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59. One experiment was also tried in which 10 female mice were exposed simultaneously to radiation and oxygen, with another 10 mice exposed to oxygen only. Unfortunately, these mice could not be observed during the radiation because of danger to the observer; and when observations were resumed, 8 of the experimental and 7 of the control mice were already dead. Since no average survival time could be stated, these results are not listed in the table. Female mice are significantly less sensitive to oxygen than males. At a pressure of 5 atm, the female survival times were so widely dispersed that experimentation was difficult. For this reason, simultaneous exposures to radiation and oxygen could be tried only in males.

Plant Materials Used by Primitive Peoples to Affect Fertility

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RECENT publications (*1–3*) have stressed the need for finding inexpensive and harmless oral agents capable of controlling human fertility. Numerous agents are known which affect fertility, both in a positive and a negative sense but have side effects, some of which are undesirable. One method of finding useful materials is the screening of naturally occurring substances to discover those with the optimum characteristics that will guide chemists to the synthesis of the ideal drug.

As work goes forward on other approaches, it may be profitable to consider the information acquired by ancient and more remote peoples concerning the use of herbs and various plant materials for fertility control purposes. Such information, almost completely unevaluated, is available in fragmentary form about many plants found in all latitudes. It comes primarily from the collected folklore of primitive peoples, from the literature of so-called "popular medicine" of Western cultures, from 19th-century books on medical botany, and from old *materia medica.*

Information from such sources is to some extent held in question by modern investigators who often dismiss the accounts as superstitions or "old wives' tales." Confidence in such sources of information may be strengthened, however, by recognizing examples of valuable drugs recently isolated from plants used by primitive peoples for generations.

1. Many soils have been claimed to cure human ills; molds from them provide us today with valuable antibiotics (*4*).
2. The powerful antithrombic agent "Rutin" is found in *Ruta graveolens.*
3. Muscle relaxant Tubo-Curare is extracted from the Indian arrow poison of Guiana (*5*).
4. The heart-regulating agent, cratioaegolic acid, and other unidentified active substances are found in *Crataegus oxyacantha* (*6*).
5. The alkaloids of Indian *Rauwolfia serpentina* reduce blood pressure and act as a general sedative (*7*).
6. The glucoside Foliandrin from the oleander shrub provides a cardiac stimulant of great value to elderly patients (*8*).
7. The coronary stimulant "khellin" is obtained from *Amni visnaga* (*9*).
8. The antimalarial "Febrifugine" from Hydrangea (ancient Chinese Chang-Shan roots) has been isolated and synthesized very recently (*10*).

Even greater confidence may be gained by referring to the recent scientific literature (*2*) on the desert herb, *Lithospermum ruderale,* used by Indians in the southwestern part of the United States for fertility control purposes.

The authors, working separately at first, have accumulated a list of more than 100 plants reported to contain substances that affect human reproduction. These have been classified into three categories:

Oc—so-called oral contraceptives thought to cause temporary sterility.

Oc_1—substances which in certain doses are believed to interfere with implantation or gestation but which might well prove to be in class *Oc* if used in smaller concentrations.

Oc_2—emmenagogues, plant materials believed to affect menstruation, many of which after investigation might be put in class *Oc* when their active principles have been isolated and their therapeutic activity determined.

Sixty of the plants for which full scientific names are available and for which there is some information (though mostly unscientific) have been selected for inclusion in the compilation of Table 1. The plant names have been listed alphabetically and the category (*Oc*, Oc_1, or Oc_2) is shown. It is stressed that, so far as is known, none of the plant materials (excepting Lithospermum extracts) have been studied from the standpoint of deleterious side effects. Some of the plants listed are known to contain poisonous substances—any indiscriminate use would be dangerous.

TABLE 1. Selected list of plants reported to contain substances that affect human reproduction.

Botanical name	Common name	Country and group	Use; comments
Achillea millefolium L. (*11*)	yarrow	N. Europe	*Oc*, Oc_2. Powdered plant mixed with normal diet (25–50% conc) to suppress estrus; hot infusion used
Ananas comosus L., Merr. (*sativa* L.) (*12*)	pineapple	Malaya	Oc_1. Unripe pineapple juice taken raw, sometimes salt added
Anodendron paniculatum A.DC. (*13*)	leurapaseikitong creeper	Assam	Oc_2. Root crushed in water taken 3 or 5 times a day at intervals of 2–3 hr to aid parturition
Apocynum androsaemifolium L. (*14*)	dogbane	N. America	*Oc*. Roots boiled with water and liquid drunk once a week
Arisaema triphyllum (L.) Schott (*15*)	indian turnip	N. America (Hopi)	*Oc*. Decoction of powdered, dried root, 1 tsp in ½ glass cold water strained and drunk prevents conception for 1 yr; two tbs hot infusion renders permanent sterility
Aristolochia clematitis L. (*16*)	birthwort	Hungary	*Oc*, Oc_2. Seed parts used to prevent fertility and menstrual pain
Asarum canadense L. (*17*)	wild ginger	N. America	*Oc*. Root and rhizome boiled slowly in a a little water for a long period; decoction drunk by women
Asclepias hallii Gray (*18*)	milkweed	Colorado (Navaho)	*Oc*. Infusion of plant drunk after childbirth
Asclepias syriaca L. (*19*)	petits-cochons	Quebec, Canada	*Oc*. Handful of roots and rhizomes dried and powdered, infused for 20 min in pint of water and drunk to produce temporary sterility
Asparagus officinalis L. & *acutifolia* L. (*20*)	asparagus	S. Europe	*Oc*, Oc_1. Fresh or dried berry decoction drunk as contraceptive; fruit or plant infusion drunk to induce menstruation
Asplenium adiantum-nigrum L. (*22*)	black spleenwort	India-Himalayas	*Oc*. Considered in Yunani system of medicine to produce sterility in woman
Bahia dissecta (Gray) Britton (*18, 23*)	"twisted medicine"	N. America (Navaho)	*Oc*. Infusion of roots boiled 30 min, drunk by women during menstruation; said to be used by both sexes
Begonia balmisiana Ruiz. (*24*)	begonia	C. America	Oc_2. Promotes menstruation
Byrsonima crassifolia H.B.K. (*25*)	nanche	C. America (Oaxaca)	Oc_1. Bark, leaves, and fruit used to expel placenta; roots used by Indians of Oaxaca to produce expulsion
Caladium seguinum Vent. (*26*)	poison arum	S. America (Indian)	*Oc*. "Heard of plants used by Indian women to render temporary or permanent sterility; on two occasions evidently Araceae"; stops spermatogenesis and follicle growth in rats

TABLE 1.—(*Continued*)

Botanical name	Common name	Country and group	Use; comments
Callicarpa sp. (*27*)	argerarger	Torres Straits	*Oc.* Young leaves well chewed until women's bodies are saturated with the juice swallowed; causes permanent sterility
Capsella bursapastoris (L.) Medic. (*28*)	hirtentaschelkraut	N. Europe	*Oc.* Powdered plant mixed with normal diet (25–50% conc) to inhibit the estrus cycle; hot infusion used as emmenagogue
Cnicus benedictus L. (*Carbenia benedicta* Adans) (*29*)	thistle	N. America (Quinault Indians)	Oc_1. Brewed and taken as tea
Castilleja linariae-folia Benth. (*30*)	indian paint brush	N. America (Hopi)	*Oc.* "A decoction of this plant was sometimes used—as it dried up the menstrual flow"
Caulophyllum thalictroides (L.) Michx. (*31*)	squaw root	N. America (Chippewa Indians)	Oc_1, Oc_2. Strong decoction of 5–30 g powdered root taken to expedite parturition and menstruation
Chenopodium album L. (*32*)	Weisser gansefuss	Hungary	*Oc.* Powdered plant mixed with normal diet (25–50% conc) found to suppress estrus cycle
Cicuta maculata L. (*33*)	spotted cowbane	America (Cherokee)	*Oc*, Oc_1. Women chew and swallow roots on 4 consecutive days to produce permanent sterility
Cocos nucifera L. (*34*)	green coconut	Pacific Isles	*Oc*, Oc_1. Milk used; "too much may be injurious." People in Java afraid to drink milk of coconuts (ripe or unripe) because it is believed to diminish libido or fertility
Cordia quarensis Gürke (*35*)	os segi	Africa (Masai)	Oc_1. Pieces of root chewed by girls
Daemia extensa R.Br. (*36*)	phala kantaka	India	*Oc.* Leaves used in the preparation of a purgative medicinal oil for amenorrhea and dysmenorrhea
Dalbergia terruginae Roxb. (*ferruginea* Roxb.?) (*37*)	balibagan	West Indies	Oc_1. Decoction of wood of stem or root used as emmenagogue, and in doses to induce expulsion of fetus
Dioscorea sativa L., var. Rotunda (*38*)	tjarri	Cape York, Australia (Kawadji)	*Oc.* Tuber eaten raw early morning on empty stomach; woman lies down and drinks nothing all day in attempt to become permanently sterile
Dryopteris filix-mas (L.) Schott (*21*)	malefern	Europe	Oc_1. German women used root to produce expulsion of fetus and sterility; Tartar women used seeds for same purpose
Entada scandens Benth. (*38*)	pi'ala	Australia (Kawadji)	*Oc.* Generally eaten raw, sometimes roasted; taken in early morning on empty stomach, after which woman lies down and does not drink throughout the day
Epimedium alpinum L. (*39*)	barrenwort	N. Europe	*Oc.* Finely ground leaves; 5 drams taken in wine after menstruation prevents conception for 5 days; root causes sterility
Eriogonum jamesii Benth. (*18, 23, 40*)	antelope sage	Arizona (Navaho)	*Oc.* Root boiled for 30 min and 1 cupful drunk by woman during menstruation to prevent conception; used by both sexes

TABLE 1.—(*Continued*)

Botanical name	Common name	Country and group	Use; comments
Eupatorium odoratum L. (*41*)	xtokabal	C. America (Zapotec)	Oc_2. Root used; plant consecrated to goddess of pregnancy and childbirth
Frasera speciosa Dougl. (*42*)	deer's tongue	Nevada (Shoshone)	*Oc.* ". . . a half cupful taken once in a while" as a contraceptive
Geranium robertianum L. (*43*)	ruprechtskraut	C. Europe	*Oc*, Oc_2. To stop excessive hemorrhage at menstruation
Gossypium herbaceum L. (*44*)	cotton root	S. America	*Oc.* Creoles give a decoction of plant root for contraceptive; also give seeds to mothers to increase lactation
Hedera helix L. (*45*)	ivy	Mediterranean	*Oc.* The finely pulverized berries drunk after purification; dose of 1 dram causes sterility
Helleborus niger L. (*46*)	christmas rose	Europe	Oc_1. Solid extract of root, 3–5 grains, taken to induce expulsion of the fetus
Leucaena glauca Benth. (*47*)	ipil-ipil	W. Indies and Central America	Oc_1, Oc_2. Decoction of root and bark used
Licuala sp. (*48*)	win	Solomon Isles (Buka)	*Oc.* Outer part of root chewed and swallowed by both sexes
Lithospermum arvense L. (*32*)	gromwell	C. Europe	Oc_1. Powdered plant mixed with normal diet (25–50% conc) and used to suppress the estrus cycle
Lithospermum ruderale Dougl. (*49*)	nemishaw or stoneseed	Nevada (Shoshone)	*Oc.* Cold water infusion of roots taken daily for 6 mo insures sterility
Lomatophyllum reflexum Boj. (*50*)	hassn.	Madagascar	Oc_2. One or two budding flowers eaten is powerful emmenagogue
Lygodium dichotomum Sw. (*51*)	asam	Solomon Isles (Buka)	*Oc.* Root chewed with betel and some of mixture swallowed
Mallotus sp. (*48, 52*)	haholon	Oceania (Buka)	*Oc.* Scrapings from root chewed with betel mixture and swallowed
Montanoa tomentosa Cery. (*54*)	zoapatle	C. America (Zapotec)	Oc_1, Oc_2. Used for difficult parturition and postpartum uterine hemorrhages
Nasturtium officinale (*55*)	cresson	W. Europe	Oc_1. Cooked or eaten raw, it assists menstruation and removes fetus
Origanum majorana L. (*56*)	marjoram	Germany	Oc_1. Taken as a tea during menstruation
Phoradendron flavescens Nutt. (*57*)	American mistletoe	California (Indians of Mendocino County)	Oc_1. Tea made from leaves
Plantago lanceolata L. (*58*)	spitzwegerich	C. Europe	*Oc.* Powdered plant mixed with normal diet (25–50% conc) suppresses estrus
Polygonum hydropiper L. (*59*)	water pepper	C. Europe	*Oc*, Oc_2. Liquid extract of powdered plant used
Populus alba L. (*60*)	white popular	Mediterranean	*Oc.* Popular superstition that the bark taken with the kidney of the mule causes sterility
Rosmarinus officinalis L. (*61*)	rosemary	C. America (Opata)	*Oc*, Oc_1, Oc_2. Tea made of rosemary and the "ocean artemisia" for fertility control
Ruta graveolens L. (*62*)	rue	Europe and S. America	Oc_1, Oc_2. Hot decoction of plant, 1 oz to 1 pt of water, allowed to stand for 8 hr and then drunk to promote menstruation; larger doses induce fetal expulsion

TABLE 1.—(*Continued*)

Botanical name	Common name	Country and group	Use; comments
Sanguisorba officinalis L. (*58*)	garden burnet	C. Europe	*Oc.* Powdered plant mixed with normal diet (of mice)
Semecarpus anacardium L. (*63*)	pavak or agni tree	India (Hindu)	*Oc.* Roots cooked in sour rice water and taken for 3 days at end of menstrual period produces sterility
Smilacina stellata (L.) Dest. (*64*)	false solomonseal	Nevada (Indians)	Oc_1, Oc_2. Root infusion regulates menstrual disorders; conception prevented by tea of leaves, ½ cup daily for 1 wk
Urena lobata L. (*65*)	wuzawuza	New Ireland	Oc_1. Leaves chewed and juice swallowed
Viburnum prunifolium L. (*66*)	black haw	Italy	Oc_1, Oc_2. Relieves dysmenorrhea and controls fertility; hot decoction taken 4 or 5 days before menstrual period
Vitex agnus-castus L. (53)	monchpfeffer	C. Europe	*Oc.* Sterility increased with increasing doses; retardation of estrus observed in female rats
Vitex negundo L. (?) (*67*)	paparau	Solomon Isles (Buka)	*Oc.* Root scrapings chewed with betel mixture and swallowed

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The Occurrence of a Group Transfer Involving Enzyme (phosphoglucomutase) and Substrate[1]

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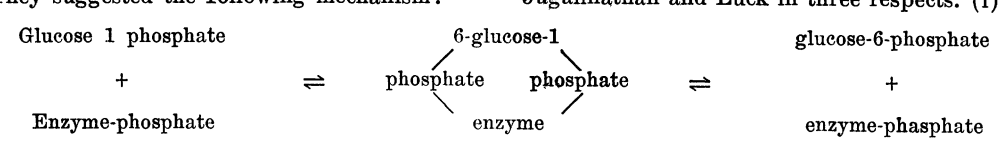
THE transfer of a reactive group involving substrate and enzyme was postulated by Doudoroff, *et al.* (*1*) for sucrose phosphorylase. This was based on the interchange of phosphate between glucose-1-phosphate and radioactive inorganic phosphate in the presence of the enzyme. Jagannathan and Luck (*2*) later suggested a similar transfer mechanism for phosphoglucomutase, based on the exchange of radioactive phosphate between glucose-1-phosphate and a proposed enzyme-phosphate. They suggested the following mechanism:



As is indicated in the diagram, the enzyme-phosphate could combine with glucose-1-phosphate or glucose-6-phosphate to form a double link with glucose through two phosphate bonds. This compound could yield enzyme-phosphate and glucose-1-phosphate or glucose-6-phosphate by a split of the appropriate bonds.

Recently, Najjar (*3*) reported direct evidence of a transfer of phosphate from crystalline phosphoglucomutase (*4*) to glucose-1-phosphate and glucose-6-phosphate with a net synthesis of glucose-1,6-diphosphate in relatively substantial amounts. The following two-step mechanism was therefore postulated:

Glucose-1-phosphate + phospho-enzyme ⇌
glucose-1,6-diphosphate + dephospho-enzyme; (1)
Glucose-1,6-diphosphate + dephospho-enzyme ⇌
glucose-6-phosphate + phospho-enzyme. (2)

This mechanism differs from that proposed by Jagannathan and Luck in three respects. (i) Glucose-1,6-diphosphate is an actual reactant that accumulates in the medium as a product of the interaction of either of the hexose phosphates and the phosphorylated enzyme rather than as a part of a transient enzyme-substrate complex, (ii) The enzyme exists in a phosphorylated state as well as in a dephosphorylated state, rather than in the phosphorylated state alone. (iii) This mechanism also accommodates glucose-1,6-diphosphate in a manner quite befitting its coenzymatic function.

The validity of this mechanism was established by

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