運動與性激素

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摘　要

一般了解類固醇對骨骼肌合成效應可增強競技表現。最近許多研究也針對體能活動對性類固醇影響進行探討。本篇之目的在於探討運動後血液中性激素之變化。根據神經內分泌生理學，性類固醇分泌是經由一精密的機制所調控，其中下視丘—前垂體—性腺軸線及細胞內環單磷酸腺甘在合成及分泌性類固醇扮演著重要的角色。最近動物實驗結果顯示，運動引發血漿性類固醇經由乳酸濃度上升刺激性腺細胞內環單磷酸腺苷增加導致性類固醇分泌增加，而非經由性促素之調控。

Exercise and Sex Hormones

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Abstract

It has been well established that anabolic effect of steroid hormones on skeletal muscle and then robust athletic performance. Recent studies have focused on the effect of physical exertion on sex hormones. The purpose of this review is to examine blood levels of sex hormone following exercise. Upon basic neuroendocrine physiology, sex hormones are regulated by a sophisticate mechanism in which hypothalamus-anterior pituitary-gonadal axis and intracellular cyclic adenosine monophosphate play an important role in synthesis and release of sex steroid hormones. Animal study demonstrated that exericse raised blood sex steroid via post exercise wich elevated lactate to stimulate an increase in intracellular cyclic adenosime monophosphate in gonodal tissue and not regulated by gonadotropic hormones.

壹、前　言

一般了解神經內分泌系統所合成及分泌之性腺激素影響骨骼肌成長及功能。近年來，許多研究顯示運動會影響血液中性腺激素之濃度，結果發現人類進行強度40 %—80%、30-45分鐘之運動後不論性別都引發血清雄性激素上升3%—37%。發現重量訓練後血漿游離睪固酮上升與肌力之增加顯著相關。當進行次最大強度(sub-maximal)運動時則發現血漿睪固酮濃度不變(23,96)或下降(6)。雌性類固醇素也會隨著運動強度之增加而上升(21,37)。Jurkowski et al.(37)檢測運動強度對卵巢分泌雌性素之影響。由於性腺激素之合成及分泌不但與動物生殖成長有關，也和運動能力關係密切，因此受到許多生理學學者注意而進行深入研究。

貳、性類固醇激素

一、睪固酮(Testosterone)：

睪丸之萊氏細胞(Leydig cell)合成及分泌95%睪固酮。萊氏細胞以醋酸鹽(acetate)合成膽固醇或細胞外低密度脂蛋白(low density lipoprotein; LDL) 供應之膽固醇(cholesterol)為原料，在細胞內先轉化成妊娠酮(pregnenolone) 再經由許多酵素作用後合成之類固醇激素(steriod hormones)(28)。此外，微量睪固酮由腎上腺皮質合成及分泌。在人類成年男性血漿、每日尿中排泄量及分泌量分別約為7.0 ng/ml、0.7 ng/day、及7000 μg/day。成年女性血漿、尿液、及每日分泌量分別約為0.4 ng/ml、0.04 ng/day、及300 μg/day(51)。成年女性血漿中微量睪固酮相信與引發性慾有關(29)。

由於性類固醇激素不溶於水，睪固酮進入血流需與血漿中大分子蛋

白結合(88,89,90)。人體血流中睪固酮只有3%呈游離狀態(free form)、而42%、39%、16%分別與睪固酮—雌二醇—結合球蛋白(testosterone-estradiol-binding- globulin; TeBG)、球蛋白(albumin)、及其他血漿蛋白結合(88,89,90)。由於游離狀態及蛋白結合睪固酮濃度直接影響睪固酮之代謝速率(101)。這些蛋白具有類似儲存庫及保護睪固酮被代謝之作用(89,90)。

睪固酮作用在許多靶細胞(target cells)前需要先經5α還原酵素(5α-reductase)之作用轉換為二氫睪固酮(dihydrotestosterone; DHT)，才能進入細胞核內產生生理作用。有研究顯示睪固酮可使肌肉中蛋白質合成率上升與分解率下降。其中之機轉，一般以為與刺激細胞中DNA之轉錄(transcription)過程有關。因為睪固酮具脂溶性，所以可穿透具兩層脂質的細胞漿膜。一但進入細胞中睪固酮就與細胞溶質(cytosol)中的接收器(receptor)相結合(32)。睪固酮在性腺以外主要靶細胞是骨骼肌(18)。這些激素—接收器結合體可轉錄(transcription)促進位於細胞核中具有合成肌肉中收縮蛋白DNA之基因密碼(genetic code)(28,32,63)後從細胞核中mRNA轉譯(translation)至細胞溶質中作用結果使得肌肉蛋白合成率增加(32)。

進入細胞後，睪固酮可代謝為活性更高之類固醇或在組織中活性減弱並與膽汁或尿素相結合後排出體外。經由5—α—還原胺(5-α reductase)作用後睪固酮成為活性更高之二氫睪固酮，刺激雄性生殖器官及皮膚之細胞分裂。睪固酮代謝為活性較低硫化類固醇(steroid sulfate)或在肝臟代謝為尿甘酸(glucuroides)後排出體外。睪固酮在腦及乳房等組織經aromatization成為生物活性較強之雌性素(estrogen)，即雌二醇(estradiol)(101)。

許多組織都受睪固酮作用所影響。除藉由賽氏細胞(Sertoli cells)

調控精子生成(spermotogensis)，也可調節於其他與生殖有關附屬組織之功能。這些組織包括前列腺(prostate)(64,67,100)、副睪(epididymis)(11,51,64,100)、儲精囊(seminal vesicle)(58,67,98,100)等。其他組織如神經系統(28,67)、腦垂體(2,64,67,86)、下視丘(64,67)、骨骼(28,67)、腎臟(67)、肝臟(67)、及肌肉組織(28,67)等均受睪固酮之影響。

二、助孕酮(Progesterone)：

助孕酮(progesterone)係雄性素與雌性素合成時之前期產物。雌性動物由卵巢黃體(corpus luteum)，顆粒細胞(granulosa cell)及胎盤可合成及分泌類固醇激素。助孕酮主要生理作用是維持妊娠。助孕酮與雌二醇(estradiol)作用促使子宮進入分泌期(secretory phase)而準備卵子著床(implantation)。當受精卵剛著床時，需要受前垂體分泌黃體促素所調控之黃體分泌助孕酮維持子宮內膜(endometrium)達10-13天。一但超過黃體分泌助孕酮期間，除非胎盤開始合成並分泌足量之人絨膜性促素(human chorionic gonadotropin; hCG)維持黃體，否則妊娠將在受精卵剛著床時數日內因黃體分解(luteolysis)，助孕酮濃度下降而終止(29,101)。

助孕酮也具有防止子宮過早收縮(premature contraction)之作用。以競爭性抑制物質阻斷助孕酮與細胞質內受器相結合可導致妊娠終止(101)。West(101)認為助孕酮可抑制子宮收縮波之擴散而阻止協同而強力之子宮收縮。因為常發現兔子助孕酮可抑制子宮收縮，雖然具有爭議(39)，但Csapo(16)將這現象稱為助孕酮阻斷(progesterone block)。由於人類之分娩與血液助孕酮濃度無關，分娩時注射大量助孕酮也無法終止分娩進行(39)。然而支持助孕酮阻斷學說者認為血液助孕酮濃度無法精

準反應出子宮組織附近助孕酮濃度，因助孕酮可在胎盤合成而就近傳遞至附近子宮(16)。助孕酮除了在胎盤作用外，當乳房發育到要泌乳時，也需要助孕酮作用而促進乳房小葉及小泡之發育，並使乳房小泡中細胞具有分泌乳汁之功能(35,101)。此外，許多研究顯示助孕酮可影響碳水化合物(38)及脂肪(5,43)代謝、通氣量(ventilation)(19,23)、胃排空(gastric emptying)(13)、血漿胰島素(insuline)(39,94)、生長激素(growth Hormone)(22,31)、皮固酮(cortisol)(25)、醛固酮(aldosterone)(72)、黃體促素(luteinizing hormone) 及濾泡促素(follicle-stimluting hormone)(29)。

助孕酮濃度變異性相當大。從Butcher et al.(10)報告中得知助孕酮濃度在正常雌鼠4天性週期中可由2-7 ng/ml上升至峰值46 ng/ml並在短時間內下降(10)。人類男性血漿助孕酮濃度約為0.15-0.33 ng/ml，而女性血漿助孕酮濃度在非妊娠時及進行妊娠時分別為0.1-2 μg/100ml(35)及11-32 μg/100ml(53)。此外，助孕酮之分佈具區域性。Zander et al.(105)就曾指出助孕酮濃度在胎盤附近最高，而越往週邊區域則濃度越低。

根據許多相關文獻顯示，性類固醇不論在調控下視丘及腦下腺分泌、有機體發育、性徵表現、生殖週期，妊娠及授乳時均很重要。然而，由於性類固醇濃度變化也往往受到性週期、妊娠、及採樣位置等許多因子之影響，因此以探討性類固醇變化為題目所進行實驗時需注意這些影響因子對結果之效應後，選擇適當實驗時間與固定採樣位置。

三、黃體促素(Luteinizing Hormone, LH)：

腦垂體之促性腺細胞(gonadotrophs)受下視丘性釋素之刺激後合成及分泌兩種由二個醣蛋白之次單位所組成，分子量約為30000之性促素

(gonadotropic hormones)；黃體促素(luteinizing hormone; LH)及濾泡促素(follicle-stimulating hormone; FSH)。性促素刺激動物性腺細胞上之接受器(receptors)藉由細胞內訊息傳遞物質；環單磷酸腺甘(cyclic adenosine monophosphate; cAMP)，調節雄性素(androgen)或雌性素(estrogen)之合成與分泌(28)。

黃體促素主要作用是刺激雄性動物睪丸組織中萊氏細胞分泌睪固酮，表現雄性第二性徵並促使精子生成(spermatogensis)。黃體促素對雌性動物則具有促進排卵之功能外，也將排卵後之顆粒細胞黃體化(luteinization)而成為黃體細胞。黃體細胞團組織即為黃體其中含有助孕酮及雌二醇類固醇激素以維持黃體，並為懷孕初期做準備(29)。

黃體促素分泌是受下視丘分泌性釋素所調控(28)。一般了解，性釋素先與促性腺細胞上受器結合後而活化前垂體細胞內G蛋白(G protein)再活化磷脂酵素C(phopholipase C)後，作用於分解phophatidylinositol biphophate (PIP2)成為雙醯基甘油(diacylglycerol, DAG)及1，4，5三磷酸肌醇(inositol 1, 4, 5, triphosphate, IP3)。1，4，5三磷酸肌醇可刺激細胞內儲存之鈣離子釋放而增加細胞內鈣離子濃度。雙醯基甘油則活化細胞內蛋白激酶(protein kinase C)，而引發前垂體之促性腺細胞(gonadotrophs)合成及分泌黃體促素。此外，促性腺細胞也可經由活化腺苷環化酶(adenyl cyclase, AC)使細胞中環單磷酸腺苷(cyclic AMP)濃度增加而促使黃體促素之合成與分泌(28)。

許多研究指出，除了性釋素影響黃體促素之分必外，體循環血液中性類固醇激素也可以迴饋調控前垂體分泌黃體促素。此外，黃體促素也受其他前垂體細胞之旁分泌(paracrine)及autocrine之相互影響(87,104)。研究顯示，前垂體中之內皮素(endothelin)，濾泡星狀細胞(folliculostellate cell)所分泌之介白素(interleukin-6)(103)、促性腺細

胞本身所分泌之activin(78)及angiotensin會刺激前垂體促性細胞分泌黃體促素。

四、性釋素(Gonadotrpin-Releasing Hormone, GnRH)：

性釋素(gonadotropin-releasing hormone; GnRH)是Schally et al.(84)等人在1971年從豬和羊之下視丘組織萃取物中分離出來。位於間腦(diencephalon)中央底部之神經末稍分泌10個胺基酸所組成胜肽其結構為(pyro) Glu-His-Trp-Ser-Tyr-Glu-Leu-Arg-Pro-Gly-NH(84)，Schally et al.(85)根據其生理作用將它命名為性釋素(gonadotropin-releasing hormone; GnRH)。

位於中底下視丘(medio-basal hypothalamus, MBH)以外之視前區(preoptic area, POA)中有合成性釋素之神經元細胞體。研究報告指出阻斷進入下視丘之神經路徑導致下視丘性釋素含量顯著下降(28)，顯示性釋素由下視丘中隆組織(median eminence)之神經末梢所分泌。此外，除了弓狀核及視前區本身會受到雌二醇(29)及睪固酮(28)迴饋控制之影響。如下視丘弓狀核及視前區所分泌之內嗎啡(endorphin)，正腎上腺素(norepinephrine)(75,76)，血清張力素(serotonin)，以及neurotensin，神經肽Y(neuropeptide Y)(42,74)，galanin (54)，angiotensin II(28)等這些腦部其他區域神經化學傳導物質(neurotransmitters)及神經胜肽(neuropeptides)都可直接或間接方式影響性釋素在視前區之合成及在下視丘之分泌作用。

性釋素在大鼠下視丘以每60-90分鐘一次脈衝(Pulse)方式分泌(20)。經由位於下視丘中隆(median eminence)之垂體門脈系統(hypophysial portal blood system)到達前垂體(anterior pitiuitary)。如將動物去性腺或以電化學方法刺激下視丘組織都會引發門脈血液中性釋素濃度上

升(28)。

性釋素在雌鼠之動情前期時，刺激前垂體分泌黃體促素及濾泡促素。雌鼠在動情前期午後，前垂體門脈血液中，上升之性釋素會刺激促性腺細胞分泌黃體促素，而使黃體促素在體循環血液中之濃度達到高峰(surge)進而誘發排卵(ovulation)。如以免疫技術方法，在門脈循環中注射性釋素抗體，而阻斷性釋素對促性腺細胞之作用，則可發現動情前期之雌鼠無法排卵，而雄鼠則有睪丸萎縮之現象(28)。

五、環單磷酸腺苷(Cyclic Adenosine 3':5' Monophosphate, cAMP)：

環單磷酸腺苷之作用是Sutherland及Rall在1957年所發現(95)，因環單磷酸腺苷是細胞將外界訊號傳遞至細胞內部之重要媒介，而被稱為第二信使(second messenger)(28)。

環單磷酸腺甘是三磷酸腺核(adenosine triphosphate; ATP)經細胞上活化之腺核苷環化酶(adenylate cyclase)作用所產生。對激素敏感之腺核甘環化酶是由胜肽類激素受器(peptide hormone receptor)、結合單位(coupling unit)、及catalytic cyclase三部份所構成(80)。細胞上之激素受器並不直接與catalytic cyclase部份產生交互作用，而是先與結合單位相結合(79)後形成激素・結合單位・受器之複合體。這時結合單位開始被活化並與三磷酸鳥苷(guanosine triphosphate; GTP)相結合。由於結合單位與三磷酸鳥苷結合時被活化(Active)，但與二磷酸鳥苷(guanosine diphosphate; GDP)結合時則會被去活化(inactive)。因此激素・結合單位・受器複合體之形成降低結合單位與二磷酸鳥苷結合而促進結合單位與三磷酸鳥苷之結合(12)。結合之激素・結合單位・受器・三磷酸鳥苷複合體與catalytic cyclase相結合而活化形成環單磷酸

腺苷之酵素(101)。而當環單磷酸腺甘退化(degradation)成為5'—單磷酸腺苷(5'-adenosine monophosphate; 5'-AMP)時激素引發環單磷酸腺苷濃度增加作用終止(101)。

細胞內環單磷酸腺苷濃度具有調控細胞反應之作用。在腦垂體(pituitary)，內分泌細胞經由環單磷酸腺苷調控腎上腺皮質素(adrenocorticotropin hormone; ACTH)、抗利尿素(antidiuretic hormone; ADH)、抑鈣素(calcitonin)、濾泡促素(follicle-stimulating hormone; FSH)、黃體促素(luteinizing hormone; LH)、副甲狀腺素(parathyroid hormone)、黑促素(melanocyte-stimulating hormone; MSH)、甲促素(thyroid-stimulating hormone; TSH)之分泌(101)。

許多證據顯示，任何細胞內環單磷酸腺苷濃度變化將直接導致性腺體組織之分泌反應。離體研究指出人絨膜性促素經由增加睪丸(3,77,83,99)及卵巢(92)組織內環單磷酸腺苷合成而刺激大鼠睪丸及卵巢分別釋放睪固酮(33,62,69,71,73,82, 91,93,99)及助孕酮(92)。然而，最近有研究顯示刺激組織內環單磷酸腺苷合成可抑制性腺及前垂體組織分泌(99)。Wang et al.(99)以鮭抑鈣素(salmon calcitionin; sCT)刺激離體性腺及腦垂體，實驗結果發現鮭抑鈣素刺激離體組織內環單磷酸腺苷濃度增加而抑制睪丸組織分泌睪固酮及腦垂體組織分泌黃體促素。

參、運動與中底下視丘—腦垂體—性腺軸線

目前有關短時間、高強度體能活動探討雄雌動物中底下視丘—腦下腺—性腺軸線反應之研究大多以不同運動方式及強度對性類固醇激素之影響為主。睪固酮及助孕酮不但與動物生殖成長有關，也和運動能力關係密切。許多研究顯示高強度運動增加內生性睪固酮(9,15,17,20,23,24,26,34,41,44,45,46,47,48,57,60,66) 、助孕酮及雌二醇之合成(7,8,

37,40,50,52,65,70)。體能活動之強度(intensity)、持續時間(duration)及方式(mode)是影響這些性類固醇分泌之因素(49)。Kuoppasalmi et al.(49)發現當受測者進行45及90分鐘高強度(3.3 min/km)與中強度(4.3 min/km)運動後，血漿睪固酮分別上升7%及21%(49)，而當男性進行30、45、60、75、及90%最大攝氧量(VO2 max)運動時，運動強度與血漿睪固酮含量呈正相關(102)。Fahey et al.(20)及Haakinen et al.(27)發現重量訓練後血漿游離睪固酮上升與肌力之增加顯著相關。當進行次最大強度(sub -maximal)運動時則發現血漿睪固酮濃度不變(23,96)或下降(6)。雌性類固醇素也會隨著運動強度之增加而上升(21,37)。Jurkowski et al.(37)檢測運動強度對卵巢分泌雌性素之影響。先以強度漸增踏車至衰竭運動測驗之結果決定大學女生（n＝9；年齡＝20-24歲）最大運動功率輸出(power output)，而後分別在黃體期（排卵後4-6）天及濾泡期（月經開始6-9天）時分別以30-35%、60-66%、及85-95%最大功率輸出代表低、高、及衰竭強度進行20分鐘運動，結果顯示，雌性素在黃體期中濃度高於濾泡期，且隨著運動強度呈直線上升之趨勢，而黃體促素及濾泡促素則不變。Jurkowski et al.(37)因此認為雌性素濃度受運動強度及月經週期之影響但不受性促素之調控。

許多研究發現運動血漿性促素濃度增加(14,47,48)或不變(48,102)。Toriola (97)發現運動後血漿睪固酮顯著增加而黃體性促素則沒有改變。實驗證據顯示黃體促素變化後20-30分鐘時才會影響睪固酮反應(1,4,36,61,68,81)，因此短時間運動雖然刺激前垂體分泌黃體促素(14,47,48)，但因黃體性促素變化反應比睪固酮慢，表示運動時性類固醇激素之變化並非經由上游前垂體分泌黃體性促素之調控所致(15)。

最近有研究探討游泳引發乳酸堆積對大鼠下視丘性釋素(GnRH)、腦垂體黃體促素(LH)、睪丸睪固酮(T)、及卵巢助孕酮(P4)分泌之影響。利

用四個月齡之雄性及雌性大鼠先進行一週之游泳訓練（每日2次；每次10分鐘）。游泳實驗前24小時，在大鼠頸靜脈置一插管。次日，大鼠泳前、涉水及以6、9、12、16、18、25升／分鐘水流強度泳後2分鐘採集血樣。大鼠進行間歇三小時游泳（水溫＝25℃；水流強度＝18升／分鐘；持續時間＝10分鐘），每次泳前及泳後10、15、30、及60分鐘採集血樣。大鼠游泳或浸水十分鐘後犧牲並收集精索靜脈及軀幹血樣。大鼠以同樣游泳，泳前及泳後10、15、30、及60分鐘採集血樣。另組大鼠在右頸靜脈及左股靜脈埋入插管24小時後以蠕動幫浦進行10分鐘乳酸(13 mg/kg/min)或生理食鹽水靜脈灌流，灌流前及2、5、10、15、30、60、及120分鐘後採集血樣（圖一）。血漿睪固酮、助孕酮、及黃體促素濃度以放射免疫法(Radioimmnuassay) 檢測。活體實驗後兩週內大鼠斷頭犧牲取出睪丸或卵巢。睪丸去鞘後均分八塊，卵巢則去鞘。每塊睪丸及卵巢組織都先分別置於34℃及37℃水浴中以Locke's溶液靜態培養90分鐘後，以含有3-isobutyl-methylxanthine (IBMX; 1 mM)之Locke's溶液，一組以乳酸(LA; 0.01-10 mM; pH=7.3)刺激，另一組則分別以人絨膜性促素(hCG; 0.5 IU/ml)及豬濾泡性促素(pFSH; 1 μg/ml)刺激60分鐘後收集培養液，組織進行蛋白質濃度檢測。培養液中睪固酮、助孕酮和睪丸及卵巢細胞內環單磷酸腺苷以放射免疫法檢測濃度。大鼠之腦垂體取出後對切一半，經由30分鐘之基礎培養後，以含乳酸(LA; 0.1-10 mM)及／或性釋素(GnRH; 10 nM)之培養液繼續培養30分鐘後收集培養液。組織立即秤重。培養液以放射免疫法檢測黃體促素之濃度。此外，取出中底下視丘(MBH)在37℃之水浴中以Locke's溶液培養90分鐘後再以含有氯化鉀(KCl; 60 mM)、乳酸(8 mM)、之培養液或Locke's溶液繼續培養30分鐘。培養液中性釋素之濃度以放射免疫法檢測。游泳10、15、30 分鐘後血漿葡萄糖、乳酸、睪固酮、及助孕酮濃度皆顯著高於安靜值。游泳30分鐘後雄

鼠血漿黃體促素濃度增加，而雌鼠黃體促素濃度不變。乳酸靜脈灌流後5-30分鐘血漿乳酸、睪固酮、及助孕酮濃度顯著高於安靜值，而黃體促素濃度不變。離體組織經過60分鐘乳酸刺激後，睪丸及卵巢細胞內環單磷酸腺苷之濃度、睪固酮及助孕酮之分泌量顯著高於基礎值。腦垂體以乳酸刺激之培養液中黃體促素濃度不變。下視丘離體實驗指出乳酸刺激性釋素分泌。結論認為游泳運動實驗模式可引發大鼠血漿葡萄糖、乳酸、睪固酮、及助孕酮之增加。而游泳運動引發血漿睪固酮及助孕酮濃度顯著上升後黃體促素才增加或不變，顯示泳後血漿睪固酮及助孕酮增加並非受黃體促素之刺激所致。此外，灌流實驗結果顯示乳酸能引發血漿睪固酮及助孕酮濃度顯著上升而黃體促素濃度不變，結果顯示乳酸具有刺激睪固酮及助孕酮分泌效應。離體實驗結果顯示乳酸具有直接刺激睪丸及卵巢增加細胞內環單磷酸腺苷濃度之效應，顯示游泳導致大鼠血漿睪固酮及助孕酮之增加，至少部分原因是由於乳酸直接刺激所致，而非由黃體促素刺激所致（圖二）(55, 56, 57)。

肆、結　語

目前國內以動物為實驗對象探討內分泌生理、神經內分泌生理、生殖生理及細胞生理等醫學相關之研究廣汎。而運動生理學多以研究人類運動對肌肉收縮、代謝、呼吸、及循環系統為主。利用短時間、高強度運動及乳酸觀察中底下視丘—前垂體—性腺軸線反應及探討乳酸對性激素分泌機轉之研究並不多見，期望藉由本篇回顧能引起國內研究人員之興趣而對相關主題做更深入之探討。

參考文獻

1. Alford, F.P., H.W.G. Baker, Y.C. Patel, G.C. Rennie, G. Youatt, H.G. Berger, and B. Hudson. Temporal patterns of circulating hormones as assessed by continuous blood sampling. J. Clin. Endocrinol. Metab. 36:108-116, 1973.
2. Armstrong, E.G. and C.A. Villee. Characterization and comparison of estrogen and androgen receptors of calf anterior pituitary. J. Steroid Biochem. 8:285-292, 1977.
3. Avallet, O., M. Vigier, M.H. Perrard-Sapor, and J.M. Saez. Transforming growth factor inhibits Leydig cell functions. Biochem. Biophys. Res. Commun. 146:574-581, 1987.
4. Baker, H.W.G., R.J. Santen, H.G. Berger, D.M. De Kretser, B. Hudson, R.J. Peperell, and C.W. Bardin. Rhythms in the secretion of gonadotropins and gonadal steroids. J. Steroid Biochem. 5:793-801, 1975.
5. Beck. P. Alteration in lipid metabolism by contraceptive steroids. J. Steroid Biochem. 6957-959, 1975.
6. Berchtold. P., M. Berger, H.J. Cuppers, J. Herrman, E. Nieschlag, K. Rudorff, H. Zimmernam, and H.L. Kruskemper. Nonglucoregulatory hormones (T4, T3, rT3, TSH, Testosterone) during physical exercise in juvenile-type diabetics. Hormone Metab. Res. 10:269-273, 1973.
7. Bonekat, H.W., M.L. Dombovy, and B.A. Staat. Progesterone induced change in exercise performance and ventilation

response. J. Med. Sport. Exerc. 19:118-123, 1987.
8. Bonen, A., F.A. Haynes, and T.E. Graham. Substrate and hormonal responses to exercise in women using oral contraceptives. J. Appl. Physiol. 70:1917-1927, 1991.
9. Brisson, G.R., M.A. Volle, M.D.M. Desharnais, and M. Tanaka. Pituitary-gonadal axis in exercising man. Med. Sci. Sports Exerc. 9:47, 1977. (Abstract)
10. Butcher, R.L., W.E. Collins, and N.W. Fugo. Plasma concentration of LH, Fsh, prolactin, progesterone and estradiol-17-β throughout the 4-day estrous cycle of the rat. Endocrinology 94:1074-1078, 1974.
11. Calandra, R.S., J.A. Blaquier, E.J. Castillo, and M.A. Rivarola. Androgen dependency of the androgen receptor in rat epididymis. Biochem. Biophys. Res. Commun. 67:97-102, 1975.
12. Cassel, D., and Z. Selinger. Mechanism of adenylate cyclase activation through the β-adrenergic receptor: catecholamine-induced displacement of bound GDP by GTP. Proc. Natl. Acad. Sci. USA. 75:4155-4159, 1978.
13. Chen, T.S., M.L. Doong, F.Y. Chang, and P.S. Wang. Effects of sex steroid hormones on gastric emptying and gastrointestinal transit in rats. Am. J. Physiol. 266:G171-176, 1995.
14. Cumming, D.C.L.A. Brunsting, G. Strich, G. Greenberg, A.L. M. Ries, and R.W. Reproductive hormone increase in response acute exercise in men. Med. Sci. Sports Exerc. 18:369-373,

1986.

15. Cumming, D.C., and G.D. Wheeler. Exercise, training, and male reproductive system. In Bouchard, C., R.J. Shephard, and T. Stephens (Eds.), Physical activity fitness and health: International proceeding and consensus statement. Human Kinetics Publisher. 1994.
16. Csapo, A. In: Progesterone: Its regulatory effects on the myometrium. New York: Ciba Foundation Study Group No. 34, 1969.
17. De Boer, D., E.G. De Jong, J.M. van Rossum, and R.A.A. Maes. Doping control of testosterone and human chorionic gonadotropin: a case study. Int. Sports Med. 12:46-51, 1991.
18. Deschenes, M.R., C.M. Maresh, L.E. Armstrong, J. Covault, W.J. Kraemer, and J.F. Crivello. Endurance and resistance exericse induce muscle fiber type specific responses in androgen binding capacity. J. Steroid Biochem. Mole. Biol. 50:175-179, 1994.
19. Dombovy, M.L., H.W. Bonekat, T.J. Fillams, and B.A. Staats. Exercise performance and ventilatory response in menstrual cycles. J. Med. Sci. Sports. Exerc. 19:111-117, 1987.
20. Fahey, T.D., R. Rolph, P. Moongee, J. Nagel, and S. Mortara. Serum testosterone, body composition, and strength of young adults. Med. Sci. Sports Exerc. 1:31-34, 1976.
21. Fox, E.L., R.W. Bowers, and M.L. Foss. Exercise and the En-

docrine System. In: The Physiological Basis for Exercise and Sport. Brown & Benchmark. Dubuque, IA, Inc., 5th edition, 1993, chap. 21, pp. 602-603.

22. Frantz, A.G., and M.T. Rabin. Effects of estrogen and sex differences on secretion HGH. J. Clin. Endocrinol. Metab. 25:1470-1480, 1965.

23. Galbo, H., L. Hummer, I.B. Petersen, N.J. Christensen, and N. Bie. Thyroid and testicular hormone responses to graded and prolonged exercise in man. Eur. J. Appl. Physiol. 36:101-106, 1977.

24. Gawel, M.J., D.M Park, J. Alaghband-Zadeh, and F.C. Rose. Exercise and hormonal secretion. Postgrad. Med. J. 55:373-376, 1976.

25. Genazanni, A.R., T. LeMarchand-Berand, M.L. Aubert, and J. R. Felber. Pattern of plasma ACTH, HGH, and cortisol during the menstrual cycle. J. Clin. Endocrinol. Metab. 41:431-437, 1975.

26. Guglielmini. C., A.R. Paolini, and F. Conconi. Variations of serum testosterone concentrations after physical exercises of different duration. Intl. J. Soprts Med. 5:246-249, 1984.

27. Haakinen, K., A. Pakarinen, M. Alen, H. Kauhanen, and P. Komi. Relationships between training volume, physical performance capacity, and serum hormone concentrations during prolonged training in elite weight lifters. Int. J.

Sports. Med. 8:61-65, 1987.

28. Hadley, M.E. Hormones and male reproduction physiology. In: Endocrinology, 3rd ed. Prentice-Hall, Englewood Cliffs, NJ, 1992.
29. Hadley, M.E. Hormones and female reproduction physiology. In: Endocrinology, 3rd ed. Prentice-Hall, Englewood Cliffs, NJ, 1992.
30. Hankin, H.R., E. Murono, T. Lin, and J. Osterman. Morning and evening human Leydig cell responses to hCG. Acta Endocrinol. 95:560-565, 1980.
31. Hansen, A.P., and J. Weeke. Fasting serum growth levels and growth hormone response to exercise during normal menstrual cycles and cycles of oral contraceptives. Scand. J. Clin. Lab. Invest. 34:199-205, 1974.
32. Hedge, G.A., H.D. Colby, and R.L. Goodman Clinical endocrine physiology, W.B. Saunders Co., Philadelphia, 1987.
33. Hodgson Y.M., and D.M. De Krester. The temporal response of rat testes to HCG stimulation during sexual maturation. Int. J. Androl. 7:203-214, 1984.
34. Jeżova, D., and M. Vigas. Testosterone response to exercise during blockade and stimulation of adrengeric receptors in man. Am. J. Clin. Nutr. 33:1010-1018, 1981.
35. Johansson, E.D.B. Progesterone levels in peripheral plasma during the luteal phase of the normal human menstrual cycle measured by a rapid competitive protein binding technique.

Acta Endocrinol. 61:591-606, 1969.
36. Judd, H.L., R. Rebar, G. Vandenberg, and S.S.C. Yen. Effect of luteinizing hormone releasing factor on Leydig cell function. J. Clin. Endocrinol. Metab. 38:8-13, 1974.
37. Jurkowski, J.E., N.L. Jones, C. Walker, E.V. Yunglai, and J.R. Sutton. Ovarian hormonal responses to exercise. J. Appl. Physiol. 44:109-114, 1978.
38. Kalkhoff, R.K.. Effects of oral contraceptive agents on carbonhydraft metabolism. J. Steroid. Biochem. 6:949-956, 1975.
39. Kao, C.Y. In Cellular biology of the uterus, edited by R.M. Wynn. New York: Appleton-Century-Croft, 1967.
40. Kanaley, J.A., R.A. Boileau, J.A. Bahr, J.E. Misner, and R. A. Nelson. Substracte iodation and GH responses to exercise are independent of menstrual phase and status. Med. Sci. Sports. Exec. 24:873-880, 1992.
41. Karvonen, J., E. Peltola, J. Saarela, and M.M. Nieminen. Changes in running speed, blood lactic acid concentration and hormone balance during sprint trining performed at an altitude of 1860 meters. J. Sports Med. Phys. Fitness. 30: 122-126, 1990.
42. Khorram, O., K. Y.F. Pau, and H.G. Spies. Biomodal effects of neuropeptide Y on hypothalamic release of gonadotropin-releasing hormone in conscious rabbits. Neuro-endocrinology 45:290-297, 1987.

43. Kim, H. J., and R. J. Kalkhoff. Sex steroid influence on triglyceride metabolism. J. Clin. Invest. 56:888-896, 1975.
44. Kindermann, W., A. Schnabel, W. M. Schmitt, G. Biro, J. Cassens, and F. Weber. Catecholamines, growth hormone, cortisol, insulin and sex hormones in aerobic and anerobic exercise. Eur. J. Appl. Physiol. 49:398-399, 1982.
45. Kraemer, W. J. Endocrine responses to resistance exercise. Med. Sci. Sports Exer. (Suppl. 20):S152-S157, 1988.
46. Kraemer, W. J., L. Marchitelli, S. E. Gordon, E. Harman, J. E. Dziados, R. Mello, P. Frykman, D, McCurry, and S. J. Fleck. Hormonal and growth factor responses to resistance exercise protocol. J. Appl. Physiol. 69:1442-1450, 1990.
47. Kuoppasalmi, K. Plasma testosterone and sex-hormone-binding globulin capacity in physical exercise. Scand. J. Clin. Lab. Invest. 40:411-418, 1980.
48. Kuoppasalmi, K., H. Naveri, M. Harkonen, and H. Aldercreutz. Plasma cortisol, androstenedione, testosterone and luteinizing hormone in running exericse of different intensities. Scand. J. Clin. Lab. Invest. 40:403-409, 1980.
49. Kuoppasalmi, K., H. Naveri, S. Rehunen, M. Harkonen, and H. Adlercreutz. Effect of stenguous anaerobic running on plasma growth hormone, cortisol, luteinizing hormone, testosterone androstenedione and estrone and estraiol. J. Steroid Biochem. 7:823-829, 1976.
50. Lamont, L. S., P. W. R. Lemon, and B. C. Bruot. Menstrual cycle

on blood lactate. J. Phys. Sports Med. 14:159-163, 1986.
51. Larminat, M.A., A. Monsalve, E.H. Charreau, R.S. Calandra, and J.A. Blaquier. Hormonal regulation of 5α-reductase activity in rat epididymis. J. Endocr. 79:15-165, 1978.
52. LaVoie, J.M., N. Dionne, R. Hellie and G.R. Brisson. Menstrual cycle phase dissociation of blood glucose homestasis during exercise. J. Appl. Physiol. 62:1084-1089, 1987.
53. LeMaire, W.J., P.W. Conly, A. Moffett, and W.W. Cleveland. Plasma progesterone secretion by the corpus luteum of term pregnancy. Am. J. Obstet. Gynecol. 108:132-134, 1970.
54. Lopez, F.J.I. Merchenthaler, M. Ching, and M.G. Wisniewski. Galanin: A hypothalamic-hypophysiotropic hormone modulating reproductive functions. Proc. Natl. Acad. Sci. USA 88:4508-4512, 1991.
55. Lu, S.S., C.P. Lau, Y.F. Tung, S.W. Huang, Y.H. Chen, H.C. Shih, S.C. Tasi, C.C. Lu, S.W. Wang, J.J. Chen, and P.S. Wang. Lactate and the effects of exercise on testosterone secretion: Evidence for the the involvement of a cAMP-mediated mechanism. Med. Sci. Sports Exerc. 29:1048-1054, 1997.
56. Lu, S.S., C.P. Lau, Y.F. Tung, S.W. Huang, Y.H. Chen, H.C. Shih, S.C. Tasi, C.C. Lu, S.W. Wang, J.J. Chen, and P.S. Wang. Lactate stimulates progesterone secretion via an increase in cAMP production in exercised female rats. Am. J. Physiol. 271:E910-E915, 1996.

57. Lu, S.S., P.S. Wang, and J.J. Chen. Effect of swim on the production of sex steroid hormones in rats. Abstract submitted to The Twelfth Joint Annual Conference of Biomedical Sciences, 1997.

58. MacConnie, S.E., A. Barkan, R.M. Lampman, M.A. Schork, and I.Z. Beitins. Decreased hypothalamic gonadotropin releasing hormone secretion in male marathon runners. N. Engl. J. Med. 315:411-417, 1986.

59. MacDonald, C., L. Williams, P. McTurk, F. Fuller, E. McIntosh, and S. Higgins. Ioslation and characteristration of genes for androgen-responsive secretory proteins of rat seminal vesicles. Nucleic Acids Res. 11:917-930, 1983. 110. MacDougall, J.D., W.G. Reddan, C.R. Layton, and J.A. Dempsey. Effects of metabolic hyperthermia on performance during heavy prolonged exercise. J. Appl. Physiol. 36:538-544, 1974.

60. Maresh, C.M., M.R. Cook, H.D. Cohen, C. Graham, and W.S. Gunn. Exercise testing in the evaluation of human responses to powerline frequency fields. Aviat. Space Environ. Med. 59:1139-1145, 1988.

61. Marshall, J.C., D.C. Anderson, T.R. Fraser, and P. Marsoulis. Human luteinizing hormone in man: Studies of metabolism and biological action. J. Endocrinol. 56:431-43 9, 1973.

62. Martikainen, H., I, Huhtaniemi, and R. Vihko. Response of

peripheral serum sex steroids and some of their precursors to a single intramuscylar injections of hCG in adult men. Clin. Endocrinol. 13:157-166, 1980.

63. Martin, C.R. Endocrine physiology, Oxford University press, New York, 1985.

64. Martini, L. The 5α-reduction of testosterone in the neuroendocrine structure. Biochemical and physioogical implications. Endocr. Rev. 3:1-25, 1982.

65. Mastrogiacomo, I., D. Toderini, G. Bonanni, and D. Bordin. Gonadotropin decrease induced by prolonged exericse at about as 55 percent of the VO2max in different phases of the menstrual cycle. Intl. J. Sports Med. 11:198-203, 1990.

66. Metivier, G., R. Gauthier, J. de al Chevotriere, and D. Grymala. The effect of acute exercise on the serum levels of testosterone and luteinizing (LH) hormone in human male athletes. J. Sports Med. Phys. Fitness. 20:235-237, 1980.

67. Mooradian, A.D., J.E. Morley, and S.G. Korenman. Biological actions of adnrogens. Endocr. Rev. 8:1-28, 1987.

68. Naftolin, F., H.L. Judd, and S.S.C. Yen, Pulsatile patterns of gonadotropins in man: The effect of clomiphene with and without testosterone. J. Clin. Endocrinol. Metab. 36:285-288, 1973.

69. Nankin, H.R., E. Murono. T. Lin. and J. Osterman. Morning and evening human Leydig cell responses to hCG. Acta Endocrionl. 95:560-565, 1980.

70. Nicklas, B.J., A.C. Hackney, and R.L. Sharp. The menstrual cycle and exercise: performance, muscle glycogen, and substrate responses. Intl. J. Sports Med. 10:264-269, 1989.
71. Nseuh, A.J.W, M.L. Dufau, and K.J. Catt. Regulation of LH receptors in testicular interstitial cells by gonadotropin. Biochem. Biophys. Res. Commun. 72:1145-1152, 1976.
72. Oparil, S., W.N.N. Ehrlich, and M.D. Lindheimer. Effect of progesterone on renal sodium handling in man: Relation to aldosterone excretion and plasma renin activity. Clin. Sci. Mol. Med. 49:139-147, 1975.
73. Padron R.S., J. Wischusen, B. Hudson, H.G. Burger, and D.M. deKretser. Prolonged biphasic response of plasma testosterone to single intramuscular injections of human chorionic gonadotropin. J. Clin. Endocrinol. Metab. 50:1100-1104, 1989.
74. Parker, S.L.S.P. Kalra, and W.R. Crowley. Neuropeptid Y modulates the binding of a gondatropin-releasing hormone (GnRH) analog to anterior pituitary GnRH receptor sites. Endocrinology 128:2309-2316, 1991.
75. Pau, K.Y.F, K.M. Orstead, D.L. Hess, and H.G. Spies. Feedback effects of ovarian steroids on the hypothalamic-hypophyseal axis in the rabbit. Biol. Reprod. 35:1009-1023, 1986.
76. Pau, K.Y.F, and H.G. Spies. Estrogen-dependent effects of norepinephrine on hypothalamic gonadotropin-releasing hor-

mone release in the rabbit. Brain Res. 339:15-23, 1986.
77. Petersson, F., R.G.G. Andersson, A.A.S. Berg, and M. Hammar. Early effect of hCG on human testicular cyclic AMP content, protein kinase activity, in-vitro progesterone conversion and the serum concentrations of testosterone and oestradiol. Int. J. Androl. 11:179-186, 1988.
78. Roberts, V.T., C.A. Peto, W. Vale, and P. Sawchenko. Inhibin /activin subunits are costored with FSH, LH in secretory Neuroendocrinology 56:214-224, 1992.
79. Rodbell, M. The role of hormone receptors and GTP-regulatory proteins in membrane tranduction. Nature 284:17-22, 1980.
80. Ross, E.M., and A.G. Gillman. Biochemical properties of hormone-sensitive adenlyate cyclase. Ann. Rev. Biochem. 49:533-564, 1980.
81. Roth, J.C., M.M. Grumbach, and S.L. Kaplan. Effect of synthetic luteinizing factor on serum testosterone and gonadotropins in prepubertal, pubertal and adult males. J. Clin. Endocrinol. Metab. 37:680-686, 1973.
82. Saez, J.M., and M.G Forest. Kinetics of human chorionic gonadotropin-induced steroidogenic response of the human testis. Plasma testosterone: Implications for human chorionic gonadotropin stimulation test. J. Clin. Endocrinol. Metab. 49:278-283, 1979.
83. Sakai, A., R. Sakakibara, and M. Ishiguro. Human chroionic

gonadotropin-rich A Chain hyrid protein: A hormone analog for the study of signal transduction. J. Biochem. 105:275-280, 1989.

84. Schally, A.V., A. Arimura, Y. Baba, R.M.G. Nair, H. Mastuo, T.W. Redding, and L. Debeljuk. Isolation and properites of the FSH and LH-releasing hormone. Biochem. Biophys. Res. Commun. 43:393-399, 1971.

85. Schally, A.V., A.J. Kastin, and A. Arimura. The hypothalamus and reproduction. Am. J. Obstet. Gynecol. 114:423-441, 1972.

86. Schally, A.V., T.W. Redding, and A. Arimura. Effect of sex steroids on pituitary responses to LH-and FSH-releasing hormone in vitro. Endocrinology 93:893-902, 1973.

87. Schwatz, J., and R. Cherny Intercellular communication within the anterior pituitary influencing the secretion of hypophysial hormones. Endocr. Rev. 13:453-475, 1992.

88. Schoultz, B., and K. Carlstorm. On the regulation of sex hormone binding globulin-a challenge of an old dogma and outlines of a alternative mechanism. J. Steroid Biochem. 32:327-334, 1989.

89. Selby, C. Sex hormone binding globulin: orgin, function and clinical significance. Ann. Clin. Biochem. 27:532-541, 1992.

90. Siiteri, P.K., and N.H. Simberg. Changing concepts of active androgens in blood. J. Clin. Endocrinol. Metab. 15:247-258,

1986.

91. Sharpe, R.M. HCG-induced decreased in availability of rat testis receptors. Nature. 264:644-646, 1976.

92. Shih. H.C., S.C. Tasi, Y.H. Chen, C.C. Lu, Y.C. Chiao, C. Liaw, M.M. Kau, S.W. Wang and P.S. Wang. Effect of triiodothyronine on progesterone production in rat ovaries. Proceeding of the 16th annual the Endocrinology Society of the R.O.C. and Diabetes Association of the R.O.C. 1994. (Abstract).

93. Smals, A.G.H., G.F.F.M. Pieters, J.I.M. Drary, T.J. Benrrad, and P.W.C. Kloppenborg. Leydig cell responsiveness to single and repeated human chorionic gonadotropin administration. J. Clin. Endocrinol. Metab. 49:12-14, 1979.

94. Srivistava, M.C.N.W. Oakley, C.V. Tompekins, P.H. Sonksek, and V. Wynn. Insulin metabolism, Insulin sensitivity and hormonal responses to insulin infusion in patients taking oral contraceptive steroids. Eur. J. Clin. Invest. 5:425-433, 1975.

95. Sutherland, E.W., and T.W. Rall. Fractionation and characterization of a cyclic adenine ribonucleotide formed by tisses particles. J. Biol. Chem. 232:1077-1091, 1958.

96. Sutton, J.R., M.J. Coleman, J. Casey, and L. Lazarus. Androgen responses during physical exercise. Bri, Med. J. 1:520-522, 1973.

97. Toriola, A.L., and D.N. Mathur, and O.A. Dada. Serum elec-

trolyte sprinters after submaximal exercise. J. Sports Med. Phys. Fitness. 26:5-7, 1986.

98. Veneziale, C.M. Specific protein synthesis in isolated epithelium of guinea-pig seminal vesicles. Biochem. J. 166:155-166, 1977.

99. Wang, P.S., S.C. Tsai, G.S. Hwang, S.W. Wang, C.C. Lu, J.J. Chen, S.R. Liu, K.Y. Lee, E, J. Chien, C.H. Chien, H.Y. Lee, C.P. Lau, and C.L. Tasi. Calcitonin inhibits testosterone and luteinizing hormone secretion through a mechanism involving and increase in cAMP production in rats. J. Bone Miner. Res. 9:1583-1590, 1994.

100. Wenderoth, U.K., F.W. George, and J.D. Wilson. The effect of a 5α-inhibitor on androgen-mediated growth of the dog prostate. Endocrinology. 113:569-573, 1983.

101. Whan, K.S., N. Ichimaru, M. Kagimura, and M. Ishii. Effects of nutrition condition's on relationships between anaerobic threshold and lactate threshold. J. Human Ergol. 18:181-189, 1989.

102. Wilkerson, J., S. Horvath, and B. Gutin. Plasma testosterone during treadmill exercise. J. Appl. Physiol. 49:249-253, 1980.

103. Yamaguchi, M.N., N. Matsuzaki, K. Hirota, A. Miyake, and O. Tanizawa. Interleukin-6 possibly induced by interleukin 1β in the pituitary gland stimulates the reease of gonadotropins and prolactin. Acta Endocrinol. 122:201-205,

1990.

104, Yu, W.H., and S.M. Mccann. Feedback of follicle-stimulating hormone to inhibit luteinizing hormone and stimulate follicle-stimulating hormone reease in ovariectomized rats. Neuroendocrinology 53:453-459, 1991.

105. Zander, J., K. Holzmann, A.M. von Mustermann, B. Runnehbaum, and W. Silver. In: The fetuo-placental unit. Edited by A. Pecile and C. Finzi. Amsterdam: Excerpta Medica Foundation, 1969.