a Developing Country

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British Medical Journal, 1972, 4, 719–722

Summary

Children's hospitals in developing countries carry an enormous patient load. Available facilities must be organized to provide essential care for all. At the Red Cross Children's Hospital in Cape Town this has been achieved by the development of an emergency ward attached to the outpatient department. It is suggested that this concept should be applied in large hospitals of other developing countries.

Introduction

Oliver and Fage[1] listed South Africa as the first country on the continent to witness an appreciable movement of rural Africans to urban areas. They dated this phenomenon from the early 1920s, when secondary industries producing for the local market were first established. The ensuing 50 years have seen this pattern recur in every country in Africa. There are now vast conurbations of people in whom increasing sophistication and the awareness of the advantages of modern treatment have created a demand for hospital care which far exceeds the available facilities. The economic structure of developing countries provides their administrators with a choice —either a limited service of high standard for the fortunate few while the rest are turned away, or the organization of available facilities in such a way that the essentials of adequate care are provided for all who seek it. In Cape Town, at the Red Cross Children's Hospital, the latter course was chosen, and this report indicates the extent to which the aim of essential care for all has been achieved through the concept of an emergency ward.

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Case Load

Children who attend the hospital are drawn predominantly from greater Cape Town, which has a population of 1,064,468.