生大黄的实验研究以及在重症肝炎、肝昏迷中的应用

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内容提要　本文报道了用家兔 32 只分组进行中毒性肝炎的实验。结果表明，生大黄组家兔死亡数及肝脏显著坏死的动物只数较少。用生大黄清洁肠道（生大黄 12g 加温水 1000 ml）配合其他方法治疗 11 例重症肝炎（1983～1984 年），死亡 4 例，病死率为 36.3%；而 1982 年以前的 22 例重症肝炎，除不用生大黄外，其病情与治疗方法与本组基本相似，但死亡 17 例，病死率 77.3%。另外，7 例肝硬化，共发生 12 次肝昏迷，用生大黄清结肠道或灌胃加西药治疗，其中 11 次清醒。

生大黄已广泛用于治疗内、外科等多种疾病。近三年来我们对生大黄进行了中毒性肝炎的实验研究，并用以治疗重症肝炎、肝昏迷，现报道于下。

动 物 实 验

一、方法：本实验用家兔 32 只，体重1.65～2.55 kg。实验分六组同时进行，除正常对照组外，其余各组分别用下列药物每天灌胃 1 次。人参组用30%红参煎液 1 ml/kg，生大黄组用 20% 生大黄煎液 1 ml/kg，生大黄加人参组用红参及生大黄煎液（浓度同上，剂量为二者相加），活血凉血组用 120% 活血凉血汤（赤芍60g　葛根30g　丹皮15g　生地15g）1 ml/kg，中毒对照组用生理盐水 1 ml/kg。

上述 6 组动物于实验第 1、8、16天测体重及采血，于第 2 天开始分别灌药。除正常对照组外，第 6 天并用30%CCl_4麻油溶液 1 ml/kg注射于家兔大腿内侧皮下，第 8 天、16天切取肝标本。

二、结果：中毒前 6 组平均体重均有增加，其中以大黄组较为明显。中毒后 2 天，GPT、GOT 均有大幅度升高，中毒后 10 天，GPT 均未恢复正常，除正常对照组外，各组之间无差异（$P>0.05$），而 GOT 均已恢复正常。肝脏病理检查以具有显著坏死特征（包括大块、亚大块、桥状坏死）作为统计标准，中毒后 2 天与10天以大黄组家兔的肝脏显著坏死数较少，且中毒后的家兔死亡数也以大黄组最少（见附表）。

附表　各组中毒前后的比较

组别	家兔数（只）	死亡数（只）	体重 (kg)**		肝脏显著坏死的家兔数（只）	
			中毒前	中毒后	中毒后 2 天	中毒后 10天
人参组	6	1	+0.12	−0.03	6	3
生大黄组	5*	0	+0.17	+0.03	3	0
人参+生大黄组	6	2***	+0.12	+0.06	5	1
凉血活血组	6	2	+0.09	−0.09	5	3
中毒对照组	6	2	+0.07	+0.01	6	0
正常对照组	3	0	+0.07	+0.02	0	0

*　原为 6 只，但在中毒前已死亡 1 只

**　"+"表示体重增加，"−"表示体重减轻

***　其中 1 只在抽心血后因心包积血而死亡，1 只因流产后死亡。

临 床 治 疗

一、重症肝炎：我科在1983～1984年间共收治重症肝炎11例，其中男 8 例，女 3 例，平均年龄 37.6±12.8 岁。11例中，属急性重肝 2 例，亚急性重肝 7 例，慢性重肝 2 例。本组除用能量合剂、血浆、抗生素、驱氨、凉血活血汤等治疗外，在病情高峰期每天用生大黄清洁灌肠（生大黄 12 g 煎水加温水至

1000ml) 1次，灌肠一般为二周左右。经治疗后11例中4例死亡(急性与慢性重肝各2例)，病死率36.3%。而我院于1982年以前的22例重肝，病情与本组基本相似，除不用生大黄外，治疗方法也大致相仿，其病死率为77.3%(17/22)。

二、肝硬化、肝昏迷：对1983～1985年间7例晚期肝炎后肝硬化患者除采用一般治疗肝昏迷的措施外，对肝昏迷者并用生大黄灌肠治疗（剂量与方法同上)，对合并有食道静脉出血者在插入三腔管后用生大黄12g煎液从胃管中注入。7例肝硬化患者共出现12次昏迷，经综合治疗后11次神志清醒，另1例次因属临终前昏迷所以未能逆转。昏迷者多数在治疗后24小时内神志转清，个别在48小时内清醒。对4例次因食道静脉大量出血者，在三腔管的胃管中注入大黄粉后，有2例次未出现昏迷，另有2例次昏迷后随着肠道中积血排出后神志迅速转清。

讨　论

生大黄具有多方面的药理作用，如泻下、利胆、保肝、解热、止血、抗感染、导泻、清除内毒素等，本文的实验也证明生大黄具有减少中毒性肝炎家兔的死亡数及减少肝脏显著坏死数的作用。近三年来，我们已常规用生大黄治疗重症肝炎、肝硬化肝昏迷、急性菌痢、流行性出血热等常见传染病。在急、慢性肝衰竭时，肠道内的许多有毒产物将加重肝脏的负担，由于肝衰竭患者的免疫功能低下，肠道的条件致病菌繁殖，因而肝衰竭患者常出现肠胀气及肠道感染，细菌产生的毒素可进一步加剧肝损害，从而促使或加重肝昏迷。为此，我们用生大黄以及时清除肠道中的粪便、致病菌及毒素（包括粪便中的与细菌产生的)。经初步使用表明，应用生大黄清洁肠道最主要的优点为：（1）清除腹气胀。以往重肝患者常出现难治性腹气胀，经用大黄后则几无腹气胀出现；（2）有防治肠道感染、消化道出血及迅速排除消化道积血等作用，因而是防治肝昏迷的一种较好的辅助性措施，没有新霉素所致的明显消化道反应。

小剂量维生素K_3穴位注射治疗腹痛76例的观察

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我科于1984～1985年夏秋季，在肠道门诊，以穴位注射小剂量维生素K_3治疗76例感染性腹泻所致的腹痛，取得了显著疗效。

病例选择及治疗方法　本组76例均为成年患者，临床诊断均符合急性感染性腹泻，其中急性菌痢3例，急性胃肠炎58例，细菌性食物中毒15例，全部患者均伴有腹部剧痛或难以忍受的阵发性绞痛；无加杂症和严重的心、肺功能不全。治疗：取单侧(左、右均可)足三里穴，皮肤常规消毒，采用$4^1/_2$或6号注射针头，直刺1～1.5cm，患者感酸胀后即缓注维生素K_3 1mg(0.25ml)(上海第一制药厂出品，批号821201)。

疗效观察　穴位用药自起针时起，至患者腹痛消失或明显减轻时，计算用药后止痛起效时间。76例结果为：1分钟内起效者6例(7.9%)，1～5分钟起效者54例(71.0%)，6～10分钟内起效者8例(10.6%)，11分钟以上起效者8例(10.6%)，除1例25分钟外，止痛起效时间均在20分钟之内，其中68例(89.5%)在10分钟之内，最快短于1分钟。以上76例均经一针治疗奏效，总有效率100%。

体　会　往年我们对感染性腹泻引起的腹痛，采用阿托品0.5～1.0 mg或维生素K_3 4～8 mg肌肉注射止痛，两者止痛效果基本一致。止痛起效时间多在15～30分钟。近2年用维生素K_3穴位止痛，从而避免了阿托品引起的口干、视力模糊、心悸以及易诱发青光眼急性发作和尿潴留等副作用。采用本疗法具有用药少、止痛奏效快、作用持久、操作方便、安全而又无副反应等优点，值得试用。

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Treatment of Experimental Liver Injury with Chinese Herbal Medicine Queen Tablet

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The effect of herbal mixture Queen Tablet (QT) on the liver injury by carbon tetrachloride in the rat was evaluated. Liver injury was induced in female Sprague Dawley rats (initial weight 120～140 g) by a combination of oral phenobarbital (0.5 g/L in the only drinking water provided) and CCl_4 inhalation. Animals received CCl_4 2～3 times a week for 8 weeks and a closed chamber for periods ranging between 2 and 10 minutes. The animals were divided into 4 groups, Group A: QT only, Group B: CCl_4 plus phenobarbital, Group C: CCl_4 plus phenobarbital plus QT, Group D: normal control. For a measure of demethylation by the P_{450} enzyme system, the Kel was measured initially and just before sacrificed. Protein bound hydroxyproline was measured in the livers at sacrifice by the method of Rojkind and Gonzale.

The deaths of Group A, B, C and D: 0/32, 9/32, 1/32 and 0/11. The liver weight /body weight: 2.89%, 4.29%, 3.73% and 2.74%. The hepatic protein bound hydroxyproline: 3.47 ± 0.7, 9.58 ± 1.5, 13.0 ± 1.9 and 5.71 ± 0.7 (μmol). The aminopyrine Kel ($\times 10^{-2}$) initially: 10.93 ± 0.28, 10.54 ± 0.54, 10.53 ± 0.39 and 11.64 ± 0.27; finally: 8.25 ± 0.25, 11.49 ± 0.48, 11.11 ± 0.40 and 8.23 ± 0.44. Histology % cirrhotic: 0, 9/28, 1/32 and 0.

These data suggest that QT is effective in reducing the liver injury by carbon tetrachloride and phenobarbital. There was a significant reduction in mortality and in the ratio of liver weight to body weight. Histologic cirrhosis was diminished in the Group receiving QT compared to those receiving only carbon tetrachloride and phenobarbital. The effect seems to be independent of the P_{450} enzyme system as QT did not appear to effect demethylation by this enzyme system in the presence of carbon tetrachloride and phenobarbital.

(Original article on page 36)

Experimental Studies on Mechanism of Anti-Platelet Aggregation Action of Motherwort

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Seventeen IcR mice of either sex weighing 22～28 g were used for investigating the effect of motherwort (MW) on cAMP and cGMP concentration of platelets. The animals received 0.05 ml/100 g body weight of MW preparation via tail vein (contains crude drug 2g/ml). Control animals received same dose of normal saline. Studies on cAMP and cGMP concentrations of platelets were done to PRP, obtained from blood drawn via internal carotid artery thirty minutes after drug administration. An experiment was also designed for detecting the effect of MW on PGI_2 level of vessel wall. 0.5 ml/100 g body weight of MW or normal saline were introduced into jugular vein of male Sprague-Dawley rats weighing 250～300 g under 3% sodium pentothal anesthesia. Five minutes later, a fragment of carotid artery 1 mm in length was resected and preserved in ice water after washing. Still 5 minutes later, platelet aggregation test induced by ADP was done to the PRP isolated from aortic blood to which MW or normal saline was then added.

Experimental data reveal that MW can cause a significant increase of platelet cAMP concentration ($P < 0.01$ as compared with controls) and also inhibit platelet aggregation but has no influence on the PGI_2 level of the vessel wall. The results suggest that MW may possess a β-adrenergic pharmacologic action that raises the cAMP concentration of platelets through the inhibitory action of phosphodiesterase. (Original article on page 39)

Experimental Study of *Rheum Officinale* Baill in Treating Severe Hepatitis and Hepatic Coma

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Experimental study of *Rheum officinal* Baill in treating 32 rabbits with toxic hepatitis showed that mortality of rabbits became lower and pathologic changes in the liver became less severe. In the period of 1983～1984, 11 patients with severe hepatitis were treated with *Rheum officinale* Baill enema combined with other methods. 4 of the patients died (36.3%). However, 17 of 22 severe cases treated with the same methods without using *Rheum officinale* Baill before 1982 were dead (77.3%). Moreover, 11 of 12 attacks of hepatic coma in 7 cases with advanced hepatic cirrhosis had been brought back to consciousness by using *Rheum officinale* Baill and other methods.

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