



Male Contraception in 2024

Day of the Young GP

UZ GHENT

24/02/2024

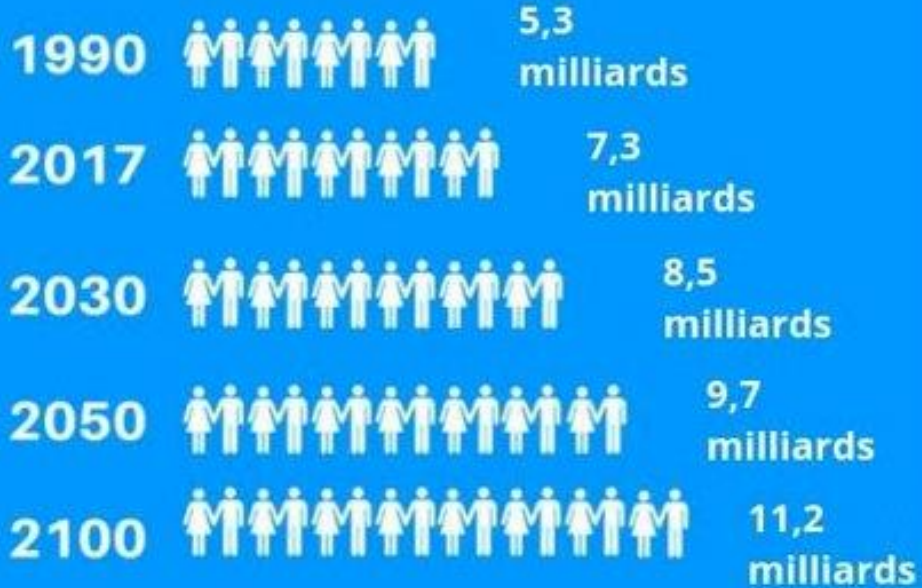
D. Murillo M. D.

CHU St-Pierre

Brussels

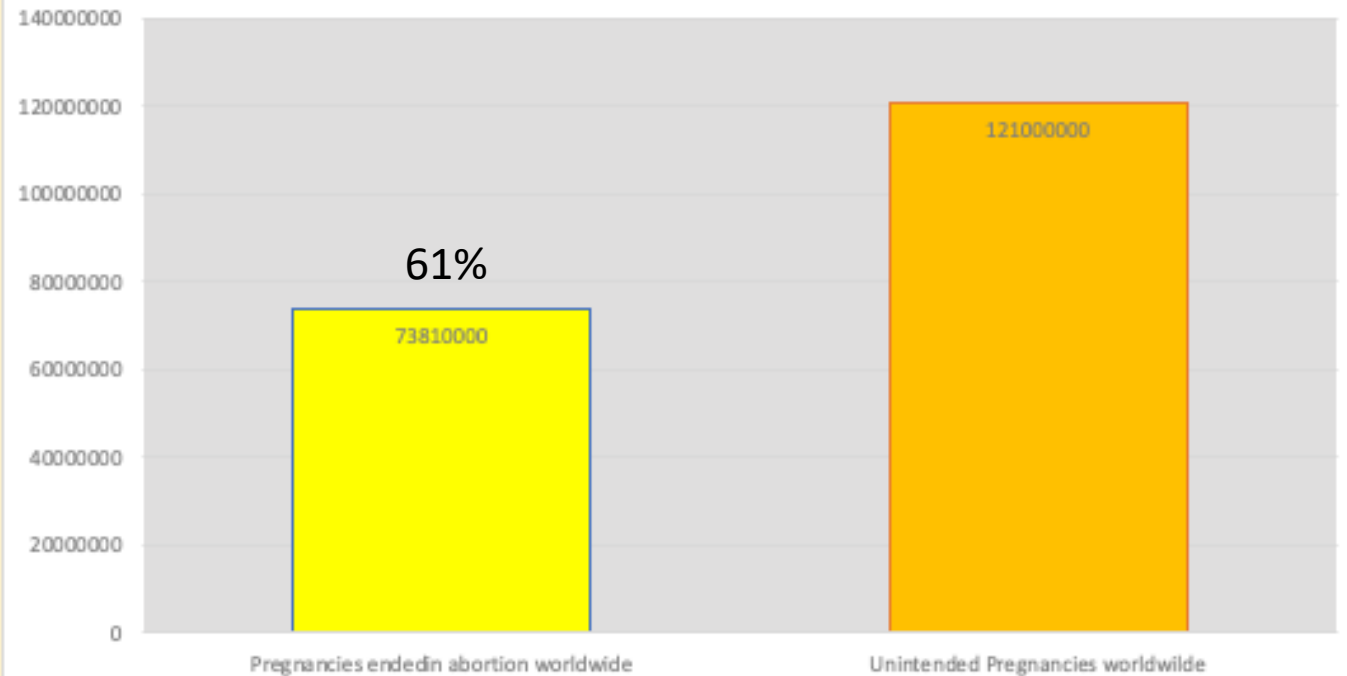
LA POPULATION MONDIALE

Projections jusqu'en 2100



Source: Nations Unies, Division de la population
(Département des affaires économiques et sociales)

Unintended Pregnancies worldwide J. Bearak & al , Lancet 2020



“Seeing the Unseen: The case for action in the neglected crisis of unintended pregnancy”
UNFPA report - March 2022

ACTIVDOCTORS ONLINE

Male Contraceptives

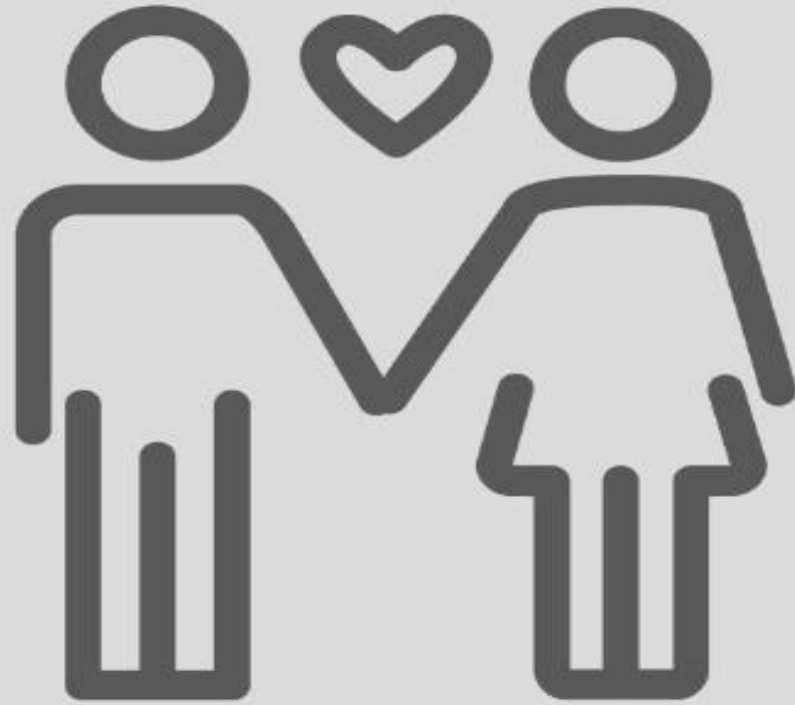
- Condom
- Vasectomy
- Abstinence
- coitus interruptus

NEWEST CONTRACEPTIVE METHODS FOR WOMEN

- Condom
- Female condom
- Oral contraception
- Hormonal ring
- UID
- Contraceptive injection
- Surgical sterilization
- Implant
- Coitus interruptus
- Calendar rhythm method
- Vaginal douche
- Contraceptive patch
- Diaphragm / cap

WWW.DRELIST.COM





Condom



Vasectomy

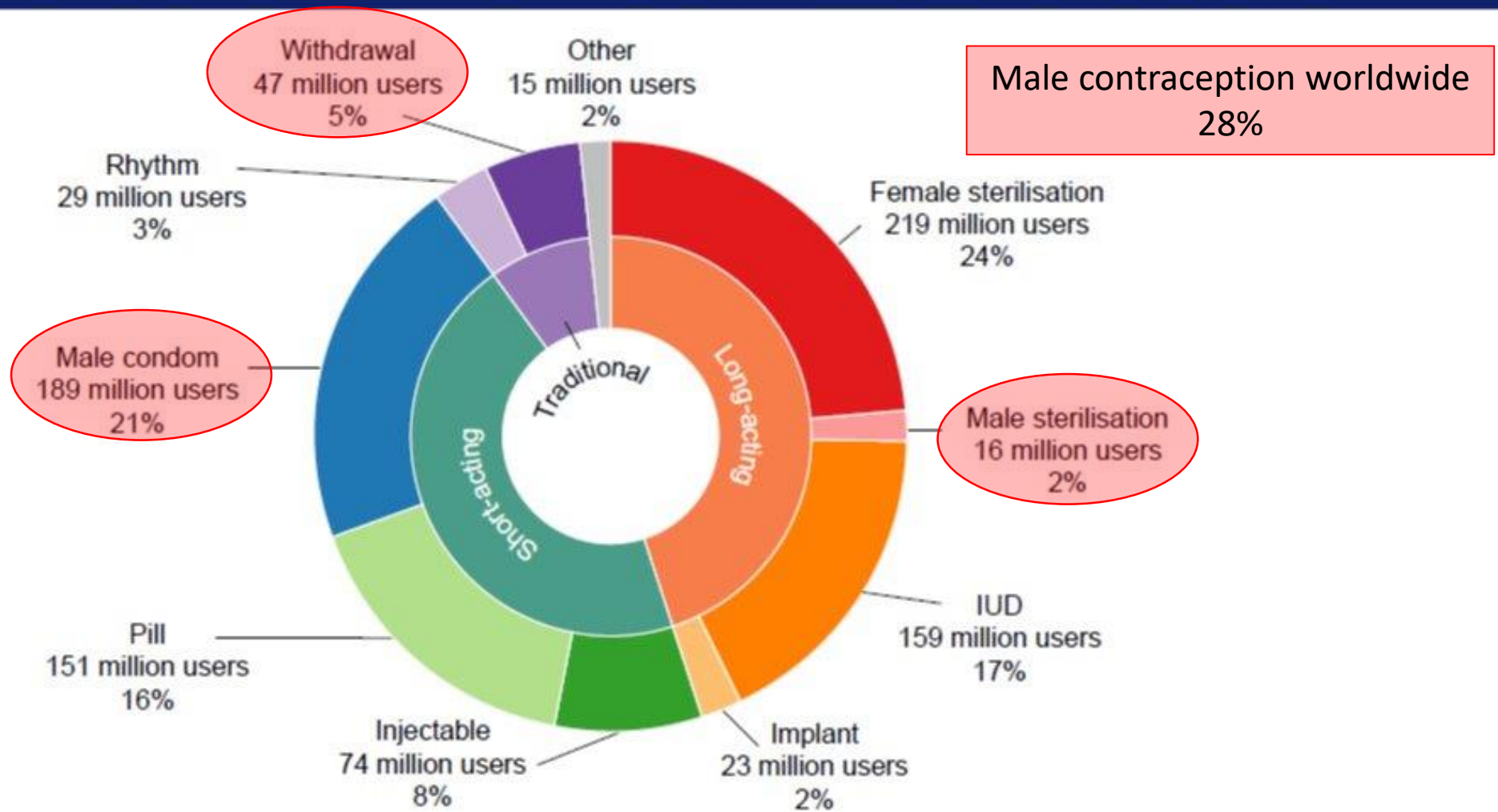


Abstinence



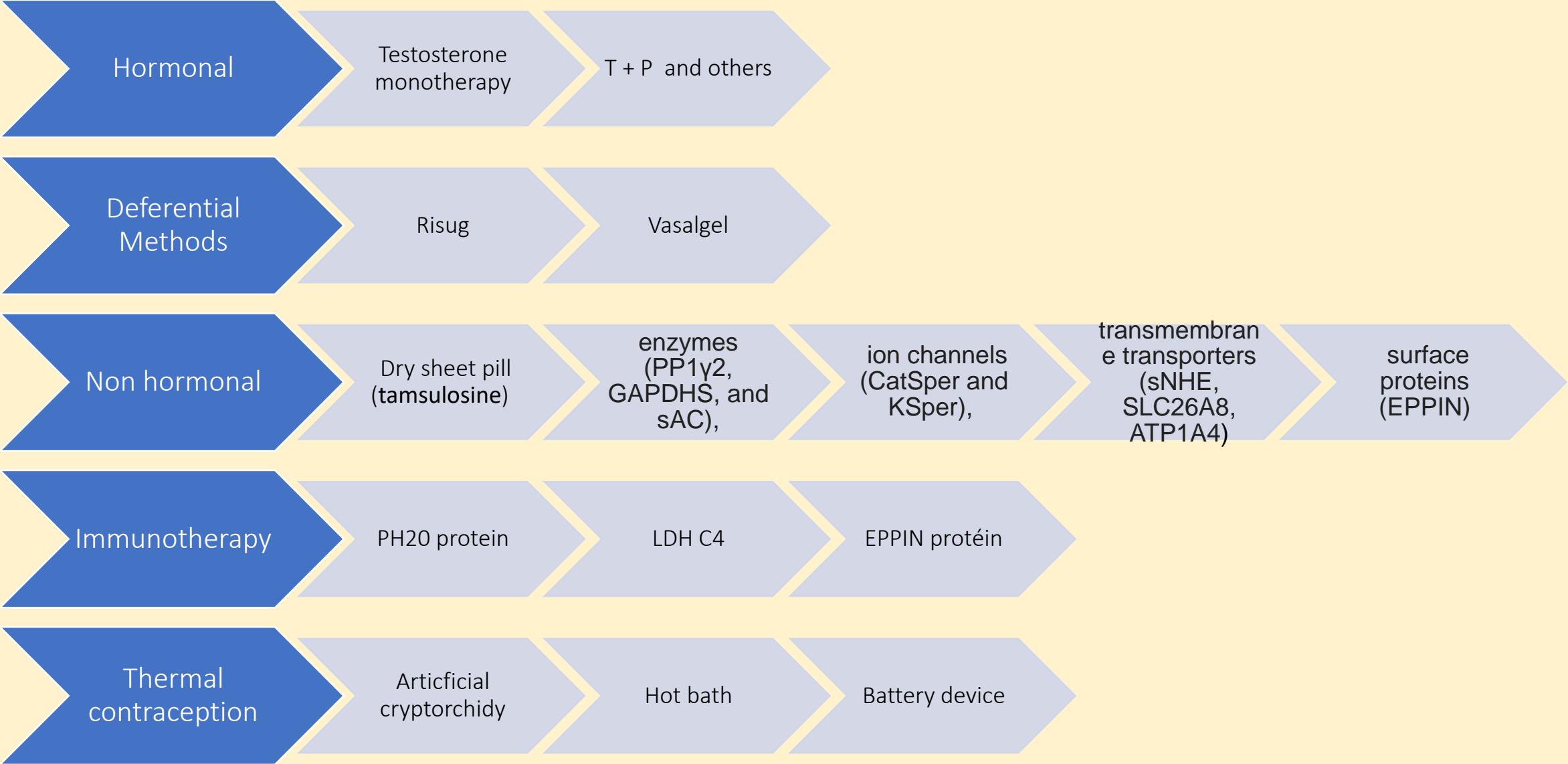
coitus interruptus

Figure 2. Estimated numbers of women of reproductive age (15-49 years) using various contraceptive methods, worldwide, 2019



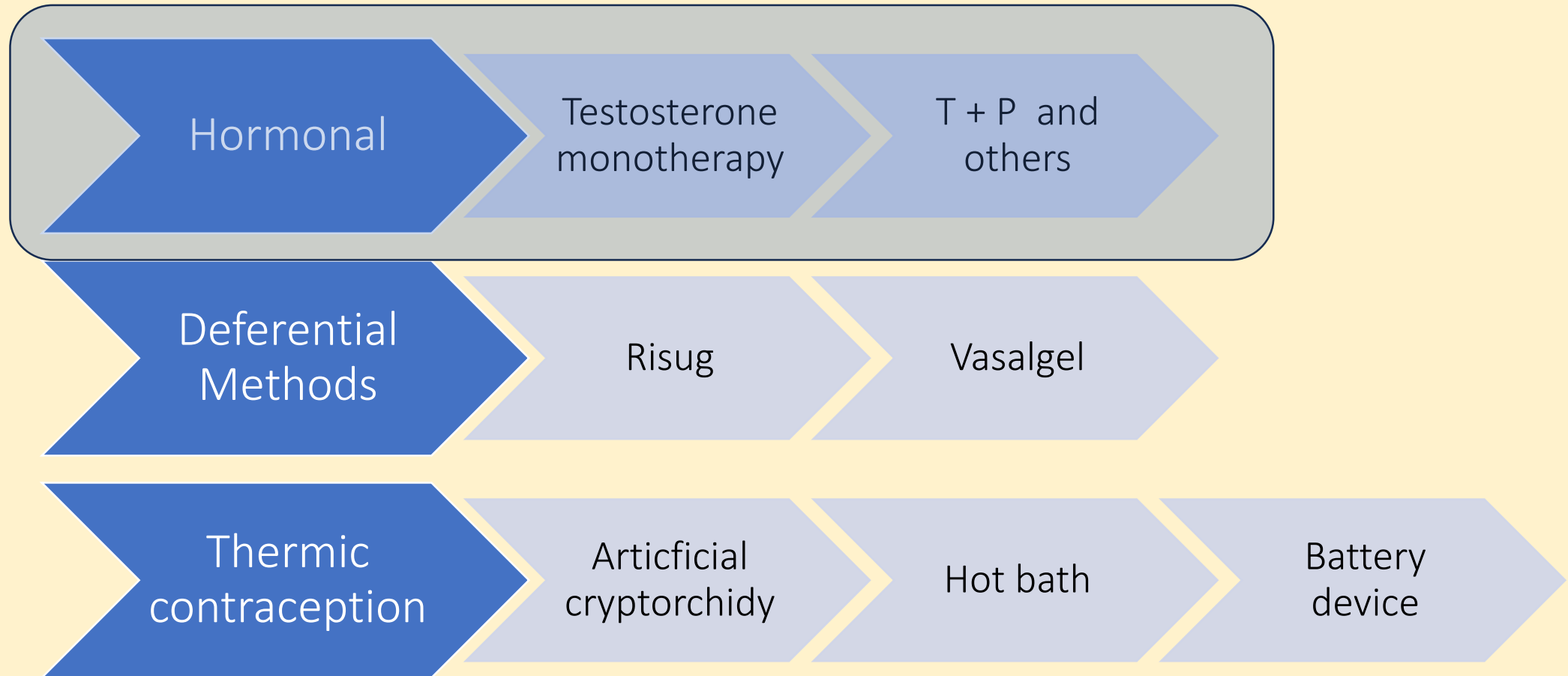
Data source: Calculations are based on the data compilation *World Contraceptive Use 2019*, additional tabulations derived from microdata sets and survey reports and estimates of contraceptive prevalence for 2019 from *Estimates and Projections of Family Planning Indicators 2019*. Population-weighted aggregates.

Research in male contraception



Research in male contraception

Human studies



Hormonal male contraception

WHO studies "proof of concept" 1990-1996

THE LANCET

MEDICAL SCIENCE | VOLUME 336, ISSUE 8721, P955-959, OCTOBER 20, 1990

Contraceptive efficacy of testosterone-induced azoospermia in normal men

WORLD HEALTH ORGANISATION TASK FORCE ON METHODS FOR THE REGULATION OF MALE FERTILITY

Published: October 20, 1990 - DOI: [https://doi.org/10.1016/0140-6736\(90\)92416-F](https://doi.org/10.1016/0140-6736(90)92416-F)

- 556 normal men normal semen.
- Multicentric - 9 countries.
- 200mg Testostérone E/weekly
- 89% men: spermogram <5millions sp/ml between 52 et 100 days.
- Pearl Index 0,8 à 1,4 for sperm < 3 Millions / ml
- Reversible
- Male contraceptive threshold: <1 Million de spz /ml.

FERTILITY AND STERILITY
Copyright © 1996 American Society for Reproductive Medicine

Vol. 65, No. 4, April 1996
Printed on acid-free paper in U. S. A.

Contraceptive efficacy of testosterone-induced azoospermia and oligozoospermia in normal men

World Health Organization Task Force on Methods for the Regulation of Male Fertility*†‡§

World Health Organization, Geneva, Switzerland

Side-effects

Acne

Weight gain(1-2 kg muscular mass)

Libido modifications (increase)

Mood swings

Lipidic profile modification & increase of hematocrit

Drop-out: 32.8%

Table 3 Number of Discontinuations and Cumulative Life-Table Rates

Reason	No. of subjects	Cumulative rate*
		%
Technical reasons		
Nonsuppression	8	2.4 (1.2 to 4.8)
Escape from suppression	4	1.3 (0.5 to 3.4)
Protocol violation	3	0.8 (0.3 to 2.5)
Injection problems	21	5.1 (3.2 to 7.9)
Medical reasons		
Pregnancy	17	4.7 (2.9 to 7.5)
Suppression phase	7	1.9 (0.9 to 3.9)
Efficacy phase	10	3.2 (1.7 to 5.8)
Other medical reasons	35	9.4 (6.7 to 13.2)
Personal reasons	50	12.2 (9.1 to 16.1)
Loss to follow-up	10	2.7 (1.4 to 5.1)
All discontinuations	148	32.8 (28.5 to 37.7)

* Cumulative life-table discontinuation rate at 1 year since start of injections, except for efficacy phase discontinuations for which rate 1 year since entry into efficacy is shown. Values in parentheses are 95% CI.

Testostérone en
monothérapie

Association
Testostérone +
Progestérone

Association
Testostérone + agoniste
ou antagoniste de la
GnRH

Associations
Testostérone +
estrogène

Association
Testosterone anti-
androgènes

Long Acting Reversible
Contraception
masculines (LARC)

Mommers & al, 2008;
Behre & al, 2016
Gu & al, 2003 and 2009



Table 1. Efficacy studies.

Regimen	Enrolled subjects	Sperm concentration threshold (million/ml)	Subjects reaching threshold	Subjects entering efficacy	Subjects completing efficacy	Pregnancy rate N (%/couple-year)
TE 200 mg/week ⁷	271	azoospermia	157	157	119	1 (0.8)
TE 200 mg/week ⁸	399	< 3 (reduced from < 5)	349	268	209	4 (1.4)
TU 1000 (loading) + 500 mg/4 week ⁹	308	< 3	299	296	280	1 (2.3)*
Depot MPA 300 mg/12 week testosterone pellets 800 mg/24–16 week ¹⁰	55	< 1	53	51	30	0 (0)
TU 1000 (loading) + 500 mg/4 week ¹¹	1045	≤ 1	855	855	733	9 (1.1)
TU 1000 mg + NETE 200 mg/8 week ¹²	320	≤ 1	274	266	111 [§]	4 (1.57)

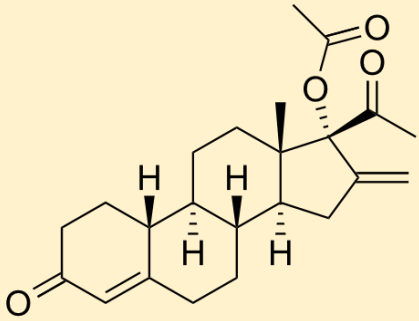
*One pregnancy was attributed to sperm rebound.

[§]Trial terminated before the planned end of the study.

MPA, medroxyprogesterone acetate; NETE, norethisterone enanthate; TE, testosterone enanthate; TU, testosterone undecanoate.

Nouveaux dérivés stéroïdiens

Etudes en suppression des gonadotrophine et/ou spermatogénèse

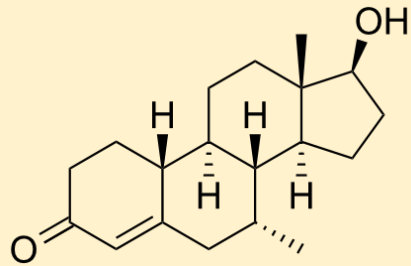


• **NESTORONE**
Progestin (gel)

Segesterone Acetate

- Inhibiteur gonadotrophines

Mahabadi et al. 2009
Ilani et al. 2012
Roth et al 2014
Anawalt et al. 2019

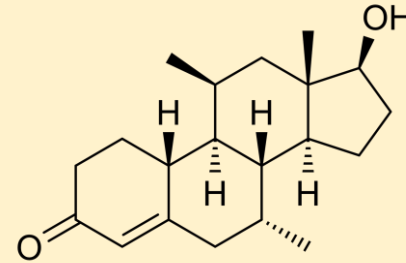


• **TRESTOLONE or MENT**
Androgen (Implants)

7 alpha-méthyl-19 N
Testosterone acetate

- Inhibiteur compétitif récepteurs androgène et progestérone

Garci Becerra et al. 2012
Walton et al. 2007

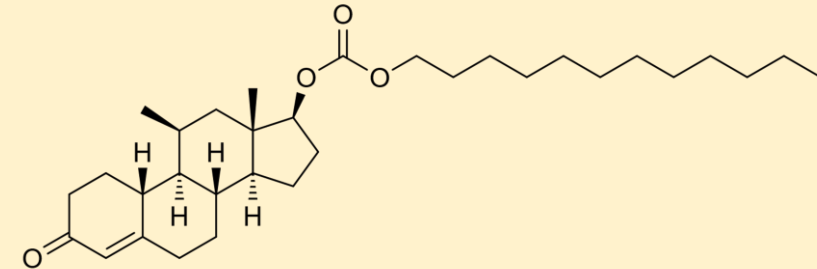


• **DMAU**
Androgen (oral)

Dimethandrolone undecanoate

- Inhibiteur compétitif récepteurs androgène et progestérone

Surampudi et al. 2014
Thirumalai et al. 2018
Nguyen et al. 2020



• **11β-MNTDC**
Androgen (oral)

11β-methyl-19-
nortestosterone-17b
dodecylcarbonate

- Activité progestative

Wu et al. 2019

Supprimer l'épinglé Afficher

Société d'Andrologie de Langue Française La Contraception Masculine

La parole est à : Cité International...



Société d'Andrologie de Langue Française La Contraception Masculine

Nestorone/Testosterone Transdermal Gel for Male Contraception

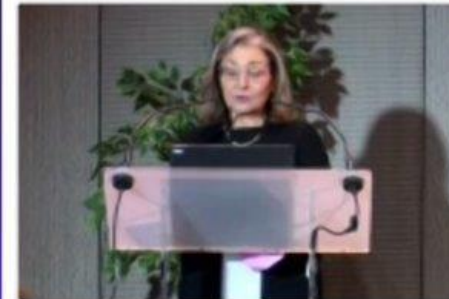
REGINE SITRUK-WARE, MD
POPULATION COUNCIL, NEW YORK, NY, USA

Paris, 20 Janvier 2023



Jeunes Scientifiques - Vendredi 20 Janvier 2023

Réactiver le son Démarrer la vidéo Participants 46 Discuter Partager l'écran Réactions Applications Quitter



**Clinical Evaluation of Daily Application of Nestorone® (NES) and
Testosterone (T) Combination Gel for Male Contraception (Phase 2 b)
Current Status**

Etude Phase 2 B

420 hommes enrôlés en 11/22

Phase de Suppression complétée 03/2023

Phase efficacité terminée 03/2024

Fin étude 09/2024



Société d'Andrologie de Langue Française

La Contraception Masculine

La parole est à : Cité International...

• Is NES/T Gel efficacious?

Efficacy

- Most men (90%) showed suppression of sperm output to < 1 million/ml

Adverse events

- Acne, weight gain, insomnia, dry skin,
- Libido increased, libido decreased, mood swings, depressed mood

Bridging studies on a combined gel with decreased T dosage

- Pharmacokinetics study of combined Nes T gel compared to T gel applied daily for 28 days
- Prevention of skin transfer of Nes and T leading to secondary exposure of females to these hormones



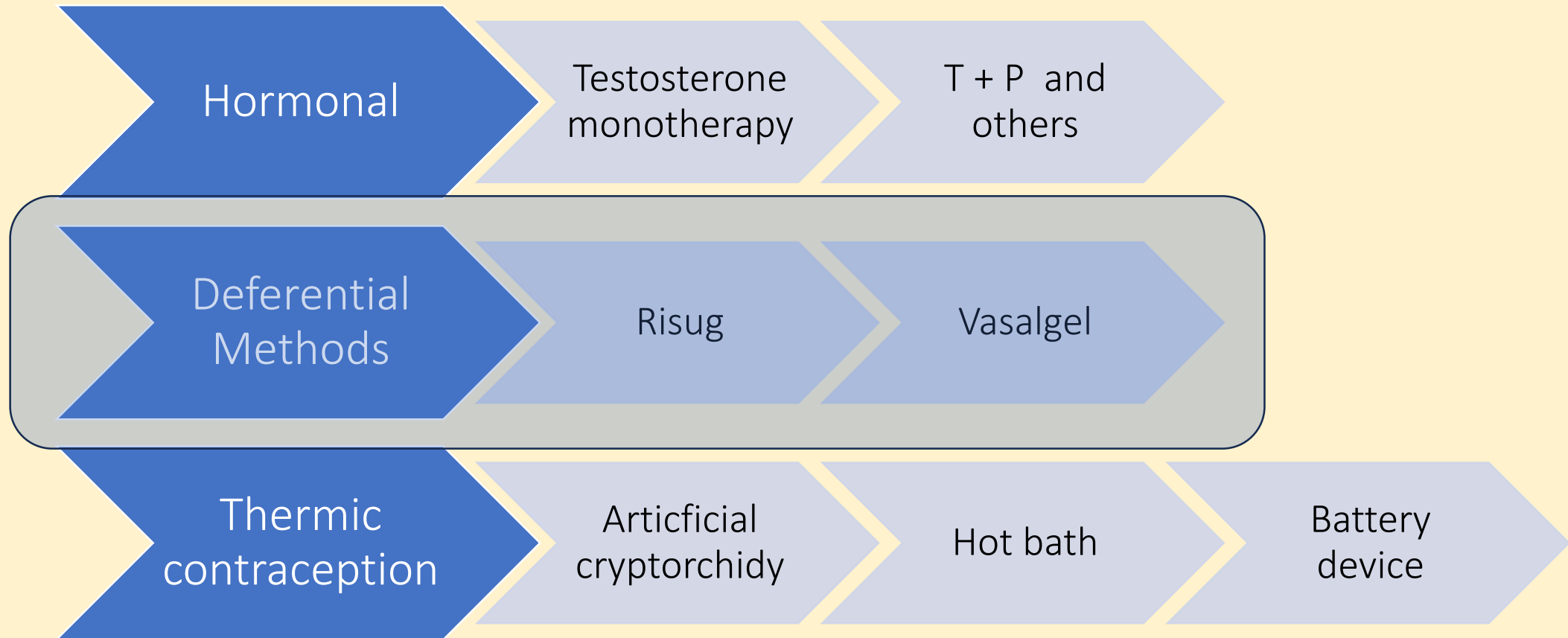
Probably the first hormonal contraceptive for man?

Hormonal contraception conclusions

1. Proven efficacy, PI equivalent to female hormonal contraception: many phase II studies have proven this.
2. The side effects are similar to those of female contraception (or even less severe).
3. Long-term effects on the prostate and bone density are unknown. However, long-term treatments for hypogonadism are reassuring.
4. Ethnic and individual variation in contraceptive response remains to be resolved (reason unknown).
5. Phase III studies on oral forms, gels, injections and implants should enable products to be marketed.
6. Very promising new compounds

Research in male contraception

Human studies



Reversible vasectomy

RISUG (India) Phase III

VASALGEL (US) Phase II

Fondation Parsemus=> Plan A™: (Next Life Science) Durée efficacité prévue: 10 ans

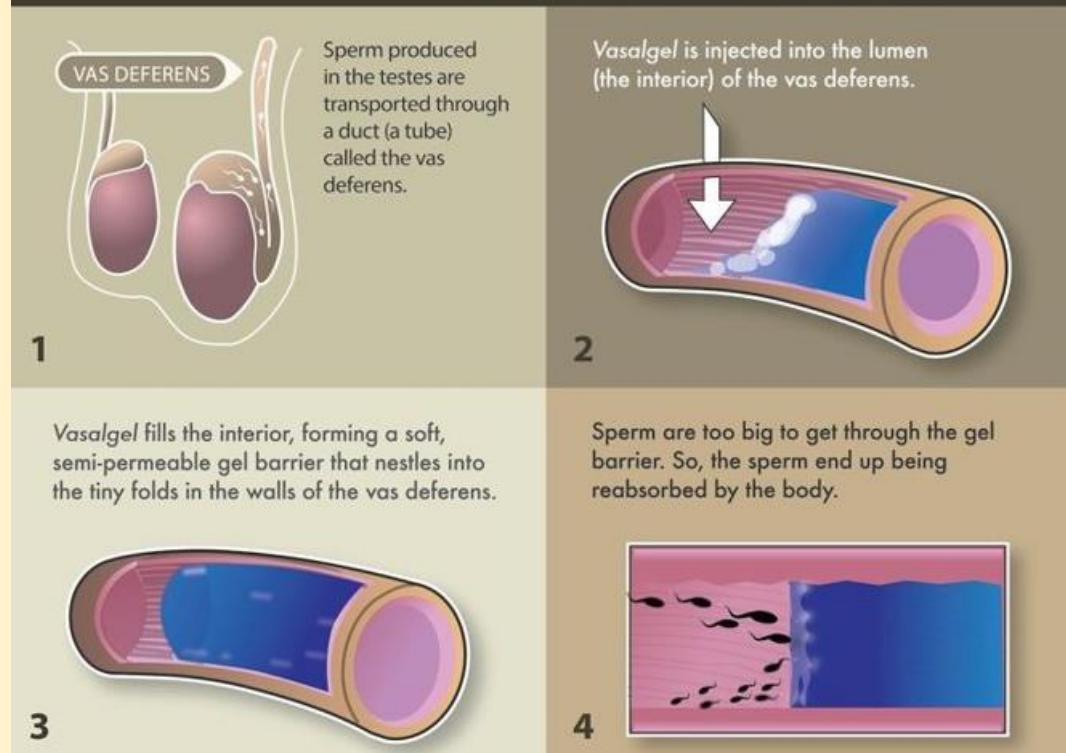
ADAM (US) phase I-II?

Ultrasound guided intradefereferential injection

- Very efficient
- Little side effects
- Unproven Human reversibility



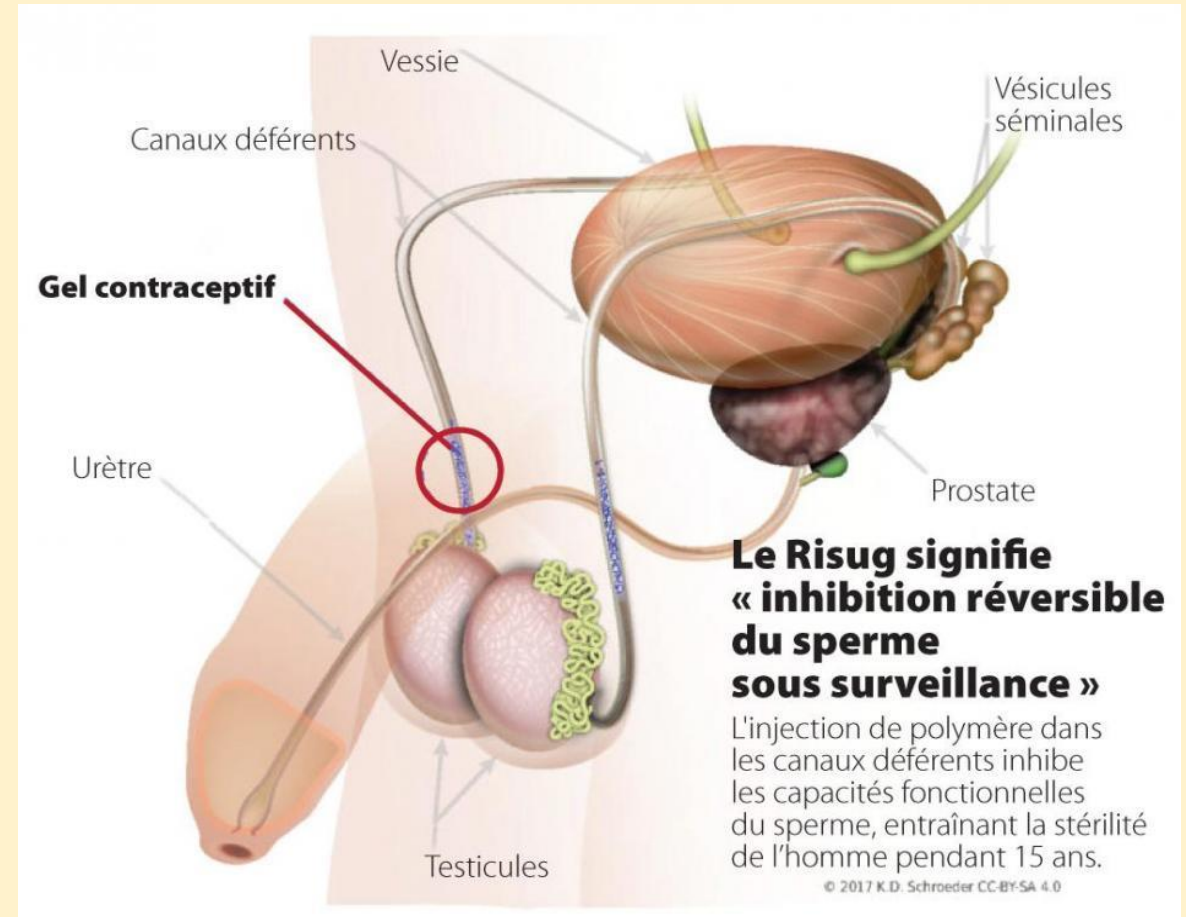
How does Vasalgel™ work?



RISUG HOW IT WORKS?



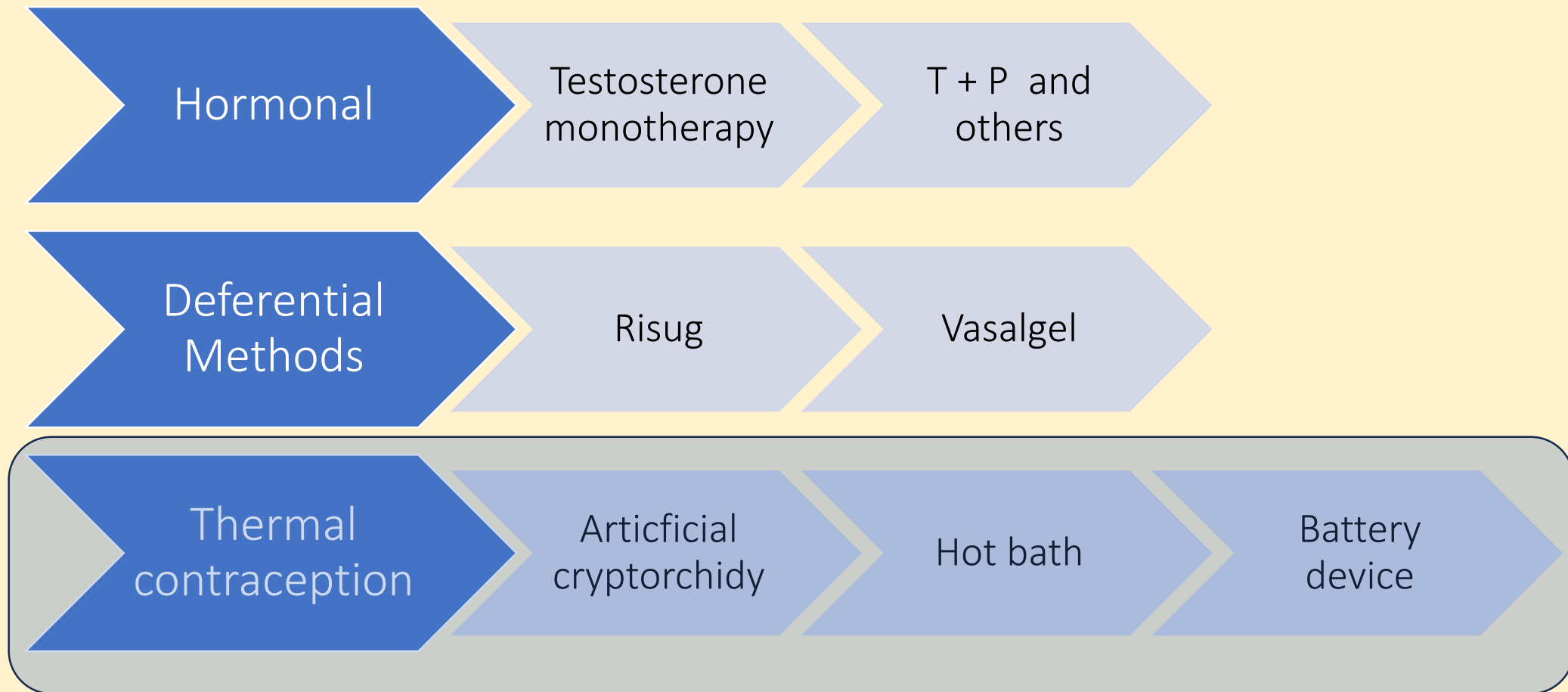
- Spermatozoa wall alterations
- Immobilisation
- Impaired Acrosomal reaction



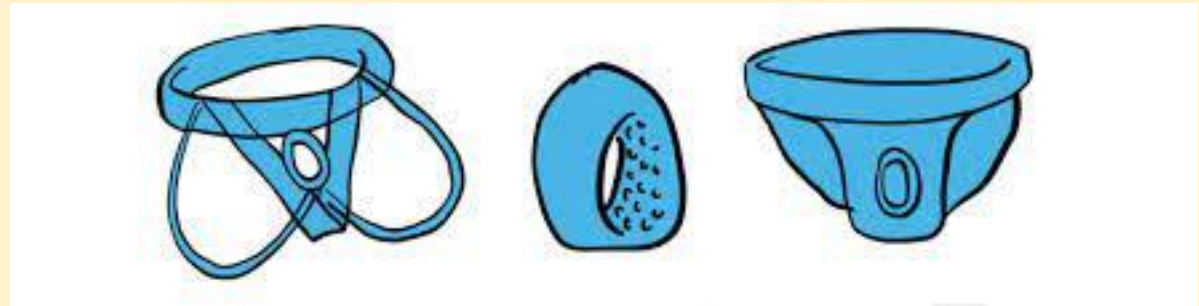
- [Indian J Med Res.](#) 2014 Nov; 140(Suppl 1): S63–S72.

Research in male contraception

Human studies



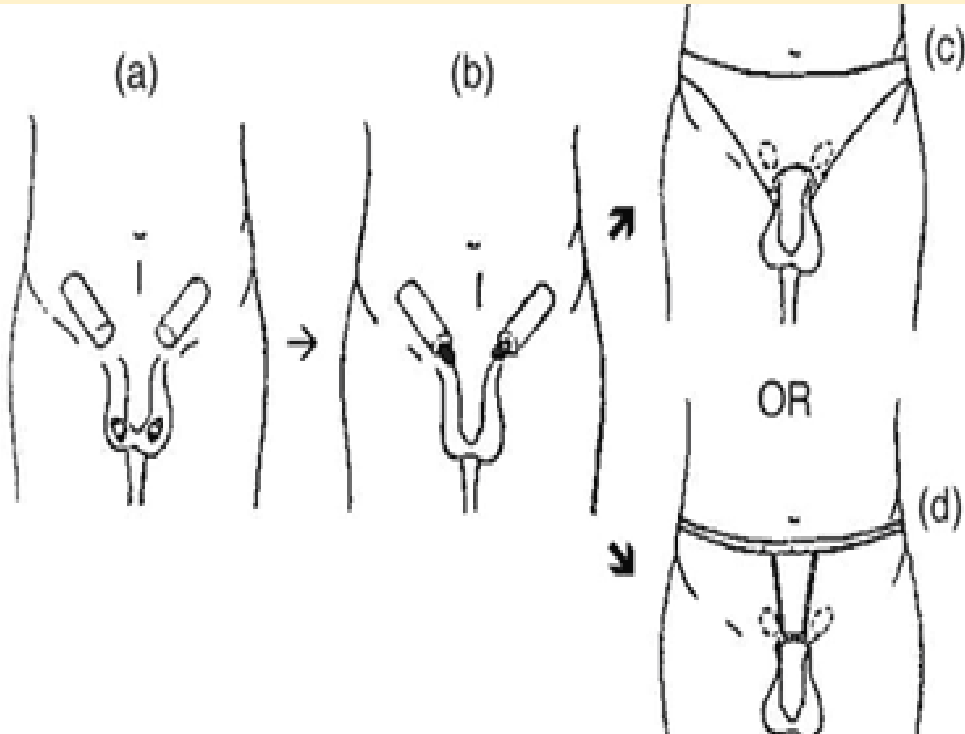
Thermal methods



Artificial cryptorchidism by jockstrap

Contraceptive efficiency

Mieusset – Bujan 1994



international journal of andrology 17:186-191 (1994)

The potential of mild testicular heating as a safe, effective and reversible contraceptive method for men

ROGER MIEUSSET and LOUIS BUJAN

Centre de Stérilité Masculine and CECOS Midi-Pyrénées, Hôpital La Grave, Toulouse, France

Essais cliniques de CM Thermique

Efficacité contraceptive : 3 études publiées

1991 (24h/j) : 28 couples, 252 cycles d'exposition : 0 grossesse.

Shafik

1992 (24h/j) : 14 couples, 126 cycles d'exposition : 0 grossesse.

Shafik

1994 (15h/j) : 9 couples, 159 cycles d'exposition : 1 grossesse,
consécutive à une mauvaise utilisation de la méthode.

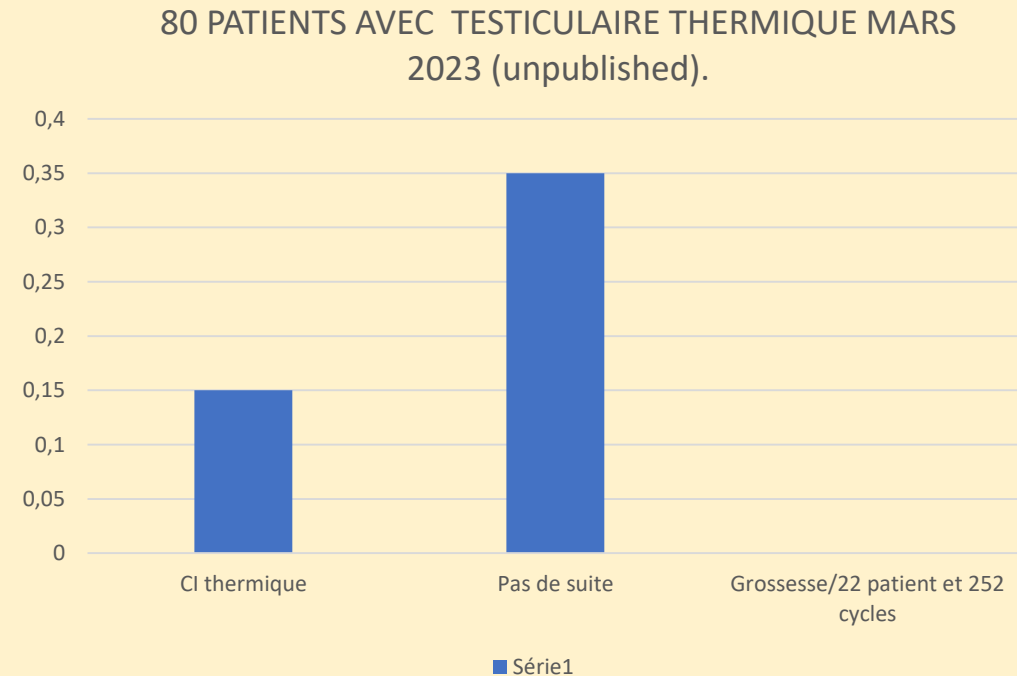
Mieusset- Bujan

51 couples : 0 grossesse sur 536 cycles d'exposition

Personal data 03/2023

80 patients

- 35% do not initiate CMT
- 15% have an IC
- 22 patients uses as unique contraceptive
- No pregnancy reported /252 cycles.



To date: no pregnancy reported in more than 50 patients since 2021.

Enquête transversale sur les dispositifs de contraception par remontée testiculaire : sécurité, acceptabilité, efficacité.

TESTIS_2021

THÈSE

Présentée et soutenue publiquement à la Faculté de Médecine Hyacinthe BASTARAUD
des Antilles et de la Guyane
Et examinée par les Enseignants de ladite Faculté

Le 11 janvier 2023

Pour obtenir le grade de

DOCTEUR EN MEDECINE

Par
GUIDARELLI Manon

I. Flow chart

Le diagramme de flux de l'étude est représenté en Figure 1.

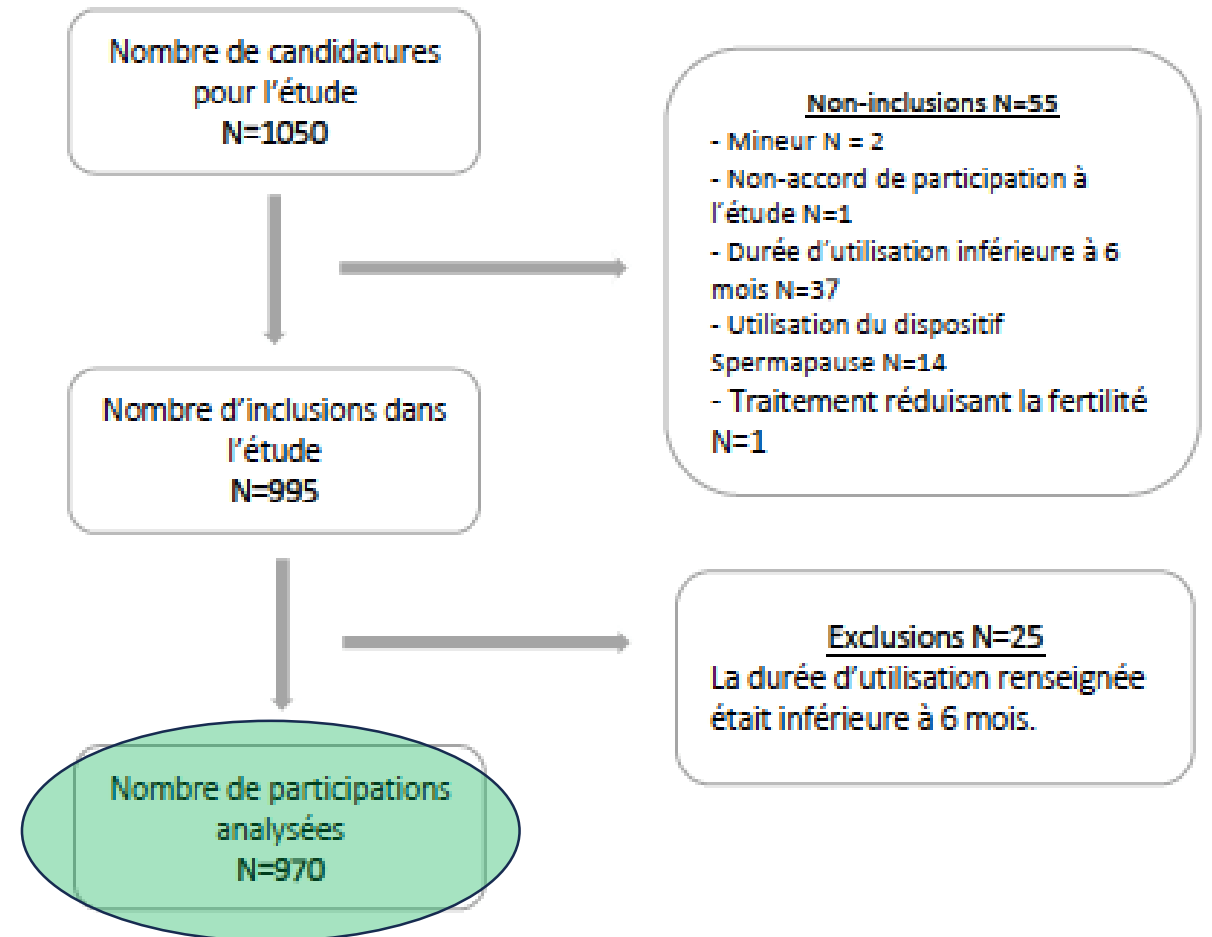


Figure 2. Diagramme de flux de l'étude TESTIS-21.

Contraception efficiency

Tableau 19. Durées d'exposition (en nombre de cycles féminins) à une contraception par remontée testiculaire (en mois). TESTIS_2021.

	Durée d'exposition totale à la CRT (mois) N=966	Durée d'exposition efficace (mois) N=568	Durée d'exposition efficace 1 an N=183
Somme (en mois)	13634	6386	3727
Nombre de grossesse	6	0	0
Indice de Pearl	0,53	0	0

Note : Durée totale = nombre de mois d'exposition sur toute la durée d'utilisation de la CRT ; Durée efficace = nombre de mois d'exposition depuis l'atteinte du seuil contraceptif et en l'absence de contraception supplémentaire ; Durée d'utilisation efficace 1 an : nombre de mois d'exposition depuis au moins un an d'atteinte du seuil contraceptif et en l'absence de contraception supplémentaire.




« LA CONTRACEPTION MASCULINE EXISTE
AUJOURD'HUI EN FRANCE. CESSONS DE DIRE QU'ELLE
EST POUR DEMAIN, SI LES HOMMES, LES MÉDECINS,
LES POUVOIRS PUBLICS EN ACCEPTENT L'IDÉE ET
LA MISE EN PRATIQUE, ELLE PEUT ÊTRE UTILISÉE
DÈS AUJOURD'HUI EN ALTERNANCE AVEC LA
CONTRACEPTION FÉMININE ET PERMET LE PARTAGE
DES RESPONSABILITÉS ET DES RISQUES.
ELLE CONSTITUE UN FACTEUR DE L'ÉGALITÉ
FEMMES-HOMMES. »

ET
TOUT LE
MONDE
se fait

ARDECOM



Collectif "Thomas Bouloù"
contraceptions testiculaires
& responsabilité masculine



COSO

Design process



COSO



Pad chauffant + batterie



Androswitch



Certification course

August 2022 - Sept. 2023

March 2023 - July 2023

2024 - 2026

Jan. 2027



Design of the clinical study

The clinical study of Andro-switch is currently being designed. Our partners are working on its development and defining the size of the panel, the necessary duration and the modalities of the study. This work will have to be validated by the authorities in order to launch the study at the end of 2023.



Andro-switch production compliance

In order to launch the clinical study, Andro-switch rings must be produced in compliance with the Medical Device Quality standard (ISO 13485:2016). Once the production unit is set up, a new generation of Andro-switch can be validated by the authorities to start the study.



Clinical study

At the beginning of 2024, the clinical study will begin. In total, a panel of about 200 men will be monitored in their use of Andro-switch for almost three years on several sites in France.



CE marking audit and market access

Following the clinical study, an audit conducted at Thorème will verify the conformity of the product and the proof of its safety and performance. This type of audit is carried out by bodies notified by the European Commission. If this audit is positive, Andro-switch can be declared compliant with the requirements of the European Medical Device Regulation.

Conclusion part one: Male contraception in 2023

Facts

- Today, only ancestral and inefficient techniques are available
- Many concepts explored
- Neglected development
- No interest of the pharma industry

Potential

- Enhancing contraceptive diversity
- Men education in their own fertility control
- Evolution of male sexual stereotypes
- Potential to reduce unintended pregnancies

Male contraception Practical aspects

First consultation

- Medical and Andrological history:
 - STD, orchitis (mumps), prostatitis
 - Surgical history (testicular, scrotal or inguinal and torsion...)
 - Androgen therapy?
 - Ejaculatory or erectile dysfunction.
- Andrological examination check:
 - Penis / uretra
 - Testicles: position/ palpation (mass?)/ volume
 - Epididymes and vas deferens presence
 - varicocoeles (Valsalva)
 - Inguinal hernia (Valsalva)



Male contraception Practical aspects

- The spermogram: 3-5 days of sexual abstinence (WHO standards 2010)

Table A1.1 Lower reference limits (5th centiles and their 95% confidence intervals) for semen characteristics

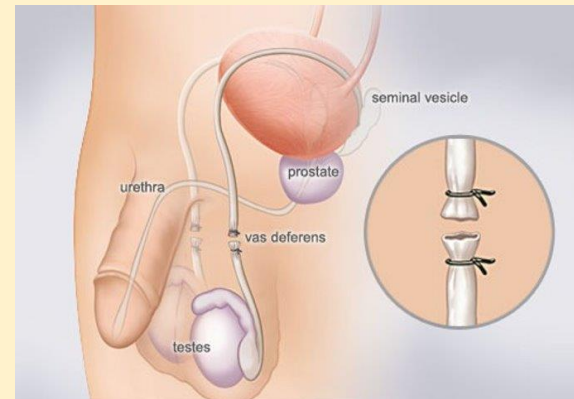
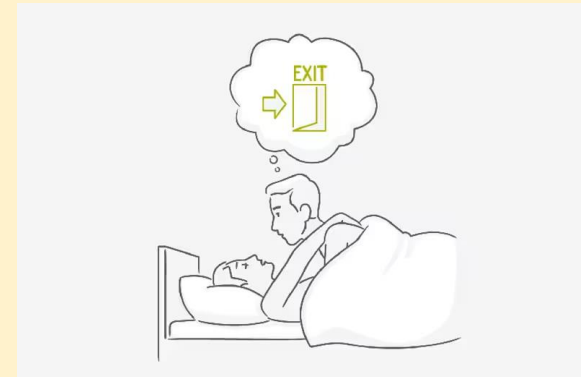
Parameter	Lower reference limit
Semen volume (ml)	1.5 (1.4–1.7)
Total sperm number (10^6 per ejaculate)	39 (33–46)
Sperm concentration (10^6 per ml)	15 (12–16)
Total motility (PR+NP, %)	40 (38–42)
Progressive motility (PR, %)	32 (31–34)
Vitality (live spermatozoa, %)	58 (55–63)
Sperm morphology (normal forms, %)	4 (3.0–4.0)
<i>Other consensus threshold values</i>	
pH	≥ 7.2
Peroxidase-positive leukocytes (10^6 per ml)	< 1.0
MAR test (motile spermatozoa with bound particles, %)	< 50
Immunobead test (motile spermatozoa with bound beads, %)	< 50
Seminal zinc (μmol /ejaculate)	≥ 2.4
Seminal fructose (μmol /ejaculate)	≥ 13
Seminal neutral glucosidase (mU/ejaculate)	≥ 20

Contraceptive threshold: < 1 Million spz/ml

Male contraception Practical aspects

What is known:

- Coitus interruptus
 - 5% of World population
 - Pearl Index (PI): optimal= 4% Real life conditions= 27% (WHO 2005)
- Condoms
 - 21% of World population
 - PI optimal= 3-5% Real life conditions: 10-15%
 - Prevention of STD'S
- Vasectomy
 - 2% of World population
 - PI= 0,15%
 - Permanent
 - For men with complete family



Male contraception Practical aspects

Hormonal contraception (Off label prescription)

Soufir, Mieusset: *Andrologie* (2012) 22:211-215

- Men <45 years old (prostate): Over 45 vasectomy is preferred.
- Contra indications:
 - history of phlebitis or thrombo-embolism
 - Cardiac (hypertension...), hepatic pathology (obstructive jaundice, steatosis),
 - Prostatic adenoma
 - Renal failure
 - Epilepsy,
 - sleep apnea
 - psychiatric conditions (psychosis, aggressivity),
 - Acne
 - Family history of prostate cancer: 1 case in the 1st degree, 2 in the 2nd degree
 - Tobacco: >5cig/d and alcoholism
- **Informed consent is required**

Male contraception Practical aspects

Hormonal contraception (Off label prescription)

Soufir, Mieusset: *Andrologie* (2012) 22:211-215

Clinical examination

- BMI <30
- Normal BP <14/9
- NO acne.

Biology

- Normal hematocrit
- Normal liver, kidney, lipid profile

Normal spermogram (WHO 2010):

- Conc >15 M/ml
- Progressive mot >32%
- Normal forms: >4%

Male contraception Practical aspects

Hormonal contraception regimen (Off label prescription)

Soufir, Mieuxset: *Andrologie* (2012) 22:211-215

- Testosterone Enanthate 200mg IM/week (Androtardyl) for maximum 18 months.
- 50 €/month non-reimbursed by social security
- Drug interactions: neuroleptics /antidepressive medication /glucocorticoids/ spironolactone/ketokonazole and others antimycotics
- Other drugs are tested and available such as Testostérone Undécanoate: 1000mg IM /12 sem (116€) alone or associated with progestatives as implants of etonorgestrel 143€/3 years).

Male contraception Practical aspects

Hormonal contraception: follow up: 18 months

- Spermogram threshold < 1 million spz/ml.
 - Achieved between 1 and 3 months of treatment (inhibition phase).
- What if contraceptive threshold not reached in 3 month:
 - continue another 1-2 months and re-evaluate
 - stop treatment if no response after 4-5 month of contraceptive use.
- Spermogram controls every 3 months (control of compliance and contraceptive efficacy)
- A physical and biological examination is recommended every 6 months.
- Reversibility: Average time to recover a normal sperm concentration is estimated at 3 - 4 months.

Hormonal contraception: side-effects

- Acne
- Changed libido (usually increased)
- Aggressivity, depression, mood swings
- Weight gain (1-2 kg) (muscular mass)
- Modification of lipids and increase in hematocrit (+2 %).

- Interruption for medical reason: 16% in WHO enanthate study

- If Abnormal blood pressure or blood parameters: **stop contraception.**

Male contraception Practical aspects

Thermic contraception

Soufir, Mieusset: *Andrologie* (2012) 22:211-215

daytime artificial cryptorchidism (15h/d) 7d/7d

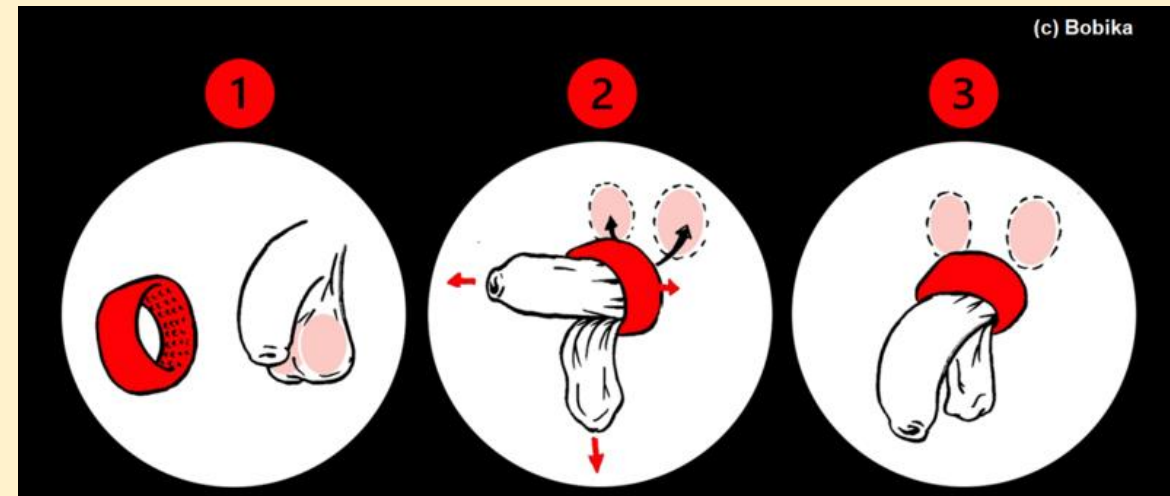
- Contra-indications:
 - History of current or former (treated) testicular descent disorders: cryptorchidism, ectopia
 - Inguinal hernias treated or not
 - Testicular cancer.
 - Varicocoeles grade 3
 - Significant obesity
 - Perineal skin lesions (psoriasis, eczema)

Male contraception Practical aspects

Thermic contraception: Assessment:

Soufir, Mieusset: *Andrologie* (2012) 22:211-215

- No biological assessment needed
- Normal genital examination
- Normal spermogram (WHO 2010):
 - Conc >15 M/ml
 - Progressive mot >32%
 - Normal forms: >4%



Male contraception Practical aspects

Thermic contraception: What options?

Soufir, Mieusset: *Andrologie* (2012) 22:211-215

these devices have unfortunately no medical publications nor EC label confirming their effectiveness or security.

Ring



Jockstrap



Boxer



<https://pointpointpoint.org/contraceptions-testiculaires/>

<http://www.contraceptionmasculine.fr/>

<https://thoreme.com/>

Artificial cryptorchidism: how to do it?



ARDECOM

<https://www.contraceptionmasculine.fr/>

Male contraception Practical aspects

Thermic contraception

Soufir, Mieusset: *Andrologie* (2012) 22:211-215

- Contraceptive threshold obtained within 3-4 months.
- Where find devices? NOT in pharmacies...
 - on the internet
 - do it yourself.
- Individual variations (thermo-resistance)
- **Informed consent is required**

Male contraception Practical aspects

Thermic contraception: Follow up

Soufir, Mieusset: *Andrologie* (2012) 22:211-215

- Recommended monthly semen analysis (?) until the sixth month, then every 3 months. (to check the effectiveness and compliance of the device).
- Duration of contraception: 4 years.
- Complete recovery in terms of sperm parameters has been observed for such a duration (between 6-9 months)
- During recovery phase, contraception of the partner is advised (chromosomal abnormalities)

Conclusions: Male Contraception

Practical aspects

Hormonal contraception for men have proven efficacy equivalent to female contraceptives.

It's still no drug officially recognized

- Many studies, many hormone regimen
- No male contraceptive medication currently officially available
- Protocol of Off-label prescriptions of different testosterone derivatives (expensive) and no refund from social insurance
- Actual protocols with weekly injections of testosterone and rigorous follow up induce reluctance and low compliance in patients.
- Hormonal gel of Nestorone/Testosterone expected on market in 2028, at best.

Conclusions: Male Contraception

Practical aspects

Thermic contraception for men have proven efficacy equivalent to female contraceptives.

There is still no device officially recognized

- Easy/Low tech/no drug dependent technique very popular in younger generations.
- Lack of medical data on its effectiveness and security but seems effective
- No device officially available (do it yourself or internet: ring)
- Possibility to initiate protocol with well-informed patients
- EC certification and medical evaluation are starting.
- On the market expected around 2027