

## · 临床论著 ·

## 补肾和健脾在延缓衰老作用中的对比研究

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**内容提要** 本文通过 90 例健康老年人随机分组, 采用补肾、健脾、对照法服药 2 个月, 服药前后进行各项检验。结果表明: 补肾法和健脾法都能发挥非特异免疫功能增强剂的作用, 而在提高血浆促黄体生成激素及皮质醇水平上, 补肾法比健脾法的作用显著, 说明补肾和健脾在神经内分泌及免疫系统上延缓衰老的作用各有侧重, 而以补肾法更为广泛而显著。

关于衰老的学说不下数十种, 而以神经内分泌及免疫学说掌管整体调节, 更符合于中医的特色。中医传统认为肾为先天之本, 脾为后天之本, 而历代由于不同的学术流派对补肾或健脾谁能延缓衰老这一主张上有不同的见解。现以 90 例健康老年人分组, 采用双盲法, 从内分泌及免疫两方面, 比较补肾法和健脾法的各自作用, 以便作出评价。

**资料和方法**

一、对象选择与观察方法: 选择年龄在 60 岁以上健康老年人共 90 例, 男 58 例, 女 32 例, 平均 70 岁, 随机分为三组各 30 例, 对照组服安慰剂(蜂蜜水加赋形剂); 健脾组服人参蜂皇浆; 补肾组服安慰剂加温阳片(附片、生地、熟地、山药、补骨脂、仙灵脾等)。人参蜂皇浆与安慰剂均由上海中药一厂提供, 取补肾强身液为名, 安瓿包装, 以不同批号区别, 每日服用 2 支; 温阳片以补肾强身片为名, 每日三次, 每次 5 片。三组采用双盲法观察, 连续服药 2 个月, 在随访考核疗效时各组均有几例失访, 但在随访时此三组年龄、性别并无明显差异, 服药前后分别作各项检验。

另设 4 组为考核新建立免疫指标可靠性而用, 即健康成人组 41 例, 平均 31 岁; 老年肿瘤

临床治愈组 26 例, 为经治疗已存活 5 年以上者, 平均 69 岁; 老年肿瘤转移组 11 例, 为已有明确转移灶患者, 平均 65 岁; 成人肿瘤转移组 17 例, 平均 49 岁。

二、实验室检查: 血标本制备系于上午 8 时左右, 抽取肝素抗凝血 5ml, 低速离心, 取上清血浆冰冻( $-35^{\circ}\text{C}$ )保存待测内分泌有关指标; 剩下细胞部分用淋巴细胞分离液(上海试剂二厂)分离淋巴细胞, Hank's 液洗涤 2 次, 用含 10% AB 血清的 1640 液重悬细胞, 分别调节细胞浓度至  $2.5 \times 10^6$  细胞/ml 作自然杀伤(NK)细胞活性测定, 并调节细胞浓度至  $1 \times 10^6$  细胞/ml 作 ConA 淋转测定。另以 2 ml 血分离血清,  $-35^{\circ}\text{C}$  保存待测血浆中免疫复合物(CIC)。

1. NK 细胞活性测定: 采用  $^{51}\text{Cr}$  标记靶细胞法, 由中国科学院上海细胞生物研究所协助完成。

2. ConA 淋转率: 采用  $^3\text{H}$ -TdR 参入法。

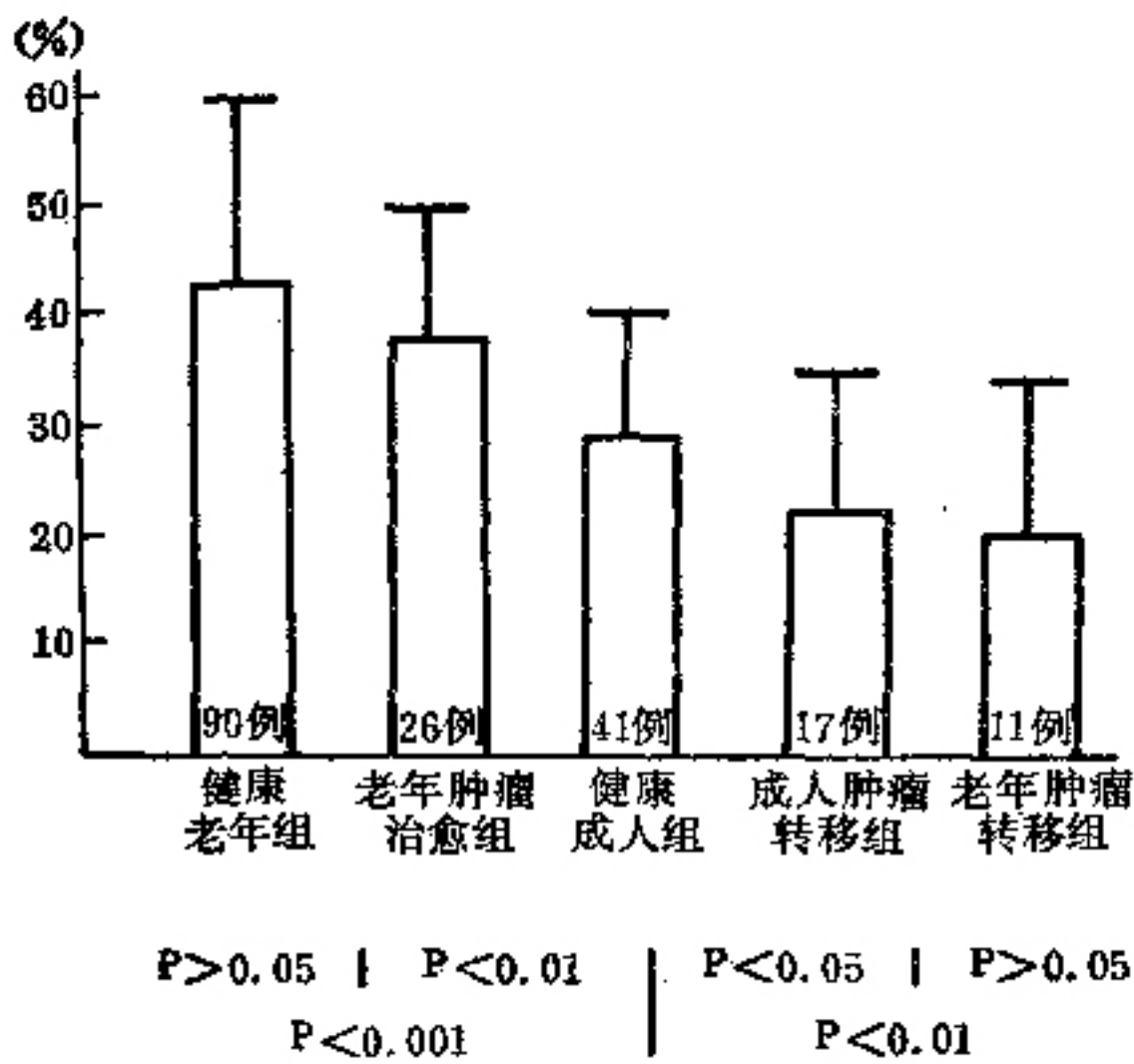
3. CIC 测定: 采用聚乙二醇沉淀法。

4. 血浆促黄体生成激素(LH)、促卵泡刺激素(FSH)、皮质醇(F), 均以放射免疫法测定, 试剂盒来自上海生物制品研究所。

三、统计方法: 样本均数比较用 t 检验中的配对比较和组间比较。内分泌激素指标用几何均数计算均值, 用反对数 t 检验。

## 结 果

### 一、各组NK细胞活性的比较：见附图。



附图 各组NK细胞活性比较

图中可见健康老年组NK细胞活性  $M \pm SD$  为  $42.6 \pm 17.1\%$ ；老年肿瘤临床治愈组为  $37.0 \pm 14.5\%$ ；健康成人组为  $28.0 \pm 13.8\%$ ；成人肿瘤转移组为  $22.1 \pm 13.8\%$ ；老年肿瘤转移组为  $19.3 \pm 17.0\%$ ，各组间比较显示，健康老年组的NK细胞活性显著高于健康成人组，老年肿瘤临床治愈组则介于前两者之间，仍明显高于健康成人组。已有明显转移灶的肿瘤患者不论老年人还是成年人，都明显低于健康成人。这表明，已经转移的恶性肿瘤患者免疫功能

能开始崩溃，因此NK细胞活性在各组中最低，已经临床治愈的老年肿瘤患者则保有老年人的特点，仍明显高于健康成人。从以上各组比较亦说明本文NK细胞活性检测的可靠性。

### 二、补肾和健脾对神经内分泌免疫方面的作用

1. 健康老年组和健康成人组的比较：内分泌方面的血浆皮质醇老年组为  $16.84 \pm 5.34 \mu\text{g/dl}$ ，成人组为  $14.20 \pm 3.92 \mu\text{g/dl}$ ， $P > 0.05$ ；FSH老年(男)组为  $11.67 \pm 7.52 \text{mIU/ml}$ ，成人(男)组为  $4.85 \pm 1.58 \text{mIU/ml}$ ， $P < 0.001$ ；LH老年(男)组为  $8.40 \pm 4.78 \text{mIU/ml}$ ，成人(男)组为  $4.41 \pm 1.31 \text{mIU/ml}$ ， $P < 0.05$ 。可见老年(男)组的垂体促性腺激素FSH与LH均显著高于成人(男)组，而皮质醇并无明显差异。免疫方面的NK细胞活性老年组为  $42.6 \pm 17.1\%$ ，成人组为  $28.0 \pm 13.8\%$ ， $P < 0.001$ ；ConA淋转老年组为  $30174 \pm 11605 \text{cpm}$ ，成人组为  $57071 \pm 19223 \text{cpm}$ ， $P < 0.001$ ；CIC老年组为  $0.1536 \pm 0.0577 \text{OD值}$ ，成人组为  $0.0846 \pm 0.0440 \text{OD值}$ ， $P < 0.001$ ，可见老年组NK细胞活性与CIC值都比成人组显著升高，而ConA淋转则显著降低，这三项指标在健康老年人是显然有别于健康成人。

### 2. 三组健康老年人治疗前后的比较

#### (1) 内分泌方面：见表1。

表1 三组老年人促性腺激素及皮质醇治疗前后变化

	皮质醇 (μg/dl)			FSH(mIU/dl)			LH (mIU/dl)		
	治 前	治 后	P	治 前	治 后	P	治 前	治 后	P
补肾组	18.19±6.427	21.71±5.547	<0.01	12.30 (7.08~21.28)	13.18 (8.51~20.42)	>0.05	4.46 (2.09~9.55)	8.71 (3.31~21.88)	<0.01
	n=21			n=8 (男)			n=14(男)		
健脾组	16.33±3.66	16.60±5.48	>0.5	6.92 (4.47~10.72)	8.13 (5.50~12.02)	>0.05	3.03 (1.68~3.44)	3.98 (1.89~ 7.98)	<0.05
	n=26			n=12(男)			n=14(男)		
对照组	16.07±4.80	17.57±8.11	>0.05	14.45 (7.94~26.3)	9.77 (5.50~17.38)	NS	4.01 (1.79~9.33)	3.77 (2.15~ 6.61)	NS
	n=21			n=12(男)			n=12(男)		

注：FSH与LH均用反对数法统计，( )内为范围，以上均值系用几何均数计算

表2 三组老年人NK细胞活性、ConA淋转、CIC治疗前后变化

	NK细胞活性 (%)			ConA淋转 (cpm)			CIC (OD)		
	治 前	治 后	P	治 前	治 后	P	治 前	治 后	P
补肾组	42.57±18.49	53.34±21.19	<0.001	26 726 ±10 119	31 997 ± 9 480	<0.025	0.1761±0.061	0.1359±0.047	<0.01
	n=22			n=22			n=20		
健脾组	46.74±11.97	57.69±14.26	<0.001	30 580 ±11 287	36 608 ±11 789	<0.025	0.1640±0.0412	0.1341±0.0501	<0.01
	n=26			n=24			n=20		
对照组	39.36±16.12	43.23±19.98	>0.5	33 878 ±12 856	33 423 ±12 116	>0.5	0.1667±0.0497	0.1643±0.0614	>0.05
	n=20			n=19			n=20		

表1可见补肾组治后血浆皮质醇与LH均有极显著升高(P均<0.01),健脾组仅LH有明显升高(P<0.05),对照组治疗前后则均无明显差异。

(2)免疫方面:见表2。从表2可见无论补肾组或健脾组都使NK细胞活性与ConA淋转有极显著升高(P均<0.025),CIC值则均明显下降(P均<0.01),对照组治疗前后均无明显差异。

## 讨 论

近年研究结果提示衰老的机理是综合性而非单一因素,各器官衰老速度不一,且有关的病理生理环节中可以因果交替,从而形成恶性循环而加速衰老的进程,从整体到分子水平的研究企图阐明衰老本质的学说已不下数十种。其中以神经内分泌及免疫对机体各种功能的调节作用表现为复杂的过程,只要其中一个环节发生障碍,就会引起调节失常和机体内环境紊乱,从而导致提前衰老。中医比较古老而经典对衰老的看法以《素问·上古天真论》中的一段,以女子七、男子八为基数递进的生长发育衰老曲线具有代表性,提出衰老的内因是“肾”起主导作用,但以后由于学术流派的倾向,对于补肾还是健脾能延缓衰老的主张与说法不一。其实中医传统一向着重从证效关系来判别辨证的正确性,也就是以药验“证”,本文出于此意在三组健康老年人中进行比较。

在免疫系统方面,较多的作者<sup>[1~3]</sup>认为NK细胞活性随年龄而增加,肿瘤发生早期或缓解期可正常,只有疾病进展期或转移扩散时才明显降低。本文通过老年人和成人以及各组肿瘤患者之间的对比,也看到与文献相一致的规律。老年人NK细胞活性和ConA淋转呈相反趋向,因为ConA淋转亦反映T细胞功能,与抑制性T细胞功能一般相平行。老年人CIC含量增高(与抑制性T细胞功能下降和自身抗体增高有关),使担负免疫监视功能的NK细胞活性代偿性增高。NK细胞虽然属于非特异性免疫功能,但是具有杀伤作用的效应细胞,具有抗肿瘤和病毒感染作用,而且具有高度调节功能,补肾和健脾都能使健康老年组原已偏高的NK细胞活性更为增高,显然对增强机体抗病能力是有利的,总之补肾和健脾两法都发挥了非特异性免疫功能增强剂的作用。

在神经内分泌方面,我们<sup>[4]</sup>曾采用补肾(补肾益寿片)、健脾(四君子汤)、对照(安慰剂)法在三组健康老年人(男)性腺轴上,观察到补肾组治前原已比成人降低的靶腺分泌的血清睾酮浓度经治后有明显提高,反映下丘脑调节功能的LH-RH兴奋试验出现延迟反应的机会也明显减少(P值均<0.05),而健脾组与对照组均无此作用,说明补肾法对性腺(男)轴上具有延缓衰老的作用。老年人由于靶腺的纤维化与功能减退而有垂体促靶腺激素(如FSH、LH、TSH等)的代偿性升高,但这种代偿是不完全



的,因为靶腺激素并未因此而恢复正常,故此次选择性腺轴上垂体水平的促性腺激素——LH与FSH浓度加以比较。又由于文献报道<sup>[5]</sup>人参可提高血皮质醇浓度,故又加测血浆皮质醇。从检测结果可见补肾组对老年人原已比成人提高的LH有更大程度的提高,血皮质醇浓度也有极显著提高, $P$ 均 $<0.001$ ,说明这些老人的性功能和应激能力都能由补肾法得到改善,从而延缓了衰老的进程,而健脾组中老人的LH仅略有提高,血皮质醇则无任何变化。结合两次的三组(补肾、健脾、对照)健康老年人中比较,说明补肾法在神经内分泌和免疫方面延缓衰老的作用比健脾法更广泛而显著。

我们<sup>[6]</sup>从中医“肾”本质的研究中发现肾阳虚证的主要发病环节在下丘脑(或更高中枢)的调节紊乱,鉴于下丘脑是神经内分泌免疫网的整合中枢,补肾法对神经内分泌及免疫能进行同步的整体性调整,提示补肾法之延缓衰老的作用点也在下丘脑。1980年Everitt曾提出“老化钟就在下丘脑”这一假说,本文则以药物验证,具体地用补肾药物能延缓神经内分泌免

疫方面的衰老进程,阐发与证实这一假说。

当然补肾与健脾之延缓衰老作用点是各有侧重,若老年人以消化系统功能衰退为主,或许健脾法会比补肾法发挥更大的作用,因为衰老的机理毕竟并非单一因素。所以结合临床,有选择地在老年人中应用补肾或健脾,为中医临床辨病与辨证相结合用药提供了科学依据。

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## 慢性肾炎肾气虚证患者红细胞超氧化物歧化酶变化

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笔者测试了慢性肾炎肾气虚证患者红细胞中超氧化物歧化酶(SOD)活性,发现其水平明显降低,报告如下。

**临床资料** 肾气虚患者26例,男性16例,女性10例。年龄19~69岁。均为慢性肾炎患者。肾气虚辨证按1982年全国中西医结合虚证研究及防治老年病会议拟定的标准。健康人对照组48例,男性26例,女性22例。年龄18~42岁。

**方 法** 取患者及健康人静脉血,离心后分离出红细胞,用生理盐水洗三次,然后置于冰箱内贮存待测。SOD活性测试方法根据Misra HP等建立的肾上腺素自动氧化法(*J Biol Chem* 1972; 247:3170)略加改进。

**结 果** 26例慢性肾炎肾气虚证患者SOD活性为 $16.54 \pm 5.65 \text{ u/mg 蛋白}$  ( $M \pm SD$ , 以下同)。48例健康人对照组为 $20.37 \pm 6.80$ ,两组间经 $t$ 检验比较,肾气虚组明显低于健康组,有显著意义( $P < 0.05$ ),提示肾气虚证和SOD活性下降可能有关。

**讨 论** SOD为机体内超氧阴离子自由基( $O_2^-$ )的清除剂,当SOD活性降低时,机体内的核酸、蛋白、脂质等有可能被自由基氧化,生物膜、酶等就可能损伤,从而出现一系列较广泛的病理改变。这和肾为元气之根,肾气虚,五脏皆失温煦而诸病丛生有类似之处。因此,SOD活性降低可能是慢性肾炎肾气虚证的发病机理之一。

## Abstracts of Original Articles

### Comparison of the Effects of Tonifying Kidney and Invigorating Spleen Regimen in Delaying Aging Changes

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Both the prescriptions of tonifying Kidney and invigorating Spleen were highly praised among all the aging delaying prescriptions in TCM, but it was conflicting viewed by different schools that which regimen was the better one. For answering this question, 90 healthy elder subjects were selected and were divided into three groups at random: (1) treated with tonifying Kidney regimen (TKR), (2) treated with invigorating Spleen regimen (ISR), and (3) controls. Before and after the treatment, their neuroendocrine and immune functions were simultaneously measured. The results showed that the activity of NK cell in the elderly group was higher than that in the youngsters and it could be further increased after the treatment in all these cases but the controls, which suggested that TKR and ISR had the effect of improving the nonspecific immune function. Early in 1984, TKR could improve the aging changes of the function of the hypothalamus-pituitary-testes axis was found. It raised the serum testosterone level and increased the response ability of pituitary to the stimulation of LH-RH. These effects were not observed in the control and ISR groups. In this article, the levels of serum LH and plasma cortisol were increased markedly in TKR group while the LH level was slightly increased and the cortisol level remained unchanged in ISR group were observed. All these data suggested that the effects of TKR were more significant and wider in application in delaying aging changes than that of ISR.

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### Prophylaxis and Treatment of Neonatal ABO Hemolytic Disease by TCM-WM Therapy

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Both Chinese herbal medicine and Western medicine were administered for prevention and treatment of the neonatal hemolytic disease by giving the herbal medicine of promoting the blood circulation and relieving the stasis as well as regulating the Qi (气) prescription composed of *Leonurus heterophyllus*, *Ligusticum wallichii*, *Paeonia alba*, *Angelica sinensis* and *Saussurea lappa*, making in pills to 35 pregnant women who had the history of delivering the "yellow baby" previously. It was given from 17th weeks of pregnancy up to the delivery. As for the blood group of the mothers, 34 of them were group "O", only one belonged to group "A". The titer of their serum anti-A(B) IgG were  $> 1:64$ . Meanwhile, the blood group of the fetuses were different from their mothers. Changes of the serum anti-A(B) IgG titer were followed monthly during the medication. 38 newborns were delivered by 35 mothers with one pair of twin, 2 mothers delivered twice. Cord blood bilirubin, anti-A(B) IgG titer, hemoglobin, blood group of the newborns were examined immediately after delivery. Another group of herbal medicine with the effect of clearing up the heat and removing the dampness such as *Artemisia scoparia*, *Gardenia jasminoides*, *Scutellaria baicalensis*, while several kinds of Western medicine of liver protection as luminal, glucuro lactone, prednisone were administered orally just after the birth for three days for prophylaxis. Meanwhile, the changes of symptoms and signs as well as laboratory findings of the newborns especially serum bilirubin were followed closely. The principles and methods of combined treatment according to the severity of disorders were demonstrated. Intravenous infusion of Chinese herbal medicine for clearing up the heat and removing the dampness, and supplemented with Rhubarb, photo-therapy, albumin infusion, exchange transfusion etc. were given. Comparison of the morbidity and mortality between the two groups of newborns before and after the combined therapy who were delivered by the same group of mothers showed the morbidity rates were 78.6% and 26.3%; mortality rates 56.8% and 0% respectively, which were significant statistically. The severity of the disturbance of the newborn patients after the medication, 9 of them were mild, only one was rather severe with the bilirubin peak value of 22.3 mg/dl and was cured by exchange transfusion. There were no sequelae in the medication group after long-period follow-up. The mechanism of the pathogenesis was discussed from both the TCM and the WM point of view. Immunological test on mature mice were done after taking drugs. The titer of anti-A(B) IgG were decreased dramatically especially in the herbal group. Human serum immunological inhibition test and agglutinin absorption test demonstrated some drugs among the blood circulation promoter and stasis reliever, as well as heat and dampness remover served as immunological inhibitor, thus, offering the theoretical basis of the treatment for this disease.

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