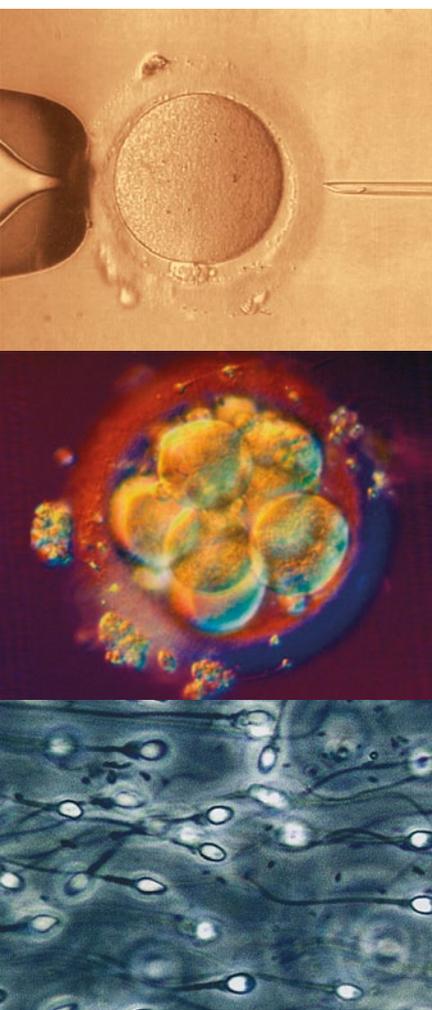


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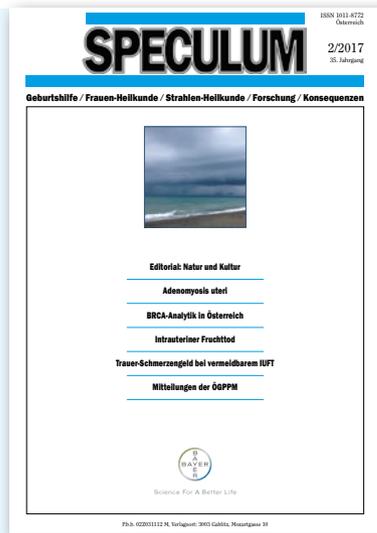
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First Steps into Gynaecological Endocrinology and Reproductive Medicine in Resource-poor Countries: An Eritrean Experience

C. Gnoth¹, H. Kaulhausen², S. Marzolf³

Background: Gynecological endocrinology and reproductive medicine within the reproductive health systems of developing countries is underappreciated and methods to incorporate basic infertility workup and treatment needs to be addressed. However, most recommendations of how to proceed in particular, though, are very general. We exemplarily report our approach in Eritrea. **Methods:** Two one-week intensive training courses on gynecological endocrinology and reproductive medicine (lectures and hands on training) were given 2011 and 2012 at the Orotta National Referral Maternity Hospital in Asmara, Eritrea. Important subjects included: education and training in contraception fertility awareness, methods to optimize fertility potential, utilization of vaginal ultrasound for cycle monitoring, performance of hysterocontrastsonography, and one-step semen preparation for intrauterine inseminations. **Results:** After two intensive courses a basic infertility work up is possible with pelvic ultrasound assessment and contrastsonography for tubal patency. Simplified intrauterine inseminations after mild ovarian stimulation are possible as well and represent the first step into assisted reproduction. All procedures are feasible and performed independently by the trainees. **Conclusions:** Basic gynecological endocrinology and infertility care in resource-poor countries is possible. The Eritrean example of intensive courses with training in hysterocontrastsonography and one step intrauterine inseminations may encourage others to follow and introduce basic infertility care into other resource-poor countries.

Key words: developing countries, infertility, fertility awareness, low-cost gynecological endocrinology and infertility treatment, simple infertility work up, Eritrea

Gynäkologische Endokrinologie und Reproduktionsmedizin in einem Entwicklungsland: Erste Erfahrungen am Beispiel Eritreas. *Hintergrund:* Der unerfüllte Kinderwunsch in einem Entwicklungsland bedeutet für betroffene Frauen ein schweres Stigma mit sozialem Abstieg und gesellschaftlicher Isolation. Ein dringender Handlungsbedarf wird heute auch von der WHO nicht mehr in Frage gestellt. Allerdings gibt es kaum Vorschläge zum Vorgehen in der Praxis. Wir berichten deshalb von unseren Erfahrungen in Eritrea. *Methodik:* Am Orotta National Referral-Hospital in Asmara, Eritrea, haben wir 2011 und 2012 jeweils einen Intensivkurs in Gynäkologischer Endokrinologie und Reproduktionsmedizin abgehalten und mit angehenden Fachärzten dort eine Sterilitätssprechstunde durchgeführt. *Ergebnisse:* Das Ursachenspektrum der Sub- und Infertilität in einem Entwicklungsland unterscheidet sich deutlich von dem in westlichen Ländern. Es handelt sich oft um junge Frauen mit entzündlichen Tubenschäden und Regeltemporstörungen bzw. Männer mit den Folgen genitaler Infektionen. Dazu kommt ein kaum vorhandenes Wissen über den Zyklus oder die zyklusabhängige Fruchtbarkeit. In beiden Intensivkursen wurden deshalb die Gebiete natürliche Fertilität, Kontrazeption, Optimierung der natürlichen Fertilität und die Infektionsprophylaxe besonders berücksichtigt. Die Interpretation von Basaltemperaturkurven zur endokrinologischen Diagnostik erlaubt das Erkennen wichtiger Pathologien auch ohne endokrinologisches Labor. Die einfache Sterilitätsdiagnostik wird erweitert durch die standardisierte Durchführung von Postkoitaltests, der Nativmikroskopie des Ejakulates und durch die Durchführung von Hysterocontrastsonographien zur Abklärung des Tubenfaktors. Auch therapeutische Schritte konnten eingeführt werden. Clomifenstimulationen und Ovulationsinduktionen sind möglich. Wichtige Prozeduren sind die intrazervikale Insemination (Nativsperma bei der häufigen Parvispermie) und intrauterine Inseminationen nach Aufbereitung des Spermias mit einem „Ready-to-use“-Einmalset. Ein andrologisches Labor ist nicht erforderlich. *Schlussfolgerung:* Das hier vorgestellte Beispiel soll Mut machen, auch in anderen sogenannten Entwicklungsländern in gynäkologischer Endokrinologie und Reproduktionsmedizin auszubilden und erste Schritte einzuführen. **J Reproduktionsmed Endokrinol 2013; 10 (1): 44–8.**

Schlüsselwörter: Gynäkologische Endokrinologie, Reproduktionsmedizin, Entwicklungsland, natürliche Fertilität, Kontrazeption, intrauterine Inseminationen, Hysterocontrastsonographie

■ Introduction

Gynecological endocrinology and infertility treatment in resource-poor countries is under appreciated within the global agenda of reproductive health, yet causes severe social and psychological suffering in affected couples. Worldwide, around 6 to 12% of couples are faced with problems of subfertility. In developing countries, population surveillance studies report a prevalence of infertility up to 25% [1]. These numbers, though, must be interpreted cautiously

because infertility is a hidden fate in traditional societies of developing countries [2]. This hidden fate causes extensive economic consequences for the childless elderly couple whereby the lack of children leads to loss of financial and family supportive security. Important known causes of infertility in developing countries are male and female infectious diseases (sexually transmitted, unhygienic obstetrics and abortion practices, female genital mutilation), ovulation disorders due to malnutrition and long-term couple separation due to mi-

gratory work or military service. Specific reasons for the lack of diagnosis and treatment in cases of infertility are (1.) poor awareness and shame, (2.) unavailability of tools for diagnosis and treatment and (3.) the high-cost of interventions [3].

This hidden problem of infertility in developing societies has gained more and more scientific attention [3–6] and the possibilities of western biomedicine and its effectiveness have attracted attention also in the general population especially

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in countries with Internet access [7]. The World Health Organization (WHO), important scientific organizations of reproductive medicine, and non-governmental organizations (NGOs) are fortunately aware of this challenge to incorporate infertility care into programs of family planning, motherhood care and reproductive health [8]; and, in addition, to adapt infertility care to local needs and resources [9]. Within the literature, though, there is very limited information as to how to implement basic and cost effective infertility services in low resource settings. This article reports our encouraging experience with first steps into infertility care in Eritrea.

The Orotta National Referral Maternity Hospital in the capital city of Asmara has the largest national delivery ward in Eritrea with more than 9,000 deliveries per year. Since 2003, the maternal mortality has decreased from 752 to 486 per 100,000 live births in 2010. With the help of "Hammer Forum", a German NGO (www.hammer-forum.de), a new maternity hospital was built and with the support and supervision of the Ministry of Health, a postgraduate medical education program in obstetrics and gynaecology was implemented in 2009 with the first batch of Ob/Gyn specialists, educated and trained in Eritrea, graduating in 2012. The gaps in the Ob/Gyn residency curriculum were filled with technical, academic, and practical assistance by external visiting faculties from Germany, the Netherlands, the USA and Sudan. Early on, officials became aware of the urgent necessity of including gynaecological endocrinology and assisted reproductive techniques into the curriculum and training of the residents. A huge demand for infertility diagnosis and treatment became obvious. Therefore, the Hammer Forum was asked to start a pilot project of implementing basic infertility care. We set-up a program of two intensive courses in gynaecological and reproductive endocrinology (GRE) and assisted reproductive techniques (ART) adapted to the needs, restricted resources and individual circumstances of the Orotta National Referral Maternity Hospital in Asmara.

■ Pre-conditions

The first intensive training course was given in March 2011. At that time the

Orotta National Referral Maternity Hospital in Asmara had an annual estimate of 10,600 outpatient visits in the outpatient department (OPD) and more than 9,000 deliveries p.a. The surgical performance comprised about 1000 caesarean sections and about 200 major gynaecological surgeries per year. The clinical and surgical work was done by six Ob/Gyn senior consultants and the five Ob/Gyn residents with support from midwives, nurses and anaesthetists.

Two ultrasound machines with an abdominal and vaginal scanner are available. Principally, hormonal assays for LH, FSH, estradiol, testosterone and progesterone are available but the capacity of performing hormonal analyses is very limited. There is one phase contrast microscope in the general clinical laboratory of the Orotta National Referral Hospital where native semen analysis can be performed.

■ Structured Intensive Courses of GRE and ART

The first intensive course for physicians (five residents in Ob/Gyn and six senior Ob/Gyn consultants (general obstetricians and gynaecologists)) was given in March 2011. It included 20 hours of lectures in the afternoon over one-week and hands on training under supervision in the outpatient department (OPD) in the morning. For the afternoon sessions on family-planning and reproductive health, medical students and midwives were invited to attend.

The content of the lectures followed the "Curriculum for Subspecialty Training in Reproductive Medicine" by the Royal College of Obstetricians and Gynaecologists of 2007 (United Kingdom, <http://www.rcog.org.uk/files/rcog-corp/uploaded-files/ED-SUBSPEC-RM-Curriculum.pdf>) and for teaching natural fertility regulation we based on own material and media from the Institute for Reproductive Health (Georgetown University, Washington, DC, USA; <http://www.irh.org>). The contents were adapted to the local needs and focused on the intended introduction of natural fertility regulation, hysterocontrastsonography, ovarian stimulation and intrauterine inseminations. In addition, the theoretical parts should also prepare the residents for their postgraduate examination in

obstetrics and gynaecology in front of an international board in February 2012.

The subjects of the first course were in detail:

- basic facts on human fertility from menarche to menopause [10]
- reproductive health with special emphasis on infectious diseases (particularly: obstetrical infections, tuberculosis) and sexually transmitted diseases
- natural methods for family planning (contraception [11–13] and fertility awareness [14, 15]) with particular emphasis on interpretation of basal body temperature charts for diagnostic purposes
- menstrual cycle physiology and menstruation disorders (primary and secondary amenorrhea, hyperandrogenaemia)
- basics of modern contraception
- diagnosis and treatment options of endometriosis
- basic pelvic ultrasound with particular emphasis on vaginal ultrasound and hysterocontrastsonography using ultrasound contrast gel and foam or saline [16–18]
- basic semen analysis and performing and interpretation of post-coital-tests [19–23]
- ART under circumstances of poor resources from intrauterine insemination to mini-ivf [24]
- basics of ovarian stimulation and cycle monitoring

In the OPD, the trainees were exposed to the relevant elements of infertility work up and were trained using case demonstrations and discussions. In addition, the trainees were taught to counsel patients about the methods of taking their basal body temperature [25–27], recording and interpreting cervical mucus symptoms which can be observed externally [28–30]. Under supervision, the Ob/Gyn residents deepened their technique of both abdominal and transvaginal vaginal ultrasound scanning. Ovarian stimulation with clomiphene, cycle monitoring for follicular development and ovulation induction with human chorionic gonadotropin (hCG) for timed intercourse were introduced. Clomiphene is on the list of urgent drugs and available in Eritrea. Progesterone for luteal phase support (100 mg vaginally) and hCG for ovulation induction were brought in.

As oral contraceptive pills (OCP) are not generally accepted and patient compliance for taking OCP's is suboptimal, we emphasized the possibilities of natural methods for fertility regulation [31, 32] in the lectures and practical training sessions. For medical doctors and midwives the two-day-method for fertility regulation was introduced [33, 34] and under supervision the residents were able to teach patients in the outpatient department. The two-day-method has been proven to be an effective method of fertility regulation for child spacing and to reduce the number of children [33]. The very important advantage of natural methods for fertility regulation is the imminent health education for women. This health education is urgently needed as the knowledge on menstrual cycle physiology, conception probabilities throughout the cycle and the prevention of infectious diseases is rather low in the general population [35]. Fortunately the interest of Eritrean women in health education and fertility regulation is high and it also allows increased self autonomy.

In February 2012 the second intensive course was given at the Orotta National Referral Maternity Hospital in Asmara to the same five Ob/Gyn residents, six Ob/Gyn consultants and an additional four new Ob/Gyn residents within the postgraduate medical education program. In between the two intensive courses, exchange of information by e-mail had taken place. Again the intensive course included hands on training under supervision in the outpatient department (OPD) in the morning and 10 hours of lectures in the afternoon over one week.

Subjects of the second course were in detail:

- interpretation of basal body temperature charts with special regard to the endocrinological diagnosis (case discussions and problems)
- endocrinological work up (clinics, laboratory tests and interpretation) for amenorrhea, hyperandrogenaemia, luteal insufficiency and bleeding disorders
- ovarian stimulation protocols with clomiphene and human menopausal gonadotropin and adequate monitoring
- basic semen analysis with video training [23]
- clinical cycle monitoring by assessing cervical index (Insler-score [15])



Figure 1: First hysterocontrastsonography (HyCoSy) performed by the OB/GYN residents in the Orotta Referral Maternity Hospital in Asmara, Eritrea. Nachdruck mit freundlicher Genehmigung aus: [Der Frauenarzt 6, 2012].

- ultrasound cycle monitoring
- assessing ovarian reserve by antral follicle count [36]
- hysterocontrastsonography (HyCoSy [18])
- indications for intracervical insemination (especially for low total semen volume, a common problem after male genital infections)
- one-step intrauterine inseminations using a simplified swim-up procedure for sperm preparation with ready to use sets

At the second visit every morning 10–20 patients with infertility problems were presented. As taught in the first course, basal body temperature charts and basic laboratory tests were discussed and analysed. If necessary, further tests were requested and their possible impact on diagnosis and treatment-strategy were discussed.

The residents and seniors were trained in transvaginal ultrasound for pelvic exploration and cycle monitoring in natural and mildly stimulated cycles. The ultrasound scans were performed with a Siemens Sonoline SI 250 ultrasound machine which was donated by Hammer Forum. Additionally, the Ob/Gyn residents and seniors were trained and able to perform hysterocontrastsonography using a newly developed and ready to use kit for hysterocontrastsonography ([17], HyCoSy, ExEm Foam®, <http://www.dikatec-medizintechnik.de/ExEmFoamKit.html>; <http://www.exemfoamkit.co.uk>) (Fig. 1).

With the German company *Gynemed* we prepared “ready to use” kits for one-step, standardized intrauterine inseminations (IUI) (<http://www.gynemed.de/Insemination-Kit.404.0.html>) based on the experience of others [37]. The kit comes complete with all the necessary materials for one IUI procedure. It is a one-step system that simultaneously selects and washes high quality sperm for intrauterine insemination. It recovers high-quality, motile sperm from semen in less than one hour. The method is very simple and takes only five minutes of actual labor time. The semen sample is simply placed into a vial at the bottom under the culture media (a modified Ham’s F-10, physiological medium with proper pH which contains NaCl, KCl, KH_2PO_4 , $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$, NaHCO_3 , $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$, Dextrose-Anhydrous, Na-Lactate, Na-Pyruvate, EDTA, Na-Alanyl-Glutamine,

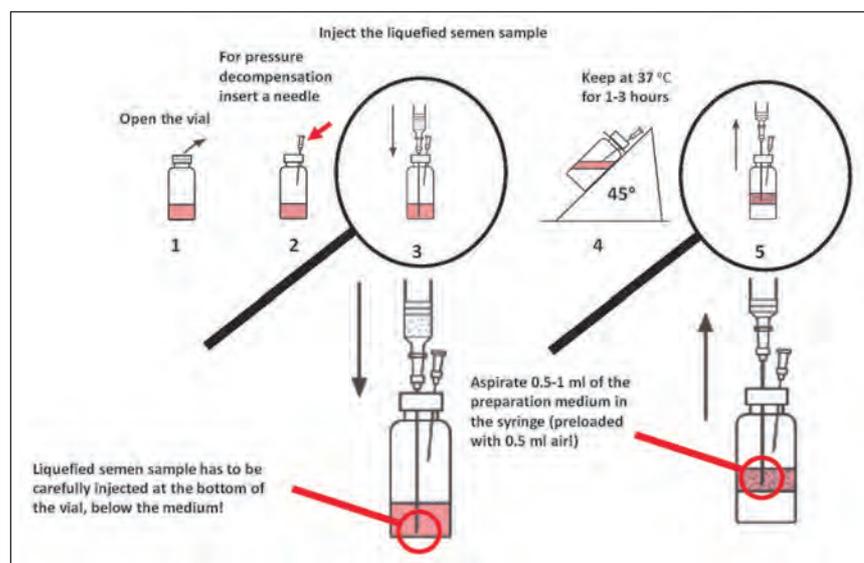


Figure 2: Sperm preparation with a modified and simplified one-step swim up method for intrauterine insemination.

water, non-essential and essential Amino Acids, 21 mM HEPES, Human Serum Albumin (5.00 g/liter), Gentamicin (10 mg/liter), Phenolred). During the incubation period (approximately 45 minutes), the healthy, motile sperm swim up out of the conical cavity and swim down into the medium where they are then aspirated and used for insemination (Fig. 2). The manufacturer recommends use of the kit if the ejaculate is normozoospermic or slightly oligo- and/or asthenozoospermic. An andrological laboratory is not necessary. The semen preparation may be performed in an OPD itself. The residents and the staff were trained to prepare semen samples and perform intrauterine inseminations.

■ Achievements

The Supervisor's Point of View

After two intensive training courses with 30 hours of lectures in GER and ART and additional hands on training under supervision the Ob/Gyn residents and the consultants were skilled in the following areas:

- fertility awareness for contraceptive use and optimising fertility for achieving a pregnancy (2008)
- basic gynaecological and reproductive endocrinology
- interpretation of basal body temperature charts for endocrinological diagnosis
- clinical and ultrasound assisted cycle monitoring
- hysterocontrastsonography for pelvic exploration and assessment of tubal patency
- basic sperm analysis
- performance and interpretation of postcoital tests
- intrauterine inseminations with a modified swim-up procedure for sperm preparation after ovarian stimulation with clomiphene citrate
- basic documentation of interventions

During the one-year interval the interest in infertility care had increased. The Ob/Gyn residents were much more aware of diagnosing infertility problems and seeing patients for these reasons in the outpatient department. The Ob/Gyn residents who completed both intensive courses may now work independently. Their knowledge was proved by taking their postgraduate examination in obstetrics and gynaecology in front of an

international board in February 2012 under supervision of the Eritrean authorities. All five residents passed the examination and now Eritrea has its first batch of specialists in Ob/Gyn educated and trained in Eritrea and licensed by the Ministry of Health.

A follow up of their achievements with a consultation service will be done per Email and a follow up visit is scheduled for 2013.

The Trainee's Point of View

Dr. Abraham Yohannes and Dr. Fithawi Girmay, Orotta Maternity Hospital, Asmara, Eritrea: *"The intensive courses and training in GE and RM opened a wide gate for further steps in this subject. The courses were very comprehensive and all the topics were discussed thoroughly. This has great impact on our way of thinking of what we had been reading in the literature and on adapting it to our case scenarios that pertain to low resource circumstances. We are now skilled to perform transvaginal ultrasound for routine pelvic examination, for follicular growth follow up, check of ovarian reserve by counting antral follicles and to do hysterocontrastsonographies. In the meanwhile 19 hysterocontrastsonographies and 2 IUI (using the readymade kit) were done independently. From the 19 patients 14 were found to have patent tubes. In four cases a clear diagnose by hysterocontrastsonography was not possible. In one case an Asherman's syndrome was diagnosed which was confirmed by hysterosalpingography later. For example, by doing saline injection for hysterosonography four patients were diagnosed to have big submucous myomas. These possibilities of vaginal ultrasound scanning with saline and/or contrast medium are a great step forward because laparoscopic techniques are available only in exceptional cases in Eritrea yet. Hysteroscopy is not possible. Despite all these achievements we suffer from shortages of the contrast medium and catheter systems for hysterocontrastsonography, HMG and HCG for ovarian stimulation and ovulation induction, progesterone for luteal phase support and readymade kits for IUI. This list was given to the Department of Family and Reproductive Health. We see many patients in urgent need of infertility care in Asmara, Eritrea."*

■ Discussion

The implementation and incorporation of two intensive courses on basic reproductive and infertility care into an existing Ob/Gyn residency program is not only feasible but provides a solid foundation and method of sustainability to address this important reproductive health issue. Infertility is an under represented problem in resource-poor countries [38] and recommendations of how to proceed have been previously very general [5, 39].

Gynecological endocrinology and infertility treatment in resource-poor countries should be part of an integrated health care program of family planning and reproductive health. Governments, non-governmental organisations and health-care professionals should target mainly at the prevention of infertility. Thereby education is the most effective solution to achieve this goal. Education programs therefore should address menstrual cycle physiology, fertility awareness for contraception or optimising fertility, infertility-causing factors, sexuality and of course applicable techniques of infertility treatment. Thereby the early diagnosis and treatment of genital infections and sexual transmitted diseases is a first important step into treatment. The audience should include midwives, physicians and other health care professionals.

Often modern assisted reproductive techniques are high cost interventions. Therefore research is needed and experiences must be gained to develop simplified approaches: simplification of diagnostic tests, simplification of assisted reproductive techniques and at a low cost level. In our experience Fertility awareness methods play an important role as a diagnostic and interventional tool and it can easily be taught.

In addition, ultrasound machines for vaginal and abdominal scanning are available in most gynaecological and obstetrical units in developing countries in the meantime. The Eritrean experience shows that with some hands on lessons, a routine vaginal ultrasound for pelvic exploration and cycle monitoring can easily be implemented in the infertility care of patients. Moreover, we assured ourselves that hysterocontrast-

sonography with reliable results is also possible as noted in other studies [40].

Using a simple phase contrast microscope, basic semen analysis for sperm cell concentration, motility, morphology and signs of infections is possible. This is an important precondition for implementing intrauterine inseminations after sperm preparations in mildly stimulated cycles [41]. Without a laboratory a simplified sperm swim-up preparation is possible without reducing the efficacy of insemination treatment [42]. Also, patient's young age compensates probably less effective possibilities of ovarian stimulation and sperm preparation techniques [43].

Experience with these first steps of infertility diagnosis and treatment will form not only the basis for further interventions like intravaginal culturing as part of a low cost "mini-IVF" [24] in the future but will also allow a successful and sustainable infertility program with the help of the Eritrean authorities at this national referral hospital. A close, computer-based follow up of treatment procedures will be initiated next year with increasing numbers of treatment cycles. This Eritrean example may encourage others to follow.

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Since 2003 the German NGO "Hammer Forum" (www.hammer-forum.de) has supported the constitution of a capable hospital and clinic for obstetrics and gynaecology in Asmara, the capital of Eritrea. The "Hammer Forum" is a German non-governmental organisation giving medical care especially to children in conflict areas worldwide, supporting programs reducing neonatal mortality (mother-child health care programs) and supporting training programs of locals to attain independency and sustainability. The "Hammer Forum" is officially recognized and financed by donations. The team members of "Hammer Forum" work without payment and "Hammer Forum" does not charge any of its activities in the different fields.

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