CORRIGENDUM

Data Collection Form.

1. **Form 4.1F question 4**, ‘other laboratory tests and results’ should have been printed in UNSHADED AREA; therefore this question may be answered for every subject.

2. **Form 7.1M question 5**, ‘other laboratory tests and results’ should have been printed in UNSHADED AREA; therefore this question may be answered for every subject.

3. **Form 7.2M question 26**, ‘leucocyte karyotype’ should read:

   26. Leucocyte karyotype
   
   1. XY  2. XO  3. XXY  4. Other abnormal (specify)
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MANUAL FOR THE INVESTIGATION AND DIAGNOSIS
OF THE INFERTILE COUPLE

1. Introduction

This manual is intended for use with the forms and flow charts for the investigation and diagnosis of the infertile couple. It is of utmost importance that each investigator participating in the programme read this manual carefully prior to the start of the study, and refer to it routinely as questions arise during the study.

The purpose of this manual is to attempt to unify and standardize both the minimal and optimal diagnostic procedures which lead to the effective management of the infertile couple.

If one wants to compare the results reported from different centres, a uniform approach needs to be adopted for at least the following procedures: the diagnostic selection of subjects for treatment of infertility; the choice of therapy; the treatment scheme; the monitoring of therapy; and the parameters of follow-up. Additionally, comparison of the results obtained in various groups of patients at the same centre, and more so, of patients treated at different centres is only possible if a well-defined and reproducible diagnostic classification and treatment method has been used.

1.1 The Forms

The instructions contained in this manual are to be used in conjunction with the forms designed for this study. The forms have been prepared with two purposes in mind—firstly, to serve as data collection instruments for this WHO sponsored study, and secondly, to serve as the clinical records for the patient if the physician so desires. Care has been taken to leave spaces for details which the physician may wish to include in the patient record.

The form booklet consists of duplicate copies of each form, to be completed by placing carbon paper between the two pages. The copy of each page is retained at the centre, while the original is sent to WHO.

1.1.1 Purpose of the Forms

The following is a list of the forms to be used for the study, and the general purpose of each.

Screening form: (Not in booklet but in separate pads).

Purposes: (a) to determine the eligibility of patients for participation in the study
(b) to determine the number of patients attending the clinic who complain of infertility.

Form 1 – Registration form and history of couple

Purpose: to register the couple as study participants, and to obtain background and general characteristics such as age, duration of marriage/union, duration of infertility etc.

Form 2 – History of female partner

Purpose: To obtain information regarding the medical history of the female partner, related to both infertility and general health.

Form 3 – Physical examination of female partner

Purpose: To obtain detailed information regarding physical signs and symptoms which may relate to infertility.

Form 4 – Diagnostic procedures for female partner

Purpose: To obtain detailed information of diagnostic value for infertility.
Form 5 – History of the male partner

*Purpose:* To obtain information regarding the medical history of the male partner, related to both infertility and general health.

Form 6 – Physical examination of the male partner

*Purpose:* To obtain detailed information regarding physical signs and symptoms which relate to infertility.

Form 7 – Diagnostic procedures for the male partner

*Purpose:* To obtain detailed information of diagnostic value for infertility.

1.1.2 Shade Coding of the Forms

The printing on the forms for this project has been shade coded in order to:

1) facilitate completion of the forms and
2) avoid spending time asking the patient questions which are not applicable.

The coding scheme is as follows:

1. *Questions* printed in UNSHADED AREAS are to be answered for every subject.
2. *Questions* printed with HATCHING (////////) are optional, and may be completed at the discretion of the physician.
3. *Responses* printed in UNSHADED AREAS indicate that the interviewer should STOP asking further questions in the particular question group (which will be in SHADED AREAS), and continue with the next question printed in UNSHADED AREAS.
4. *Responses* printed in SHADED AREAS indicate that the interviewer should continue asking further questions in the question group which are in SHAIDED AREAS. The interviewer should then continue with subsequent questions printed in UNSHADED AREAS.

Below are examples of the coding scheme:

**Examples:**

Form 2.3 19

Form 5.3 16 Number of previous marriages

Form 6.2 13 Varicocele

1. none
2. visible
3. palpable
4. valsalva positive

The above questions are answered for every subject.

Form 5.1 4 History of mumps 1. no
INTRODUCTION

In the above question, if the answer to part (1) is 'no', do not complete parts b and c and continue to the next question printed in an UNSHADED AREA.
If the answer to part (a) is 'yes', answer parts b and c and continue to next question.

Form. 1.1 7 Ethnic group

The above question is optional and is hatched.

1.2 The Flow Charts

Located at the end of the form booklet are two flow charts: 1) Flow chart for the diagnosis of infertility in the female, and 2) Flow chart for the diagnosis of infertility in the male.

The importance of these flow charts cannot be overstressed. They illustrate the diagnostic pathways which have been developed for the purposes of standardization for this and other studies dealing with infertility.

The use of these flow charts will ensure that in all centres the same symptoms and tests will result in the same diagnosis, and that for a given diagnosis, no symptom or necessary test will be overlooked. The flow charts ensure that to arrive at Diagnosis A it will be necessary to pass through points a, b, c and d. They also indicate the next stage of investigation necessary to achieve a specific diagnostic category from the results of a specific test or procedure.

AN INVESTIGATOR SHOULD INDICATE ON THE FLOW CHART FOR EACH PATIENT THE PROGRESS THROUGH THE CHART WHICH WILL EVENTUALLY REACH THE PARTICULAR DIAGNOSTIC CATEGORY.

The order in which tests and procedures are presented on the flow chart is not necessarily the same order in which they appear on the forms. The study forms are designed with the clinical situation in mind, while the flow chart is designed to achieve maximum discrimination.

1.3 Operational Working Definitions

Abnormal semen analysis: Characteristics or measurements which divert from the normal value. See normal semen analysis below.

Abortion: any termination of pregnancy (either spontaneous or induced) taking place during or before the 20th completed week of pregnancy or where the fetus weighs less than 500 grams.

Amenorrhoea, primary: The patient after the 18th birthday has never experienced spontaneous vaginal bleeding.

Amenorrhoea, secondary: Absence of spontaneous vaginal bleeding for 6 months or more.

Aspermia: Absence of seminal fluid.

Azoospermia: The absence of sperm in the ejaculate.

Consanguinity: The marriage/union of two partners who are related as first cousins or closer.

Dysmenorrhoea, idiopathic, (primary or essential): Lower abdominal pain at or about the time of menses not associated with symptoms of the premenstrual tension syndrome and not associated with a demonstrable pelvic lesion.
Dysmenorrhea, acquired (secondary): Lower abdominal pain at or about the time of menstruation associated with a demonstrable pelvic lesion.

Dyspareunia: painful vaginal intercourse.

Ectopic pregnancy: Pregnancy occurring outside the uterine cavity.

Family: Father, mother and siblings.

Galactorrhea: is present when any fluid which is not blood stained can be expressed from the breast after firm manual pressure on the areola.

Hypospadias: A developmental anomaly in the male in which the urethra opens on the ventral side of the penis or on the perineum.

Infertility, primary: The woman has never conceived despite cohabitation, exposure to pregnancy, and the wish to become pregnant for at least 12 months.

Infertility secondary: The woman has previously conceived but is subsequently unable to conceive despite cohabitation, exposure to pregnancy and the wish to become pregnant for at least 12 months. If the woman has breast fed a previous infant, then exposure to pregnancy should be calculated from the onset of regular menstruation following delivery.

Live birth: Any baby born alive whether it is now living or dead.

Molar pregnancy (including hydatidiform mole, invasive mole, chorio-carcinoma): Hydatidiform change in chorionic villi involving all or part of the placenta. Fetal parts or evidence of embryo formation may or may not be present. This definition includes the recovery of malignant trophoblastic tissue from the uterus (chorio-carcinoma).

Normal menstrual pattern: Regular menstrual bleeding at intervals of not more than 35 days and not less than 21 days i.e. 28 ± 7.

Normal semen analysis: Semen analysis in which all parameters fall within the following ranges:

- Volume: 1.5–6.0 mls
- Motility: >40% progressively motile sperm
- Viability: >60% with supravitral staining
- Density: >20 X 10⁶ spermatozoa/ml
- Agglutination: <10%
- Morphology: >50% normal forms
- WBC’s: <1 x 10⁶/ml

Oligomenorrhea: Infrequent or scanty menstruation—bleeding at intervals from 36 days to 6 months.

Presumptive evidence of ovulation: The following are taken as presumptive evidence of ovulation.

1. Pregnancy
2. The presence of a corpus luteum
3. Secretory endometrium
4. Plasma or serum progesterone greater than 5 ng/ml (15 nmol/l)
5. Pregnanediol excretion of greater than 2.5 mg/24 hours (7.5 nmol/24 h). These latter 3 parameters should be estimated 5–9 days before the anticipated onset of menstrual bleeding.

A pregnanediol excretion of between 1.5 and 2.5 mg/24 hours (4.5–7.5 nmol/24 h) and plasma serum progesterone concentration of 3–5 ng/ml (9–15 nmol/l) are suggestive of ovulation but require further evidence to confirm it.

Phimosis: Tightness of the foreskin so that it cannot be drawn back from over the glans.

Stillbirth: Any infant born dead after the 20th completed week of pregnancy weighing more than 500 grams.

Tubal patency and appearance: Tubal patency can be established by either laparoscopy and hydrotubation or by hysterosalpingography. The former technique has a lower incidence of false
negative results and provides additional information about the state of the pelvic organs (e.g. the presence or absence of adhesions).

Hysterosalpingography on the other hand gives information about the intrauterine cavity. Tubal insufflation is not a reliable way of establishing tubal patency.

2. Instructions for the Use of Study Forms

2.1 The Screening Form

This form is used to establish the eligibility for participation in the study of persons visiting the clinic and complaining of infertility. The criteria for participation in this study are as follows:
1) The couple has been infertile for one year or more during which time they have been trying to achieve pregnancy.
2) Both partners are available for interview.
3) Both partners are willing to undergo the necessary procedures once they have been explained to them.

Patients not qualifying for this study should be treated in the clinic’s usual manner. The study forms may be used for the patient’s clinical record, but copies should not be sent to WHO.

All Screening Forms should be retained at the centre, both for the qualifying and non-qualifying patients, as they may provide important information regarding the clinic workload, etc.

2.2 The Booklet Cover

2.3 Form 1 – Registration and History of the Couple

It is recommended that initially the couple should be interviewed together. Although it is recognized that in many instances this may not be possible, it is to be encouraged.

Form 1 — Registration form and history of couple

*Question No.*

0a–d Form code and study number are preprinted on each page. Enter the participating centre number and couple number in the boxes provided.

1a, b Enter the full name of (a) the male partner and (b) the female partner, family name first, on the line provided. These names should not be visible on the copy of the forms sent to WHO, in order to maintain confidentiality.

2 Enter the day, month and year of entry into the study of the couple.
3a-d  Enter the day, month and year of birth of the male partner (a) and female partner (c). If date of birth is unknown code 99 99 99 and enter estimated age in years (b, d).

5  Duration of infertility is the number of months the couple has been attempting to conceive. (N.B. If less than 12 months, the couple should not be included in study). If duration is 98 months or more, code 98.

6  The marriage/union is consanguinous if the partners are first cousins or closer.

7a, b  Optional: the ethnic groups of the (a) male and (b) female partner may be entered. This information will not be coded by WHO.

8a, b  Optional: The religion of the (a) male and (b) female partner may be entered. This information may be useful where religious law leads to sexual patterns that may affect fertility. This information will not be coded by WHO.

9a, b  Optional: The current occupation and its duration may be entered in the space provided for the (a) male partner, and (b) female partner. This may provide information regarding exposure to chemicals or trauma which may affect fertility. This information will not be coded by WHO.

10  Space provided for any additional comments.
11. Name of investigator (please print)


Signature Date


2.4 Form 2 – History of the female partner

This form should be completed in the presence of the female partner only.

0a–e Form code and study number are preprinted. Enter participating centre number, couple number in the boxes provided.

Name of subject (not on WHO copy).

1 Enter the day, month and year of this interview.

2a–b (a) If the subject has had a previous examination for infertility, code 2–’yes’, otherwise code 1–’no’.

(b) If the subject has had previous treatment for infertility, code 2–’yes’, otherwise code 1–’no’.

If the answer was yes to either 2(a) or (b), enter the details of diagnosis and treatment in the space provided. The back of the form may be used if additional room is needed.

If the subject has previously been examined but received no treatment, she is eligible for this study and future clinical trials. If the subject has received previous treatment, she is eligible only for the present study.

3a–eSince certain familial diseases may affect fertility, it is essential that the information concerning some typical diseases be recorded e.g. diabetes mellitus, thyroid disease, tuberculosis. Family is defined as father, mother and siblings.

(a) If patient has no family history of any of the diseases listed, code 1 and do not complete (b–e).

(b–e) Enter appropriate code. Specify other.
REPRODUCTIVE HISTORY

Information regarding female reproductive history is one of the most important sources of data which can lead to a diagnosis of infertility. Please take special care to obtain the most accurate information possible.

(a) If wife has never been pregnant during the present marriage/union, code 1—'no' and do not complete (b–e). Otherwise code (b–e) in the following way:
(b) Enter interval from the end of the last pregnancy in months.
(c) Enter duration of amenorrhoea following the last pregnancy, in months.
(d) Enter proper code (1, 2, 3, 4, 5, 6) for the outcome of the last pregnancy:

1 LIVEBIRTH is defined as any infant with a birth weight of 500 grams or greater, born alive whether it is now living or dead.
2 SPONTANEOUS ABORTION is defined as any termination taking place before the 20th completed week of pregnancy or the fetus weighs less than 500 grams.
3 INDUCED ABORTION
4 STILLBIRTH is defined as any infant born dead after the 20th completed week of pregnancy weighing more than 500 grams.
5 MOLAR PREGNANCY (including hydatidiform mole, invasive mole, chorio-carcinoma). Hydatidiform change in chorionic villi involving all or part of the placenta. Fetal parts or evidence of embryo formation may or may not be present. This definition includes the recovery of malignant trophoblastic tissue from the uterus (chorio-carcinoma).
6 ECTOPIC PREGNANCY is defined as a pregnancy occurring outside the uterine cavity.

(e) Code appropriately.

5a–f Code appropriately using above definitions.
6. **Total number of living children during present marriage**
   - Enter total number of currently living children resulting from present marriage/union.

7. **Number of pregnancies prior to present marriage**
   - If 00, go to question 10.
   - Enter total number of pregnancies prior to present marriage/union. If ‘none’, code 00, and do not complete items 8 and 9.

8a–f. **Number of the following prior to present marriage**
   - a. livebirths
   - b. spontaneous abortions
   - c. induced abortions
   - d. stillbirths
   - e. molar pregnancies
   - f. ectopic pregnancies
   - Enter the number of each pregnancy outcome prior to present marriage/union, using definitions in Question 4d.

9. **Total number of living children prior to present marriage**
   - Enter the total number of currently living children resulting from previous marriage/union.

10. **Postpartum or abortion complication**
    - present and/or prior to present marriage
    - 1 no 2 yes
    - Specify date and complication

11. **Methods of fertility regulation used**
   - 1 never
   - 2 only during prior marriage
   - 3 only during present marriage
   - 4 during prior and present
   - 5 premarital
   - Code appropriately. If coded 1—‘never’, do not complete Question 12.

12a–g. **Methods of fertility regulation used**
   - (a–f) For each method, code whether it was ever used by the patient and if used, the total duration of use in months.
   - (g) Specify any other birth control method which the patient has used.
MEDICAL HISTORY:

13a-e (a) Code 1—‘none’ if patient has no history of the diseases listed, and do not code b–d.
(b–d) Code appropriately.
Specify any other disease of which the patient has a history, which the physician feels is relevant, e.g. fibrocystic disease of the pancreas.

14a–d Since pelvic inflammatory disease (PID), especially recurrent episodes, may lead to tubal factors related to infertility (including obstruction, adhesions, etc.) an accurate account of history of PID, including number of episodes, treatment and months since last episode is of great importance.
(a) If no history of PID, do not code (b–d).
(b–d) Code appropriately.

15a–e As with PID, an accurate history of sexually transmitted disease (STD) is of utmost importance. If there is a history of STD, record information regarding treatment (b), months since last episode (c) enter appropriate code for d, and total number of episodes (e).
ALL INFORMATION REGARDING SEXUALLY TRANSMITTED DISEASE MUST BE KEPT STRICTLY CONFIDENTIAL.
N.B.: Information disclosing the patient’s identity must not appear on the forms sent to WHO.

16a, b If patient has history of appendicectomy, code (b) appropriately as ‘complicated’ or ‘uncomplicated’.
17a–g If patient has history of other abdominal surgery, code (a) 2 ‘yes’ and complete (b–g). Abdominal surgery includes inguinal herniorrhaphy, tubal or uterine surgery, bladder and urinary tract surgery.

18 Certain drugs, especially if used over a long term, may affect fertility. Some are known to increase prolactin levels such as tranquilizers, reserpine and phenothiazine. Others, such as steroids, may interfere with the normal feedback mechanism regulating the human reproductive system, and may lead to anovulation. Furthermore, cytotoxic drugs may affect the ovary directly, especially the germ cells. If the subject is using such a medication, code (a)—2 ‘yes’ and specify the drug by its approved name in.

**SEXUAL HISTORY**

Sexual dysfunction such as untimely or infrequent intercourse and inadequate penetration are known factors which directly or indirectly may lead to infertility. Sometimes this may be due to pain during intercourse (dyspareunia), by excessive douching, use of lubricants (with spermicidal qualities), or by inadequate knowledge of the fertile period.

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<td>20. Frequency of vaginal intercourse per month over the last 6 months</td>
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<td>21. Frequency of other sexual activity per month</td>
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<td>22. Use of lubricants</td>
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<td>23. Degree of penile penetration</td>
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<td>24. Frequency of orgasm</td>
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<tr>
<td>25. Dyspareunia</td>
</tr>
</tbody>
</table>

19 Enter the number of previous marriages.

20 Enter the average frequency of vaginal intercourse per month over the last 6 months.

21 Enter the frequency of other sexual activity per month. This includes masturbation, non-vaginal forms of intercourse, etc.

22–24 Code appropriately.

26  Code appropriately. If subject douches, give details.

27a, b  In certain ethnic or religious groups, coital activity is permitted only during particular times of the menstrual cycle. Thus, care should be taken to find out whether coitus takes place during presumed time of ovulation. Both adequate ‘knowledge’ and adequate ‘use’ of the fertile period should be coded.

**Gynaecological History**

28a, b  Enter age at menarche. If patient has primary amenorrhoea, code 99 and do not complete Questions 29–32.

If patient has secondary amenorrhoea, give duration in months (b).

**PRIMARY AMENORRHOEA:** The patient has never experienced spontaneous vaginal bleeding.

**SECONDARY AMENORRHOEA:** Absence of spontaneous vaginal bleeding for 6 months or more.

29  Enter day, month and year of the first day of the last menstrual period (LMP). If more than six months ago, the diagnostic classification is secondary amenorrhoea. If the exact day of the LMP is not remembered, code 99 for day and enter the month and year. In all cases, details of the LMP should be entered.

30a–c  This series of questions helps to differentiate between a *Regular menstrual pattern* (regular menstrual bleeding at intervals 28 ± 7 days, and *Oligomenorrhoea* (menstrual bleeding at intervals from 36 days to 6 months). Enter all numbers in days for parts (a–c). If exact length of cycle is not known, the patient’s best estimate should be entered.

31  Enter the duration in days of the average menses over the previous 6 menses.

32  Code appropriately.
33a–e  (a) If vaginal discharge is ‘absent’, do not code (b–e).
(b–e) Code appropriately. Vaginal discharge may be an indicator of infection or inflammation of the cervix.

34a–c  (a) If discharge is absent from both nipples, do not code (b) and (c).
Otherwise, code appropriately: (b) 1, 2 or 3 and (c) enter duration of discharge in months. If a blood-stained discharge is noted, malignant disease of the breast should be excluded. Discharge should be observed microscopically for the presence of fat globules. If fat globules are absent, organic breast disease must be considered. Additional comments or observations may be entered on the back of this form.

35  The investigator should enter his/her name (please print), signature and the date in the space provided.

2.5 Form 3 – Physical Examination of the Female Partner

0a–e  Form code and study number are preprinted
Enter participating centre number and couple number in the boxes provided.
Name of subject (not on WHO copy).
1, 2 Since height and weight may be signs of systemic disease directly related to infertility (e.g. anorexia nervosa) the collection of this information is important. Enter the subject's height in centimetres and weight in kilograms. See conversion tables on the back of booklet cover.
Code question 2b appropriately.
1: No significant change is a weight gain or loss of not more than 10% in past year.
2: weight loss > 10% in past year.
3: weight gain > 10% in past year.

3 The blood pressure should be taken and entered in boxes provided.

4a–g A general physical examination to detect abnormalities in the following systems or organs should be performed:
(b) Thyroid—e.g. thyroid nodules, goitre, etc.
(c) Adrenals—e.g. striae, hirsutism, virilism or other signs.
(d) Cardiovascular—e.g. pulse rate, heart sounds, ophthalmoscopy for papilloedema, haemorrhages and normality of retinal vessels.
(e) Respiratory—e.g. chest deformities, percussion, auscultation.
(f) Gastrointestinal—e.g. scars, hernial orifices, presence of hepatosplenomegaly, tenderness, abdominal masses.
(g) Neurological—e.g. gross motor or sensory abnormalities.
Specify abnormalities.

5a, b If the hair distribution is masculine (a), enter the Ferriman-Gallwey score in (b) (Appendix 1).
N.B. If sex hair is completely absent in the presence of primary amenorrhoea, this may be a sign of testicular feminization syndrome.

6a–d (a) Breast development should be coded according to the Tanner’s staging (Appendix 2).
Enter the stage in box provided.
(b–d) N.B. Only after blood has been taken for serum prolactin the breasts should be palpated and the areolar area should be squeezed to check for secretion. If no secretion is observed, code (b)—‘none’, and do not code (c–d). Should any suspicious mass be found, or should there be bloody secretion, malignant disease should be excluded.
### Pelvic Examination

1. **Vulva**: Code appropriately. If any abnormalities are noted, give details. Abnormalities may include absence, stenosis, primary atrophy, signs of inflammation or infection, tumours, ulceration, malformations, varicosities, past trauma, etc.

2. **Clitoris**: Code appropriately. The clitoris may be congenitally absent or may have been removed (either surgically or by traditional, ritual means). An enlarged clitoris greater than 2 cm in length or glans diameter greater than 1 cm may be a sign of virilism.

3. **Vagina**: (a) Vaginal examination may reveal congenital abnormalities or occlusion. Code appropriately. (b–e) Signs of infection should be noted, and if present, the infecting organism should be identified.

4. **Cervix**: (a) The cervix should be examined and classified as normal or abnormal. If abnormal code (b–i) appropriately.

5. **Uterus**: The uterus should be examined. Code appropriately and give details of all abnormalities.
13. **Genital prolapse**
   - 1 absent
   - 2 present
   - Give details

14. **Adnexa**
   - 1 normal
   - 2 abnormal
   - Give details

15. **Menstrual Category**
   - 1 Regular menstrual pattern
   - 2 Oligomenorrhea
   - 3 Amenorrhoea

16. **Additional Comments**

17. **Name of investigator (please print)**
   - Signature
   - Date

2.6 **Form 4 – Diagnostic Procedures for the Female Partner**

Oa–e  Form code and study number are preprinted. Enter participating centre number and couple number in the boxes provided.
Name of subject (not on WHO copy).
1-2 These tests should be performed for the purpose of good medical practice.

3 If urinalysis is normal (a), do not code (b-f).

4 This space is provided so that the results of any additional laboratory tests may be entered. If more space is required, use back of form.

### HORMONES

The following hormone levels should be determined when necessary for a diagnosis. Please refer to the flow chart (female) to determine the necessity of particular tests. See Appendices 3 (a) and 3 (b) for hormone analysis performed by radioimmunoassay using the Matched Reagent Programme and Standards supplied by WHO.

5a–d Prolactin levels should be estimated in every patient in whom an endocrine cause of infertility is suspected, and after genital tuberculosis and tubal occlusion have been excluded. Prolactin should be estimated by RIA using the Matched Reagent Programme and WHO Standards (Appendix 3). The value should be entered in (a) in milliunits/l and coded as ‘normal’, ‘elevated’ or ‘low’. Although less than 20 ng/ml (640 mIU/l) is considered normal, each laboratory must establish their own values for ‘normal’, ‘elevated’ and ‘low’ levels.

If prolactin is elevated the assay should be repeated within one month. Result should be entered in (c) and (d). Special care should be taken that 1) the patient is not stressed when blood is being withdrawn, and 2) blood should not be withdrawn for assay immediately following a breast or vaginal examination. A patient with amenorrhoea can have blood withdrawn any morning, but with anovulatory patients or patients in whom bleeding has been induced, blood should be taken 3–5 days after the first day of menstruation.
6a, b FSH levels should be performed only in amenorrhoeic patients who have low endogenous estrogens as described in Question 8 below. The value of the serum FSH may be entered in (a) in IU/l and/or, the urinary 24 hour excretion may be entered in (b). Normal values in IU/24 hours should be established for each laboratory.

7a, b (a) Enter the serum LH level in IU/l (b) Normal values should be determined in each laboratory.

8a–c Endogenous estrogen levels can be determined either by (a) serum estradiol levels in pmol/l, (b) total urinary estrogens in nmol/24 h or by (c) withdrawal uterine bleeding by giving medroxyprogesterone acetate by intramuscular injection daily for 2 days or 15 mg norethisterone orally daily for 5 days or 15 mg medroxyprogesterone acetate orally daily for 3 days. If no vaginal bleeding occurs, the test is negative. Any bleeding up to 1 week following the test is positive. Endogenous estrogen activity need only be assessed in amenorrhoeic patients.

**Detailed Methods**

Urinary excretion—Brown method (Estrogene-glucuronide) or RIA (Appendix 4)

9a–c Progesterone or pregnanediol estimation is a helpful diagnostic test to establish whether ovulation has occurred. Serum progesterone levels greater than 5 ng/ml (15 nmol/l) or urinary pregnanediol excretion greater than 2.5 mg/24 h (7.5 nmol / 24 h) estimated 5–9 days before the anticipated onset of menstrual bleeding is presumptive evidence of ovulation.

(a) Serum progesterone is to be estimated according to the Matched Reagent Programme using WHO standards (Appendix 3a).

Value shall be entered in nmol/l.

(b) Pregnanediol may be estimated using the method of Klopper & Michie or Shearman.

(c) The patient’s ovulatory status should be coded according to the criteria described above.
10a-b Thyroxine: In cases where prolactin is elevated, hypothyroidism should be excluded since TRH (Thyroid Releasing Hormone) is a potent elevator of prolactin. If serum thyroxine is low, the patient should be further investigated and treated for hypothyroidism. Each laboratory should establish normal values for serum thyroxine.
(a) The value should be entered in nmol/l.
(b) Code appropriately as ‘normal’, ‘low’ or elevated.
Thyroxine should be measured by the method used routinely in each laboratory.
E.g. Competitive Protein Binding Radioimmunoassay.

OTHER PROCEDURES

11. The leucocyte karyotype should always be performed if FSH (LH) levels are above normal. The method used should be that used routinely by each laboratory. The appropriate code should be entered for the result, and (4) ‘other abnormalities’ should be specified.

12. In all cases where a pituitary lesion is suspected (e.g. when prolactin is elevated) an X-ray of the sella turcica and a detailed examination of the visual fields should be performed. The technique of choice will depend upon availability, but whenever possible polytomography of the sella turcica is to be preferred to simple radiography.

13. The visual fields should be examined by an experienced neuro-ophthalmologist, using objects of different size and colour. The visual fields should be charted, and the chart retained for later comparison. A change in the visual fields or a progressive defect may be a sign of a growing tumour.

14. Other pituitary function tests (e.g. thyroid releasing hormone test, adrenal suppression) should be performed whenever pituitary abnormalities are suspected (consult flow chart). Give details of results, including which tests were performed.
15a–e (a) Code appropriately.

Tubal patency can be established by either laparoscopy and hydrotubation, by hysterosalpingography or both. The former technique has a lower incidence of false negative results and provides additional information about the state of the pelvic organs (e.g. the presence or absence of adhesions).

Hysterosalpingography, on the other hand, gives information about the uterine cavity. Tubal insufflation is not a reliable way of establishing tubal patency.

(b) Code status of tubes. This can only be determined by laparoscopy plus hydrotubation or by hysterosalpingography or both.

(c) If adhesions are present, give details. This can be determined by laparoscopy.


16 The uterine cavity can only be evaluated by hysterosalpingography or hysteroscopy. The appropriate code should be entered.

17a–c (a) Enter the day of cycle when the biopsy is obtained. If amenorrhoeic, code 99.

(b–c) Code appropriately for histology and tuberculosis culture.


The diagnosis of genital tuberculosis may be established by bacteriological examination of uterine secretions or tissue obtained by endometrial biopsy. Direct smears stained by the Ziehl-Neelsen method occasionally reveal tubercle bacilli but are often negative in cases in which guinea pig inoculation or cultures give positive results. An additional advantage of culture of the endometrium is that the drug sensitivity of the isolated organism can be determined.
Guinea Pig Inoculation

Guinea pig inoculation may reveal cases of genital tuberculosis undiagnosed by other methods. Positive results may be obtained from endometrial tissue removed by curettage, menstrual blood, or cervical mucus. Guinea pig inoculation sometimes gives positive results when histological examination of the endometrium is negative, and endometrial biopsy specimens should be examined by both methods in suspected cases. Guinea pig inoculation using endocervical secretions was found to give better results than direct examination or culture of the cervical mucus.

Cultures of Menstrual Discharge and Cervical Mucus

The diagnosis of endometrial tuberculosis may be established by bacterial examination of menstrual blood and cervical mucus. It may yield positive results even though the endometrial biopsy is negative. Examination of cervical mucus is less likely to give positive results than examination of menstrual blood.

The menstrual discharge is collected, on the second day of menstruation, through a vaginal speculum into a solution of 2 ml of isotonic sodium chloride and then cultured on Loewenstein’s or Petraghini’s medium. It is important that mucus and endometrial shreds present in the menstrual blood be included in the material inoculated. A minimum of six to eight consecutive negative cultures is necessary in order to exclude genital tuberculosis.

18a, b Ovarian biopsy should be done only in patients with high FSH whose karyotype is normal. It may confirm the diagnosis of primary ovarian failure. Since this disease is untreatable, the results of this procedure are of academic interest only. It should only be done in special circumstances, e.g. suspicion of resistant ovary syndrome.
(a) Code appropriately.
(b) Code 2—‘yes’ if additional abnormalities are found.
Specify details of abnormalities.

19 Chest X-ray (if done): code ‘normal’ or ‘abnormal’.

20 The final diagnosis should be entered and coded in the space provided. Additional comments may be added if the physician desires. See Appendix 6 for diagnostic codes.

21 Additional comments and observations may be entered here.
22. Name of investigator (please print)

Signature Date

22. Investigator should enter his/her name (please print), signature and the date in the space provided.

2.7 Form 5 – History of the Male Partner

This form should be completed in the presence of only the male partner.

Oa–e Form code and study number are preprinted. Enter participating centre number and couple number in the boxes provided. Name of subject (not on WHO copy).

1 Enter the day, month and year of the history taking.

2a–b (a) If subject has had a previous examination for infertility, code 2—‘yes’.
(b) If subject has had previous treatment for infertility, code 2—‘yes’.
If the answer was ‘yes’ to either a or b, enter the details of diagnosis and treatment in the space provided for the purpose of clinical management.
If the subject has previously been examined but received no previous treatment, he is eligible for this study and future clinical trials. If the subject has received previous treatment, he is eligible only for the present study.

3a–e Since certain familial diseases may affect fertility, it is essential that the information concerning some typical diseases be recorded i.e. diabetes mellitus, thyroid diseases, tuberculosis.
(a) If patient has no family history of any of the listed diseases, code 1 and do not complete (b–e).
(b–e) Enter appropriate code. Specify ‘other’.
4a–c  (a) If response is 'no', do not complete (b) and (c).
(b–c) Code appropriately.

5a–g  (a) If subject has no history of any disease listed code 1 — 'none', and do not complete (b–g).
(b–g) Enter appropriate code for each disease. It has been reported that some types of respiratory disease are associated with infertility. Patients with a history of fibrocystic disease of the pancreas may have congenital absence of the vas deferens. A number of men who give a definite history of childhood bronchiectasis are noted to have azoospermia due to an obstruction. In a smaller number, situs inversus, chronic sinusitis and bronchiectasis (Kartagener's Syndrome) are associated with normal sperm counts but total immotility due to alterations in the structure of the axial filament of the sperm tail. If patient has a history of high fever (39°C for 48 hours or more) within the past 6 months, seminal analysis should be done only after 6 months have elapsed and the present sperm analysis should not be regarded as definitive.

6a–d  If subject has no history of any disease listed, code 1 — 'none' and do not code (b–d). Otherwise, code (b–d) appropriately and specify any additional disease.
7a–h  (a) If subject has no history of the symptoms listed, code 1—‘none’, and do not complete (b–h).
(b–f) Code appropriately.
(g) Specify any other symptoms not listed.
(h) Code appropriately. If there were recurrent episodes, give details including diagnosis and treatment.

<table>
<thead>
<tr>
<th>7. Urinary Symptoms</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Any of the following</td>
<td>1 no 2 yes</td>
</tr>
<tr>
<td>b. Dyuria</td>
<td>1 no 2 yes</td>
</tr>
<tr>
<td>c. Urethral discharge</td>
<td>1 no 2 yes</td>
</tr>
<tr>
<td>d. Haematuria</td>
<td>1 no 2 yes</td>
</tr>
<tr>
<td>e. Frequency</td>
<td>1 no 2 yes</td>
</tr>
<tr>
<td>f. Difficulty in voiding</td>
<td>1 no 2 yes</td>
</tr>
<tr>
<td>g. Other</td>
<td>1 no 2 yes</td>
</tr>
<tr>
<td>h. Were any episodes recurrent</td>
<td>1 no 2 yes</td>
</tr>
</tbody>
</table>

Give Details of symptoms

8a–m  (a) if ‘yes’, do not complete (b–d).
Otherwise, code appropriately.
(e) If no injury to testes, do not complete (f–h).
Otherwise, code appropriately.
(i) If no torsion of testes, do not complete (j–k).
Otherwise, code appropriately.
(l) If no epididymo-orchitis, do not complete (m), otherwise, code it appropriately.

<table>
<thead>
<tr>
<th>8. Testes</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Always had both testes in the scrotum</td>
<td>1 no 2 yes</td>
</tr>
<tr>
<td>b. Not in scrotum</td>
<td>1 left 2 right 3 both</td>
</tr>
<tr>
<td>c. Type of treatment</td>
<td>1 none 3 surgical</td>
</tr>
<tr>
<td>d. Medical 4 both</td>
<td></td>
</tr>
<tr>
<td>e. Age at treatment yrs</td>
<td></td>
</tr>
<tr>
<td>f. Injury to testes</td>
<td>1 no 2 yes</td>
</tr>
<tr>
<td>g. With haematuria</td>
<td>1 no 2 yes</td>
</tr>
<tr>
<td>h. With decrease in size</td>
<td>1 no 2 yes</td>
</tr>
<tr>
<td>i. Torsion of testes</td>
<td>1 no 2 yes</td>
</tr>
<tr>
<td>j. Unilateral 2 bilateral</td>
<td></td>
</tr>
<tr>
<td>k. Treated surgically</td>
<td>1 no 2 yes</td>
</tr>
<tr>
<td>l. Epididymo-orchitis</td>
<td>1 no 2 yes</td>
</tr>
<tr>
<td>m. Left 2 right 3 both</td>
<td></td>
</tr>
</tbody>
</table>
9a–d If subject has had any surgery relevant to infertility code a–2 and specify and code surgical procedure. Surgery relevant to infertility includes all pelvic surgery. See Appendix 7 for detailed list of surgical procedures.

10 If subject has had long term use of medication possibly affecting fertility, code—2 ‘yes’ and specify drug, using approved name only. The categories of drugs include cytotoxic agents, steroids, antihypertensives, tranquilizers (known to increase prolactin), and certain antibiotics.

11 Code 2—‘yes’ if the subject’s alcohol consumption is more than 60 grams per day
   e.g. scotch whiskey contains 40% alcohol,
   60 gm = 4 double whiskies
   60 gm = 4 pints of most beer.
   Care must be taken to ascertain the exact alcoholic content of local beverages.

12 Social habits such as narcotic use, excessive sauna baths, etc. may be noted in the space provided.
**SEXUAL HISTORY**

<table>
<thead>
<tr>
<th>13. Erection</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Coital 1 adequate 2 inadequate</td>
</tr>
<tr>
<td>b. Early morning erections</td>
</tr>
<tr>
<td>1 never 2 sometimes 3 often</td>
</tr>
<tr>
<td>c. Masturbatory erections</td>
</tr>
<tr>
<td>1 never 2 sometimes 3 often</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>14. Dyspareunia</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 absent 2 present</td>
</tr>
<tr>
<td>Give details</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>15. Ejaculation</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. regularly during sexual intercourse</td>
</tr>
<tr>
<td>1 no 2 yes</td>
</tr>
<tr>
<td>b. ever</td>
</tr>
<tr>
<td>1 no 2 yes</td>
</tr>
<tr>
<td>c. nocturnal</td>
</tr>
<tr>
<td>1 no 2 yes</td>
</tr>
<tr>
<td>d. masturbatory</td>
</tr>
<tr>
<td>1 no 2 yes</td>
</tr>
<tr>
<td>e. characteristics of ejaculation</td>
</tr>
<tr>
<td>1 normal 2 abnormal</td>
</tr>
<tr>
<td>f. painful</td>
</tr>
<tr>
<td>1 no 2 yes</td>
</tr>
<tr>
<td>g. before introversion</td>
</tr>
<tr>
<td>1 no 2 yes</td>
</tr>
<tr>
<td>h. other (describe)</td>
</tr>
<tr>
<td>1 no 2 yes</td>
</tr>
</tbody>
</table>

13a–c If subject reports adequate coital erection, do not code (b) and (c). Otherwise, code (b) and (c) appropriately. Inadequate coital erection with either early morning erections with or without masturbatory erections may suggest psychological problems related to infertility. If masturbatory erection and ejaculation is possible and pregnancy is urgently desired, artificial insemination may be performed. Otherwise patient should be referred for psychological investigation and treatment.

14 If dyspareunia is present, details should be given including sexual habits, mode of intercourse and frequency.

15a–h (a) If subject reports ejaculation during vaginal intercourse, do not code (b–d). Otherwise, code appropriately. (e–h) If subject reports normal characteristics of ejaculation, do not code (f–h). Otherwise, code them appropriately.
16. **Number of previous marriages**

17. **Number of pregnancies resulting from previous marriages/unions**

18. **Length of time since last fertilization (months)**
   (code 999 if none)

19a–e. **History of sexually transmitted disease**
   1 no 2 yes
   - **Last episode treated**
     1 no 2 yes
   - **Months since last episode**
   - **Disease last episode**
     1 syphilis
     2 gonorrhoea
     3 lymphogranuloma
     4 mycoplasma
     5 non-specific, unknown
   - **Total number of episodes**

20. **Additional Comments**

21. **Name of investigator (please print)**

   Signature  Date

---

**2.8 Form 6 – Physical Examination of the Male Partner**

Oa–e. **Form code and study number are preprinted.**
Enter participating centre number and couple number in the boxes provided.
Name of subject (not on WHO copy).
Information regarding height, weight and blood pressure should be collected for the purpose of good medical practice. They may give indications of systemic disease, e.g. Addison’s disease, Cushing’s disease, hyper- and hypothyroidism. See conversion on the back of booklet cover.

A general physical examination to detect gross abnormalities in the following systems and organs should be performed:

(b) Thyroid—e.g. thyroid nodules or goitre.
(c) Adrenals—e.g. striae or other signs of adrenal disease.
(d) Cardiovascular—e.g. pulse rate, heart sounds, retinal blood vessels, etc.
(e) Respiratory—e.g. deformities, percussion, auscultation.
(f) Gastrointestinal—e.g. scars, hernial evidence of hepatosplenomegaly hernial orifices, tenderness.
(g) Neurological—e.g. gross motor or sensory abnormalities.
(h) Other abnormalities should be specified.

If the secondary sex characteristics are normal, do not complete (b). Secondary sex characteristics to be observed include body configuration, hair distribution (facial, trunk, axillary and pubic) and pubertal stage. (See Appendix 2: Tanner pubertal stage).

If signs of hypogonadism are noted (e.g. eunuchoid appearance), do visual fields (a) and test for anosmia (b) using oil of peppermint and oil of cloves. TEST FOR ANOSMIA—The solutions of the test substance should be administered in narrow-necked glass or plastic bottles kept at room temperature and held 2-5 cms. below the nose.

Examine breasts by palpation for presence of glandular tissue (gynaecomastia).
UROGENITAL EXAMINATION

With the patient standing, check the *penis* including the *urinary meatus* and palpate the penis for induration. Check *both testes* for site, position, consistency and tenderness.

Palpate the *epididymis* for abnormalities including tenderness, thickening, etc. Check the *vas deferens*. Check for *scrotal swellings*, especially for hydrocele, lymphocele and hernia. Check for the presence of *varicocele* on both sides: ‘*visible*’ if lesion can be seen, ‘*palpable*’ if lesion is felt only, and ‘*Valsalva positive*’ if the varicocele is present only on coughing or straining i.e. by an increase of intra-abdominal pressure by forcible exhalation against the closed glottis. Check the left and right inguinal canals for hernia. Check for scars in the inguinal region and for lymphadenopathies. With patient in the *knee-chest* position, perform a rectal examination to palpate the *seminal vesicles* and *prostate*. Note tenderness, soft and hard swellings of prostate.

8a–d
(a) If penis is normal, code 1, and do not complete (b–d).
(b) Code appropriately.
(c) Code appropriately.
Hypospadias may prevent normal delivery of sperm. (This can be checked by a post coital test). If the sperm analysis is normal and no sperm are found in the cervical canal post coitus, then a problem of sperm delivery is present. Hypospadias may be a sign of other developmental abnormalities.
(d) Other penile abnormalities should be noted such as indurations, scars, fistulae and balanitis.

9a–e
(a) If both testes are normal, code 1 — ‘normal’, and do not complete (b–d).
(b–d) Enter appropriate codes for both right and left testes.
(e) Measure the volume of both testes using the Prader orchidometer.

10
Code appropriately for both the right and left epididymis.
11. Vas deferens
   1. normal
   2. thickened
   3. non palpable

12. Scrotal swelling
   1. none
   2. hydrocoele/lymphocele/subcutaneous
   3. hernia

13. Varicocele
   1. none
   2. visible (grade III)
   3. palpable (grade II)
   4. valsalva positive (grade I)

14. Inguinal examination
   a. 1. normal
      2. abnormal
   b. Hernia
      1. absent
      2. present
   c. Scar
      1. absent
      2. surgical
      3. Post infection/trauma
      4. both 2 and 3
   d. Lymphadenopathy
      1. no
      2. yes

15. Rectal examination
   a. Prostate
      1. normal
      2. abnormal
   b. Firmness
      1. no
      2. yes
   c. Swelling soft
      1. no
      2. yes
   d. Swelling hard
      1. no
      2. yes
   e. Seminal vesicles
      1. non-palpable
      2. palpable

16. Additional Comments

17. Name of investigator (please print)

Signature               Date
2.9 Form 7 – Diagnostic procedures for the male partner

<table>
<thead>
<tr>
<th>0. IDENTIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Form code</td>
</tr>
<tr>
<td>b. Study number</td>
</tr>
<tr>
<td>c. Participating centre</td>
</tr>
<tr>
<td>d. Couple number</td>
</tr>
<tr>
<td>e. Name of subject (not on WHO copy)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Family</th>
<th>Given</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>GENERAL LABORATORY</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Haemoglobin (g/dl)</td>
</tr>
<tr>
<td>2. WBC (x 10^9/l)</td>
</tr>
<tr>
<td>3. ESR (optional)</td>
</tr>
</tbody>
</table>

1–3 These tests should be performed for the purpose of good medical practice. The ESR may be entered on the line provided.

<table>
<thead>
<tr>
<th>4. Urinalysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. 1 normal</td>
</tr>
<tr>
<td>b. 2 abnormal</td>
</tr>
<tr>
<td>b. Glucose</td>
</tr>
<tr>
<td>c. Protein</td>
</tr>
<tr>
<td>d. Leucocytes</td>
</tr>
<tr>
<td>e. RBC</td>
</tr>
<tr>
<td>f. Significant bacteria (&gt;10^5/mcl)</td>
</tr>
</tbody>
</table>

4a–f If urinalysis is normal (a), do not code (b–f). (b–f) Code appropriately.

5 | This space is provided so that the results of any additional laboratory tests may be entered.

| TEST | RESULT |

SEMEN ANALYSIS

The instructions in Appendix 8 are an attempt to meet the need for standardized procedures. Without necessarily prescribing ‘official guidelines’, it is intended to provide an acceptable set of procedures that would enable investigators and clinicians to compare their findings. The standardization required includes procedures for the collection, processing, examination and description of specimens of semen.

The following instructions are extracted from a manual which was developed for the research requirements of the Task Forces of the World Health Organization’s Special Programme of Research, Development and Research Training in Human Reproduction. It has been modified by the Task Force on the Diagnosis and Treatment of Infertility to render it suitable for routine clinical investigation oriented to therapy.
Enter the date the semen was obtained. The second analysis should take place not less than two weeks after the first examination.

At the time of the second analysis, enter the exact number of days since the first analysis.

A normal seminal fluid specimen should liquefy within 20 minutes of collection. As soon as this is completed the examination can begin. The age of the sample at the time of this examination should be noted. The sample volume should be measured with a graduated cylinder or a disposable, calibrated plastic pipette, and the exact volume entered to the first decimal (in ml) in the box provided. The normal range is 1.5–6.0 mls.

The appearance of the seminal fluid should be observed, and appropriately coded as either normal, bloody, yellow, mucus streaked, or yellow and mucus streaked.

It should be noted whether liquefaction of the sample occurs or not, as well as any increased viscosity. The appropriate code should be entered. Quantitative and qualitative motility, sperm agglutination, and sperm viability are evaluated according to the methods discussed in Appendix 8.

**MOTILITY**

The percentage of progressively motile sperm should be entered in 11a.

(b) Norms must be established in each laboratory. The figures quoted above should only be used as guidelines.

**AGGLUTINATION**

If agglutination is less than or equal to 10%, code 1—'no'. If agglutination is more than 10%, code 2—'yes'.
**SPERM VIABILITY**

The number of live spermatozoa can be determined by using one of several supravital staining techniques. For details see Appendix 8. The supravital staining technique makes it possible to differentiate immotile but live spermatozoa from those which are dead. It also provides a check on the accuracy of the motility evaluation. It should, therefore, be used particularly when the quantitative motility is 40% or less. The percent of live spermatozoa should be entered in the boxes provided.

**COUNTING THE SPERMATOZOA**

The sperm counts of men considered to be fertile range from 20 to 200 million/ml. However, it must be understood that pregnancies have occurred with sperm counts lower than 20 million/ml and alternatively, infertility may be encountered in patients with more than 200 million/ml. The evaluation of a man's potential fertility should therefore not be based only on sperm concentration. Due attention must be given as well to the motility, morphology and other functional properties of the spermatozoa.

The estimate of sperm density is made by counting the average number of spermatozoa in several fields under a 40X objective and multiplying it by $10^6$. For example, 40 spermatozoa/field can be considered roughly equivalent to 40 million/ml. Enter the value in the boxes provided.

**ANALYSIS OF MORPHOLOGICAL CHARACTERISTICS OF GERMINAL CELLS**

*Preparation of Seminal Fluid Smears:* See Appendix 8.

*Classification and quantitation of germinal cells and leukocytes:* At least 100 germinal cells (including both morphologically mature and immature form) are counted and classified according to the criteria presented in the photographic plates (Appendix 8). A table summarizing the cell types and their expected frequencies in a presumed normal ejaculate is presented in Annex 1 of Appendix 8.

The leukocytes are counted after being stained for differentiation between leukocytes and other round cells, as outlined above, and reported as the number x10⁶/ml. (See Appendix 9 for method). 1 x 10⁶/ml is considered normal. The number to one decimal should be entered in the box provided.
As a result of the first and second seminal analysis, the patient will be categorized into one of the following groups. The appropriate code should be entered in the box provided.

1) Normal Semen Analysis—All parameters normal
   - Volume: 1.5–6.0 mls
   - Motility: >40% progressively motile sperm
   - Viability: > 60% with supravital sperm staining
   - Density: > 20 x 10⁶ spermatozoa/ml
   - Agglutination: < 10%
   - Morphology: > 50% normal forms
   - WBC's: < 1 x 10⁶/ml.

2) Abnormal Semen Analysis
   - Any parameter or combination of parameters which diverts from normal.

3) Azoospermia
   - The absence of sperm in the ejaculate.

4) Aspermia
   - The absence of ejaculate.

These hormone levels (Plasma FSH, Plasma LH, Plasma testosterone and prolactin) should be determined when necessary for a diagnosis. Please refer to the flow chart (male) to determine the necessity of particular tests. See Appendices 3a and 3b for hormone analyses performed by Radioimmunoassay using the Matched Reagent Programme and Standards supplied by WHO.

(a) The Plasma FSH level should be entered in IU/l.
(b) Normal values should be established for each laboratory. The appropriate code should be entered.

19a, b
(a) The Plasma LH level should be entered in IU/l.
(b) Normal values should be established for each laboratory. The appropriate code should be entered.

20a, b
(a) The plasma testosterone level should be entered in nmol/l.
(b) Normal values should be established for each laboratory. The appropriate code should be entered.
21a-d  (a) The prolactin level should be entered in mIU/l.
(b) Normal values should be established for each laboratory. The appropriate code should be entered.
IF PROLACTIN LEVEL IS ELEVATED, IT SHOULD BE REPEATED, AND THE VALUE ENTERED IN (c) AND (d) AS ABOVE.

22a, b  In cases where it is difficult to decide whether the FSH is normal or low, an LHRH test (Luteinizing Hormone Releasing Hormone) should be performed using 100 μg intravenously. In cases where there is a poor response to LHRH as measured by FSH and LH one can assume the diagnosis of gonadotrophin deficiency. In cases of normal FSH basal levels and an exaggerated response to FSH, primary testicular failure should be considered.
(a) Response (FSH) should be coded according to the normal values in each laboratory.
(b) Response (LH) should be coded according to the normal values in each laboratory.

OTHER PROCEDURES

23, 24  In all cases where a pituitary lesion is suspected (e.g. when prolactin is elevated) an X-ray of the sella turcica and an examination of the visual fields should be performed. The technique of choice will depend upon availability, but whenever possible, polytomography of the sella turcica is to be preferred to simple radiography.
Whenever possible, the visual fields should be examined by a neuro-ophthalmologist, using objects of different size and colour. Visual fields should be charted, and the chart retained for later comparison. A change in the visual fields or a progressive defect may be a sign of a growing tumour.

25  Other pituitary function tests (e.g. thyroid releasing hormone test, adrenal supression tests) should be performed whenever pituitary abnormalities are suspected (consult flow chart). Give details of results, including the tests which were performed.
The leucocyte karyotype should always be performed if FSH (LH) levels are above normal. The method used should be that used routinely by each laboratory. The appropriate code should be entered for the result, and (4) —‘other abnormal’ should be specified.

In cases of azoospermia or severely low sperm count, testicular biopsy enables the confirmation of the diagnoses of obstruction, primary testicular failure or gonadotrophin deficiency. However, a testicular biopsy should be performed only if obstruction is suspected and surgical techniques are available for treating such patients. Otherwise, such confirmation will be of academic interest only. Classification of testicular histology can be found below. The appropriate code should be entered.

If surgical treatment is being considered for occlusion, the techniques of testicular biopsy and vesicolo vasography may be combined. The combined technique may be performed as follows.


The tunica albuginea is exposed through a 1-cm scrotal incision. A 5-mm incision is made through the fibroelastic tunica albuginea, and this incision is spread with a fine-angled dissecting forceps, preferably on the anterior surface of the testis. The counter pressure on the testis by the holder causes a testicular tubular bead to extrude. This is excised with a fine, sharp, curved iris scissors, and the specimen is immediately placed.

A fine suture of 4-0 plain catgut can be used to close the tunica albuginea. However, the underlying tunica vasculosa often bleeds profusely and requires the use of a mattress suture. This will not cause a significant hematoma or increase in intratesticular pressure, as occurs with arterial bleeding. The tunica vaginalis and skin are closed with single sutures of 4-0 plain catgut. A similar procedure is performed on the opposite side. Subsequent surgical exposure in the areas of these properly performed biopsies will show minimal scarring and only occasional fine adhesions at the site of the suture.

Before closing the skin incision, it is possible to grasp the vas deferens with a Bachaus towel clip and deliver it into the same incision for vasoseminal vesiculography. The sheath of the vas is incised vertically and the vas is isolated from accompanying vessels and the sheath by another towel clip. An oblique vertical vasotomy is made using a bistoury tip pointed to the center of the vas in a vertical direction. The permits instillation of 2 ml. of Salpix contrast medium cephalad through a blunt 20-gauge or 22-gauge cannula. The X-ray film may be exposed after one or both sides have been injected. The outline of the vasa deferentia and seminal vesicles, together with evidence of ‘bladder spillage’, confirms the patency of the ductal system.
CATEGORIZATION OF TESTICULAR BIOPSIES

1) Near-Normal: The seminiferous tubules show normal spermatogenesis with mild degree of desquamation of germ cells being acceptable. The Leydig cells are normal and no peritubular fibrosis is seen. If associated with azoospermia this appearance usually indicates obstruction.

2) Hypospermatogenesis: All stages of spermatogenesis can be identified but the numbers of germ cells are decreased without cessation of spermatogenesis at a specific stage. A subjective categorization can be made into mild, moderate or severe depending on the degree of germ cell loss. Peritubular fibrosis is commonly present with severe hypospermatogenesis.

3) Germ Cell Arrest: Spermatogenesis proceeds to a specific stage and no further maturation is seen. Commonly this occurs at the primary spermatocyte or spermatogonial level. Peritubular fibrosis is uncommon and Leydig cells are normal. For this diagnosis to be substantiated the histological pattern must be present in the entire biopsy and is usually associated with azoospermia.

4) Sertoli Cell only or Germ Cell aplasia: The seminiferous tubules are reduced in diameter and often show peritubular fibrosis. Only Sertoli cells are present in the epithelium and the Leydig cells appear more prominent, sometimes forming clumps.

5) Seminiferous Tubule Hyalinization: The tubules are markedly reduced and contain little or no epithelium; the latter, if present, consists of Sertoli cells only. The outline of the tubule is represented by fibrotic tissue and an amorphous basement membrane type of material. The Leydig cells frequently form continuous sheets or clumps in the intertubular tissue.

6) Immature Testis: The seminiferous 'tubules' show no lumen and consist of immature Sertoli cells and gonocytes or primitive spermatogonia. No mature Leydig cells are seen but elongated mesenchymal cells are present in the intertubular area. This is the appearance seen in prepubertal children and represents a failure of gonadotrophic stimulation of the testis if seen in a biopsy from a chronologically 'adult' male.

29–31 In cases where one suspects infections or abnormalities of the secondary sex glands (prostate, seminal vesicles and epididymis) seminal fluid biochemistry, seminal fluid culture and prostatic secretion culture can aid in the diagnosis.

29 Infection of the accessory sex glands may cause a deficiency of marker substances in the seminal plasma. Thus, impaired secretion of the seminal vesicles characterized by a decreased fructose concentration. Disturbed secretion of the prostate may result in either later or incomplete liquefaction, or increased threadiness of the seminal plasma after liquefaction, or too alkaline pH, or decreased concentration of prostatic acid phosphatase.

Code acid phosphatase (a), fructose (b) and pH (c) appropriately as 'normal' or 'abnormal'.

30–31 The diagnosis of acute prostatitis is easy since the symptoms are evident, prostatic examination is overtly pathological and cytological and bacteriological examination of the prostatic fluid is clearly abnormal. On the contrary, chronic (aspecific) infection or inflammation of the prostate or
1. Prostatic secretion culture
   - 1 negative
   - 2 positive

2. Prostatic secretion cytology
   - 1 negative
   - 2 positive

Seminal vesicles may be difficult to detect. Sometimes, the patient recalls a short period of urinary disturbance indicating a more or less pronounced attack of acute urethral prostatitis, but such episodes may have been lacking. At rectal palpation the prostate is found to be slightly tender, enlarged, oedematous or indurated. Microabcesses may occur whenever the inferior glandular part of the prostate is infected, whereas chronic infection of the superior part leads to prostatism, bladder neck fibrosis or sexual insufficiency. Cytological and bacteriological examination of the fluid obtained after prostatic expression may confirm the diagnosis. Such fluid may however be difficult to obtain and analysis of the urinary sediment after prostatic massage may then give the necessary information. In order to prove unequivocally a diagnosis of inflammation, the prostatic expression fluid should contain at least 40 leucocytes per high power field together with altered cells from the prostate or seminal vesicles. Three main spermiological alterations should be considered.

1) The presence of an increased number (>1 million/ml) of peroxidase positive leucocytes indicates an inflammatory process. It may be difficult to differentiate between granulocytes and other round cells, such as desquamated spermatoigenetic cells in the fresh ejaculate. The Endtz stain which colours peroxidase positive granulocytes brown and all other cells pink should be used (See Appendix 9).

2) Sperm culture will disclose the presence of pathological bacteria such as E. Coli, Proteus species, Streptococcus faecalis, Staphylococcus aureus, Klebsiella or Neisseria gonorrhoeae. Trichomonas infections and T-mycoplasma, chlamidia, and anaerobic bacteria may also be found.

It may however be difficult to decide whether bacteria originate from the skin or anterior urethra, and therefore should be considered as contaminants. In order to reduce contamination, the patients must be instructed to abstain from sexual intercourse for at least 3 days, they should void urine before the semen collection and clean hands, penis and genital region before masturbation. Some further clue may be obtained by the comparison of sperm culture of the split ejaculate fractions. Bacterospermia is considered to be significant if:
32. Post coital urine - sperm present
   1 no  2 yes

33. Final diagnosis (Appendix 10)
   a. 
   b. 
   c. 

34. Additional Comments

35. Name of Investigator (please print)

Signature Date

- either there is homogenous growth of 1000 or more pathogenic bacteria per ml
- or homogenous growth of at least 10,000 bacteria per ml of non-pathogenic strains, such as Staphylococcus epidermidis, Corynebacterium species, Acinetobacter calco aceticus, Serratia, anaerobic Streptococcus.

Seminal fluid culture results should be coded appropriately as 'negative' or 'positive', and details of abnormalities should be given. The same is true for the prostatic secretion culture and prostatic cytology.

In some cases of aspermia, the post coital urine test for sperm should be performed in order to differentiate between ejaculatory disturbance (no sperm in urine) and retrograde ejaculation (sperm present in urine).

Method: Subject should be asked to void prior to sexual intercourse or masturbation, and the first post orgasmic urine should be collected in a glass container. The specimen should be centrifuged and examined for the presence or absence of sperm. Code appropriately on form.

The final diagnosis should be entered in the space provided and coded. Additional comments may be added if the physician desires. See Appendix 10 for diagnostic codes.

Additional comments may be entered here.

Investigator should enter his/her name (please print), signature and the date in the space provided.
Appendix 1

Ferriman and Gallwey Hirsuties Score
Clinical Assessment of Body Hair Growth in Women

Clinical problems related to hirsuties in women have usually been approached as if there were a clear dividing line between hirsuties and the normal state. Body hair growth appears, however, to be a graded characteristic (1). A method for assessing hair growth is needed which will be quantitative and, at the same time, suitable for clinical use. A number of studies of hair growth in men and women have been reported (2-9) since the pioneer work of Danforth and Trotter in 1922 (10). The problem of assessment resolves itself into a selection of suitable sites for study, and the choice of a method for grading hair growth at any given site.

The various sites are not involved consistently in the female; for example, the face and chest may be affected in one, and the lower abdomen and thighs in another. It is clearly desirable, therefore, to study a number of sites. The idea of grading hair growth at any site according to the density and the area involved was introduced by Dupertuis, Atkinson and Elfrman (3), and developed by Garn (5). The involvement of any site with increasing hair growth tends to follow a definite pattern, so that it is not difficult to select a number of gradings at each site. Hair growth is scored according to the sum of the gradings obtained. This method is comparatively precise, since the spread of scoring is considerable. It is considered the best method devised so far for clinical use. More objective methods such as weighing or counting hairs are clinically impractical, especially if a number of sites are to be studied.

The nature of the scoring in the population at large must be known for any method before it can be of use in clinical studies. The method adopted in this department has therefore been applied to a control series of 430 women and the findings form the basis of the present communication.

Material and Methods

Adequate co-operation in an investigation of this nature was unlikely to be forthcoming from any group of subjects outside a hospital. It was therefore decided to study a consecutive series of women attending a general medical out-patient clinic. It was thought that the series would be sufficiently representative of the population at large for the purposes of this study, provided care was taken to exclude patients suffering from diseases or symptom complexes which might be associated with disturbances of hair growth (including diseases of the anterior pituitary, adrenal cortex and ovary, hypothyroidism, generalized skin diseases, menstrual disturbances and infertility). Only a few such cases were encountered. No patients came complaining of excessive hair growth, but a few had mild hirsuties. This hirsuties was considered to be constitutional in origin, and further study was not considered necessary on clinical grounds nor for the furtherance of this particular investigation.

Four hundred and thirty women were studied. Their ages ranged from 15 to 74 years.

The method of assessment was based upon that of Garn (5). Eleven sites were studied—lip, chin, chest, upper back, sacro-iliac region, upper and lower abdomen, arm and back of forearm, thigh and leg (Figs. 1 and 2). Only terminal hair growth was considered, and 5 grades were determined for each site, zero grading in each instance being an absence of terminal hair. Definitions of the gradings are shown in Table 1. The gradings for one of these sites are illustrated in Figure 3. Most of the women could be classified quite readily by this system. In some borderline cases, a subjective impression of density determined the final grading.

Results and Conclusions

The data on the 430 women, analyzed by age decades, are listed in Table 2. Study of the findings led to certain conclusions.

Age Range for Comparison of Hair Growth

It can be seen that after the age period 45-54, hair tended to increase on the face and to disappear from all other sites. A similar effect of age has been observed by other workers (2, 4, 9, 11). Adolescence is known to be a period of increasing hair growth. The age range in which the hair growth of subjects can be compared, therefore, cannot be precisely defined, but it is around 20-40 years.
Table 1. Definition of Hair Gradings at each of 11 Sites (Grade 0 at all sites indicates absence of terminal hair.)

<table>
<thead>
<tr>
<th>Site</th>
<th>Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Upper lip</td>
<td>1</td>
<td>A few hairs at outer margin.</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>A small moustache at outer margin.</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>A moustache extending halfway from outer margin.</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>A moustache extending to mid-line.</td>
</tr>
<tr>
<td>2. Chin</td>
<td>1</td>
<td>A few scattered hairs.</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Scattered hairs with small concentrations.</td>
</tr>
<tr>
<td></td>
<td>3 &amp; 4</td>
<td>Complete cover, light and heavy.</td>
</tr>
<tr>
<td>3. Chest</td>
<td>1</td>
<td>Circumferential hairs.</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>With mid-line hair in addition.</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Fusion of these areas, with three-quarter cover.</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Complete cover.</td>
</tr>
<tr>
<td>4. Upper back</td>
<td>1</td>
<td>A few scattered hairs.</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Rather more, still scattered.</td>
</tr>
<tr>
<td></td>
<td>3 &amp; 4</td>
<td>Complete cover, light and heavy.</td>
</tr>
<tr>
<td>5. Lower back</td>
<td>1</td>
<td>A small tuft of hair.</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>With some lateral extension.</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Three-quarter cover.</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Complete cover.</td>
</tr>
<tr>
<td>6. Upper abdomen</td>
<td>1</td>
<td>A few mid-line hairs.</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Rather more, still mid-line.</td>
</tr>
<tr>
<td></td>
<td>3 &amp; 4</td>
<td>Half and full cover.</td>
</tr>
<tr>
<td>7. Lower abdomen</td>
<td>1</td>
<td>A few mid-line hairs.</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>A mid-line streak of hair.</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>A mid-line bend of hair.</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>An inverted V-shaped growth.</td>
</tr>
<tr>
<td>8. Arm</td>
<td>1</td>
<td>Sparse growth effecting not more than a quarter of the limb surface.</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>More than this, cover still incomplete.</td>
</tr>
<tr>
<td></td>
<td>3 &amp; 4</td>
<td>Complete cover, light and heavy.</td>
</tr>
<tr>
<td>9. Forearm</td>
<td>1, 2</td>
<td>Complete cover of dorsal surface; 2 grades of light and</td>
</tr>
<tr>
<td></td>
<td>3, 4</td>
<td>2 of heavy growth.</td>
</tr>
<tr>
<td>10. Thigh</td>
<td>1, 2</td>
<td>As for arm.</td>
</tr>
<tr>
<td>11. Leg</td>
<td>1, 2</td>
<td>As for arm.</td>
</tr>
</tbody>
</table>

Factors Underlying Body Hair Growth

In the 20–40 age group, it was observed that in most of the women a significant growth of hair was present on the forearm and leg, though a zero grading was much the commonest elsewhere. This feature was submitted to further study, attention being directed to the 161 women between the ages of 18 and 38. Two scores were obtained for each subject, one being the sum of gradings for the forearm and leg, and the other the sum of the gradings for all other sites. The percentage incidences of the various scores obtained for the forearm and leg were calculated, as were those for all other sites. The findings are contrasted graphically in Figures 4 and 5. The 2 curves differ greatly and it is possible that 2 factors underlie body hair growth. One type of growth, with main expression on the forearm and leg, may be sexually indifferent and protective in nature. The other, with clearest expression elsewhere, may be sexually determined and related to blood hormone levels or to sensitivity of hair follicles to circulating hormone. The action of the 2 factors must overlap. For reference purposes the sum of the gradings on the forearm and leg has been termed the ‘indifferent’ score, and the sum of the gradings from all other sites, the ‘hormonal’ score. Figure 6 shows corresponding ‘indifferent’ and ‘hormonal’ scores for each of the 161 subjects; \( r \) for the group was 0.48, and this showed a significant correlation (\( P < 0.001 \)).
Assessment of Hirsuties

The score for 'hormonal' sites alone can now be employed in the study of clinical problems concerned with hirsuties in women. Examination of findings in the present series of 161 women aged 18 to 38 permitted assessment of the significance of such scores found in clinical practice. An 'hormonal' score above 5 was found in 9.9 per cent (16 women), and above 7 in 4.3 per cent (7 women), but scores above 10 were found in only 1.2 per cent (2 women).

Figure 3. Hair growth gradings—front of chest.

Figure 4. Percentage incidence of the sums of the gradings for the forearm and leg ('indifferent' scores) in 161 patients aged 18-38.

Figure 5. Percentage incidence of the sums of the gradings of the lip, chin, front of the chest, upper and lower back, upper and lower abdomen, arms and thighs ('hormonal' scores) in 161 patients aged 18-38.
## APPENDIX 1

### Table 2. Percentage Frequency Distribution of Hair-growth Gradings at 11 Sites, by Age Decades

<table>
<thead>
<tr>
<th>Age Decade</th>
<th>No. of cases</th>
<th>Sites</th>
<th>Gradings</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-24</td>
<td>75</td>
<td>Lip</td>
<td>71 18 10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chin</td>
<td>98 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chest</td>
<td>93 6 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Upper back</td>
<td>96 1 6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lower back</td>
<td>86 13 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Upper abdomen</td>
<td>100 2 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lower abdomen</td>
<td>72 18 7 2 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Arm</td>
<td>74 21 5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Thigh</td>
<td>57 27 13 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Forearm</td>
<td>9 24 62 5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Leg</td>
<td>5 11 35 46 3</td>
</tr>
<tr>
<td>25-34</td>
<td>92</td>
<td>Lip</td>
<td>81 25 11 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chin</td>
<td>89 5 6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chest</td>
<td>86 12 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Upper back</td>
<td>100 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lower back</td>
<td>88 12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Upper abdomen</td>
<td>100 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lower abdomen</td>
<td>79 12 3 5 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Arm</td>
<td>77 18 4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Thigh</td>
<td>68 14 15 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Forearm</td>
<td>14 46 36 4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Leg</td>
<td>3 4 38 53 4</td>
</tr>
<tr>
<td>35-44</td>
<td>90</td>
<td>Lip</td>
<td>47 28 19 5 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chin</td>
<td>84 5 7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chest</td>
<td>76 18 6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Upper back</td>
<td>100 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lower back</td>
<td>86 14</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Upper abdomen</td>
<td>99 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lower abdomen</td>
<td>77 20 2 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Arm</td>
<td>93 7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Thigh</td>
<td>71 11 15 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Forearm</td>
<td>40 40 20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Leg</td>
<td>9 17 46 27 1</td>
</tr>
<tr>
<td>45-54</td>
<td>83</td>
<td>Lip</td>
<td>40 32 16 10 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chin</td>
<td>86 6 6 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chest</td>
<td>93 7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Upper back</td>
<td>100 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lower back</td>
<td>88 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Upper abdomen</td>
<td>99 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lower abdomen</td>
<td>91 4 2 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Arm</td>
<td>93 7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Thigh</td>
<td>76 13 8 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Forearm</td>
<td>57 27 14 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Leg</td>
<td>25 23 46 6</td>
</tr>
<tr>
<td>55-64</td>
<td>50</td>
<td>Lip</td>
<td>38 24 20 16 4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chin</td>
<td>88 20 10 4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chest</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Upper back</td>
<td>100 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lower back</td>
<td>98 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Upper abdomen</td>
<td>100 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lower abdomen</td>
<td>94 4 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Arm</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Thigh</td>
<td>86 6 8</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>94 6 8 2</td>
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<td>Lower abdomen</td>
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### HORMONAL SCORE

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### INDIFFERENT SCORE

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Figure 6. Correspondence of 'indifferent' and 'hormonal' scores for each of the 161 patients aged 18-38.

References

Appendix 2

Tanner Pubertal Stage

Figure 1. Differing degrees of adolescence at the same chronologic age. Upper row, 3 boys all aged 14.75 years. Lower row, 3 girls all aged 12.75 years.
The genital development stages, illustrated in Figure 2, are as follows:

Stage 1. Preadolescent. Testes, scrotum and penis are about same size and shape as in early childhood.

Stage 2. Scrotum and testes are slightly enlarged. The skin of the scrotum is reddened and changed in texture. There is little or no enlargement of the penis at this stage.

Stage 3. Penis is slightly enlarged, at first mainly in length. Testes and scrotum are further enlarged than in stage 2.

Stage 4. Penis is further enlarged, with growth in breadth and development of glans. Testes and scrotum are further enlarged than in stage 3; scrotal skin is darker than in earlier stages.

Stage 5. Genitalia are adult in size and shape.

Figure 2. Standards of genital maturity in boys. (From Tanner, 1962)
The pubic hair stages, illustrated in Figure 3 for boys and girls are as follows:

Stage 1. Preadolescent. The vellus over the pubes is not further developed than that over the abdominal wall, i.e., no pubic hair.

Stage 2. There is sparse growth of long, slightly pigmented downy hair, straight, or slightly curled, chiefly at the base of the penis or along the labia.

Stage 3. The hair is considerably darker, coarser and more curled. It spreads sparsely over the junction of the pubes.

Stage 4. Hair is now adult in type, but the area covered is still considerably smaller than in the adult. There is no spread to the medial surface of the thighs.

Stage 5. The hair is adult in quantity and type with distribution of the horizontal (or classically 'feminine') pattern. Spread is to the medial surface of the thighs, but not up the linea alba or elsewhere above the base of the inverse triangle.

Figure 3. Standards for pubic hair ratings in boys and girls.
The breast development stages (Reynolds and Wines, 1948), illustrated in Figure 4 are as follows:

Stage 1. Preadolescent. There is elevation of the papilla only.

Stage 3. Breast and areola are both enlarged and elevated more than in stage 2, but with no separation of their contours.

Stage 4. The areola and papilla form a secondary mound projecting above the contour of the breast.

Stage 5. Mature stage. The papilla only projects, with the areola recessed to the general contour of the breast.

Figure 4. Standards for breast development ratings. (From Tanner, 1962)