



慢性排斥的用藥細節與病人衛教補充說明

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補充 1 – 皮膚具體用藥說明

一般而言，局部使用類固醇的時間不應超過 14-21 天，以避免發生耐受性現象。

在 14-21 天的使用後，應將用量減至每週末兩次。如有需要，可每 4-6 週重複使用（每天兩次，持續 2 週）。

類固醇製劑注意事項

Ointment 軟膏	<ul style="list-style-type: none">由於遮蔽性質，通常效力較強最具潤滑效果，但油膩在易受摩擦部位使用受限一般患者最不願接受的劑型
Cream 乳霜	<ul style="list-style-type: none">可能含有致敏的防腐劑在易受摩擦部位使用可能有乾燥效果吸收迅速，患者容易接受
Lotion 洗劑	<ul style="list-style-type: none">可能含有刺激性的酒精可用於頭皮或其他覆蓋毛髮的部位通常具有乾燥效果
Gel, solutions, spray, foam 凝膠，溶液， 噴霧，泡沫	<ul style="list-style-type: none">乾燥並迅速吸收適用於頭皮和其他覆蓋毛髮的部位通常含有刺激性的酒精或丙二醇最具乾燥效果的劑型

類固醇效價考慮事項 (Steroid Potency Considerations)

類固醇制劑的效力通常是通過血管收縮素試驗來確定的¹。

Super high and high potency 超 強效	<ul style="list-style-type: none">最大劑量為每週 50 克
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高和高效價	<ul style="list-style-type: none"> • 兒童和老年患者應謹慎使用 • 對於角化過度和苔蘚樣皮膚變化以及掌心和腳底等皮膚增厚區域更有效 • 避免在臉部或皮膚摩擦處使用
Medium and low potency 中低效價	<ul style="list-style-type: none"> • 長期使用低效價製劑通常是安全的 • 每天使用中效價製劑約 3 個月通常是安全的。 • 可用於大面積身體表面 • 適用於面部和皮膚摩擦處 • 適用於兒童和老年人

Drug Name	Strength	Formulation	Special considerations
Super High Potency 超高效價			
Clobetasol propionate	0.05%	Cream, foam, gel, lotion, ointment, shampoo, spray	Avoid axilla, groin & face Use for no more than 14 days
Flucinonide	0.1%	Cream	
Halobetasol propionate	0.05%	Cream, ointment	
High Potency 高效價			
Flucinonide	0.05%	Cream, gel, ointment, solution	Avoid axilla, groin & face Use for no more than 14 days
Triamcinolone acetonide	0.5%	Ointment	
Medium-High Potency 中高效價			
Betamethasone valerate	0.12%	Foam	
Fluocinolone acetonide	0.025%	Ointment	
Fluocinolone acetonide	0.2%	Cream	
Medium-Low Potency 中低效價			
Desonide	0.05%	Lotion, ointment	
Fluocinolone acetonide	0.025%	Cream	

Hydrocortisone butyrate	0.1%	Cream	
Hydrocortisone valerate	0.2%	Cream	
Triamcinolone acetonide	0.1%	Lotion	
Low Potency 低效價			
Desonide	0.05%	Cream	
Fluocinolone acetonide	0.01%	Cream, oil, shampoo, solution	Helpful for scalp lesions
Hydrocortisone (OTC)	1%	Cream, lotion	
Triamcinolone acetonide	0.1%	Cream	

另外類固醇外用治療考量:

Topical Calcineurin inhibitors:

- Tacrolimus (0.03%, 0.1% cream/ointment): Apply to affected area bid .
0.03% 劑量只用於兒童。
- Pimecrolimus (1% cream) : 用於患部一天二次。.

Antipruritic agents (止癢劑)

- Hydrocortisone acetate (1.0% or 2.5%)/Pramoxine HCL (1.0% lotion/cream/ointment): 用於患部一天兩次。
- Pramoxine HCL (1.0% cream/liquid/lotion/ointment): 一天兩次用於患部。
- Camphor/Menthol (0.5%/0.5% lotion): 需要時用.

補充 2 – 口腔和口腔組織慢性移植物抗宿主病的特定用藥說明

一般敏感或黏膜糜爛/潰瘍：類固醇溶液 – 對於大多數類固醇或 calcineurin 抑制劑溶液（見表），使用說明是含 5 毫升漱口 4–6 分鐘後吐出，每天最多 6 次。對於 budesonide，公布的漱口時間可長達 10–15 分鐘。漱口後 30 分鐘內應避免進食或飲用。應告知患者口腔念珠菌感染風險增加，並考慮聯合使用 nystatin 進行預防黴菌感染。

表：口腔慢性移植物抗宿主病常見局部製劑藥物

Preparation	Family	Drug	Concentration	Daily dose	Available commercially in the US
Solutions	Steroids	Dexamethasone	0.1 mg/mL (0.01%)	10 mL x3-6/d	Yes
		Dexamethasone	0.4 mg/mL (0.04%) ¹	10 mL x3-6/d	No
		Prednisolone	3 mg/mL (0.3%)	5 mL x3-6/d	Yes
		Budesonide	0.3 mg/mL (0.03%)	10 mL x2-4/d	No
		Clobetasol	0.5 mg/mL (0.05%)	5 mL x3/d	No
		Triamcinolone	1 mg/mL (0.1%)	x10/d	Yes
		Triamcinolone	10 mg/mL (1%)	5 mL x3-6/d	No
		Betamethasone ¹	0.02 mg/mL (0.002%)	10 mL x3-4/d	No
	calcineurin inhibitor	Tacrolimus (oral solution)	0.1mg/mL (0.01%)	5 mL x3/d	No
Creams/gels/ointments	Steroids	Clobetasol cream/gel	0.05%	x2/d	Yes
		Triamcinolone cream ¹	0.1%	x2/d	Yes
		Triamcinolone cream ¹	0.5%	x2/d	Yes
		Halobetasol cream ¹	0.05%	x2/d	Yes
		Betamethasone	0.05%	x2/d	Yes

	cream/ointment/gel ¹			
	Betamethasone cream/ointment ¹	0.1%	x2/d	Yes
	Betamethasone ointment ¹	0.05%	x2/d	Yes
	Fluocinonide gel	0.05%	x2/d	Yes
Other immuno-modulators	Tacrolimus ointment	0.1%	x3/d	Yes

¹Preparations that are in use for oral vesiculobullosus diseases and were suggested in the literature specifically for oral cGVHD.

疼痛處理

人工唾液和口腔潤滑油可改善口腔的舒適度。應告知患者使用非刺激性的牙膏（例如兒童牙膏）和無酒精的漱口水，以盡量減少對口腔黏膜刺激。粘性 Lidocaine (2% 溶液)，或者與 Kaolin/Pectin or aluminium hydroxide -magnesium hydroxide (Maalox)-and diphenhydramine (1:1:1)可以提供一些緩解疼痛。病人可口含 5Ml，5 分鐘後吐掉，一天不超過 5 次，過多次，可能造成 lidocaine 身性吸收。

齲齒預防：

高糖飲食應該避免。每日使用中性的 1.1% 氟化鈉- 凝膠或牙膏，可用於預防蛀牙的。中性 pH 氟化物或非薄荷味的氟產品，在口腔較敏感時，可得到較好的耐受性。已有齲齒的病人，可以考慮添加 chlorhexidine 漱口液（不含酒精），每天漱口兩次），不適用太長時間，因為它可能會導致味覺喪失和口腔染色。患者可嚼無糖口香糖，無論含木糖醇或磷酸鈣，以刺激唾液增加，防止齲齒。

過度口乾：

人工唾液和潤滑劑，如上文所建議。此外可處方：Cevimeline: 30 mg orally 3 times daily; or Pilocarpine (5 mg tablets): 5-10 mg orally 3 times daily。保濕唇膏有防曬係數 SPF > 30 為首選，可降低唇癌風險到最低。

胃酸逆流：

如果胃食道逆流是出於唾液減少。病人可受益於質子泵抑制劑(PPI)，減少胃酸對口腔黏膜的影響。

補充 3 - 眼睛的具體用藥說明：減少眼睛表面發炎局部藥物

Cyclosporine (ophthalmic emulsion 0.05%):	Apply one drop in both eyes twice a day.
Prednisolone (1.0% ophthalmic solution, e.g. Pred Forte®)	one drop in both eyes 2-4 times daily.
Fluorometholone (0.1/0.25% ophthalmic suspension)	one drop in both eyes 2-4 times daily.
Loteprednol etabonate (0.5% ophthalmic suspension)	1-2 drops in both eyes 4 times daily.

局部藥物增加眼睛濕潤：

人工淚液一天如超過 4 次，就必須使用不含防腐劑人工淚液。不含防腐劑可每 30 分鐘點一次。.

- 常見廠牌 Refresh®, Refresh Endure®, Refresh Plus®, Systane®, Bion Tears®, TheraTears®, GenTeal PF®.
- Hydroxypropyl cellulose (i.e. Lacrisert® 5 mg ophthalmic insert). Place into the cul-de-sac of the eye daily as an alternative
- Thicker formulations maybe helpful for patients requiring frequent use of artificial tears, and are most appropriately recommended at bedtime, such as Celluvisc®, and Genteal Gel ®, Lacrilube®, Hypotears® ointment

增加淚液口服藥：

- Cevimeline (30mg oral capsules): 30 mg orally three times daily
- Pilocarpine (5 mg tablets): 5-10 mg orally 3 times daily

補充 4 - 外陰和陰道的常規婦科保健和特定用藥說明

一般衛生：不考慮其他原因，建議對外陰或陰道症狀的預防或減輕不適症狀。

- 應避免機械和化學刺激物。
- 生殖器部位最好用溫水清洗，不用肥皂或女性洗產品清洗。然後自然晾乾，告知病人清潔由前方往後方向擦拭。擦少量潤膚劑或綿羊油在外生殖器，不要擦入陰道。它可提供發癢、紅腫減輕，與不正常分泌。
- 抑菌凝膠可以在用於陰道的使用。.

常規監測：最近的前瞻性研究支持在幹細胞移植之前，與移植 100 天後需常規監測。教育病人，了解移植後，可能造成性與婦科功能障礙，能夠及早發現和治療慢性排斥。自我檢查，與 3 個月內使用陰道擴張器，以確保陰道是暢通的。常規監測和早期處理，可避免外陰陰道因排斥導致後期生殖器官硬化。.

Vulvar and vaginal atrophy: (外陰和陰道萎縮)

移植後通常會出現外陰及陰道萎縮，可以是出於化療造成卵巢功能衰竭或自然絕經。由於雌激素是支持外陰和陰道上皮細胞的屏障和修復功能，雌激素替代治療可用於陰道粘膜炎、陰道萎縮的症狀（如乾燥，性交疼痛）或外陰部、或陰道 GVHD。以外用雌激素、全身口服藥或經皮途徑可用於外陰部或陰道內，應與婦科醫生或對卵巢激素治療有經驗醫師。局部和陰道內使用雌激素，可避免全身性暴露是於雌激素風險。全身性雌激素治療會有特定的風險。如果全身性雌激素是用於有子宮婦，則需要外加 progesterone 來預防子宮內膜腫瘤。雖然有傳聞證據表明，雌激素替代（全身或局部治療）對外陰部或陰道 GVHD，是一種有效的輔助治療，需要有前瞻性對照研究。

外陰部慢性排斥局部治療 (Topical Therapy for Vulvar GVHD):

- Mild GVHD: Triamcinolone acetonide (0.1-0.5% ointment). Bid as needed to control symptoms. 婦科評估每隔 6-8 星期
- Moderate GVHD: Betamethasone dipropionate (0.05% gel or ointment). Apply topically to the vulva bid to qd for up to 12 weeks. 婦科評估每隔 4-6 星期
- Severe GVHD: Clobetasol (0.05% ointment). Bid up to 8 weeks. 婦科評估每隔 4-6 星期或症狀惡化。
- Vulvar GVHD 如對局部 corticosteroids 無效: Tacrolimus (0.1% ointment). Topical application qd or bid to severe vulvar lesions under the direction of a gynecologist with experience in managing chronic GVHD or lichen planus.

Intravaginal therapy for vaginal GVHD 陰道慢性排斥內陰道局部治療

Betamethasone dipropionate (0.05% gel or ointment)	Apply 1gm intravaginal (using vaginal estrogen cream calibrated applicator) every 12-24 hours for up to 12 weeks	婦科評估每隔 4-6 星期, 或新的或症狀惡化, 考慮提早婦科評估。
Hydrocortisone (10%) in 2% clindamycin base	Apply 5 g with vaginal applicator every other night for 4 weeks	科評估每隔 4-6 星期, 亦可重覆一次治療.
Tacrolimus vaginal suppositories 0.1% (2 mg tacrolimus per 2 gram suppository)	May be used nightly for 2 months,	婦科評估每隔 4-6 星期

補充 5 – 胃腸道和肝臟的用藥說明

- **Chronic Diarrhea:** 排除感染原因。
- Probiotics 益生菌的安全性與有效性未知。
- Loperamide : Adults: 2-4 mg po prn loose stools, max daily dose of 16 mg.
Children: 0.08 to 0.24 milligram/kilogram/day in 2 to 3 divided doses can be used. 對慢性腹瀉常規使用比需要時使用要來得有效。

Irritable Bowel Type Symptoms (腸躁症狀)

- Nortriptyline : 25-125 mg po daily may be helpful for patient with symptoms similar to irritable bowel syndrome.⁵ 抗膽鹼作用可能導致假性腸道阻塞。
- Dicyclomine (10 mg capsule; 20 mg tablet; oral solution 10 mg/5ml): Adults: 20 mg orally four times a day. 兒童的安全性和有效性尚未確定。抗膽鹼作用可能導致假性腸道阻塞。

Malabsorption (吸收不良):

- Pancreatic enzyme replacement:
- 每餐前服用，½ 與零食一起服用。這可對脂肪吸收不良導致腹瀉和體重減輕的病人有幫助。Various brand names include: Creon®, Zenpep®, Pancreaze®, Ultresa®, Viokace®, Pertzye®. 通常與質子泵抑制劑一起處方，以避免胃中脂肪酶失活。

Abnormal liver tests(肝功能不正常)

- Ursodeoxycholic acid : Adults: 250-300 mg orally 3-4 times daily, Children: 10-15 mg/kg daily divided three times a day or alternatively < 15 kg – 150 mg po daily, 15-29 kg - 300 mg po daily, > 30 kg – 300 mg po BID.

補充 6- 肺排斥的具體用藥說明

Albuterol (multiple formulations of inhalation aerosols and solutions): Adults: 1-2 puffs every 4-6 hr as needed or nebulized 2.5 mg 3-4 times daily, Children: 4 years and older, 1-2 puffs every 4-6 hr. Age 2 to 12 years, nebulized 1.25 or 0.63 mg 3-4 times daily.

- Beclomethasone : Adults (12 years and older): Oral inhalation, 2 puffs (42 mcg each) 3-4 times daily or double strength 2 puffs (84 mcg each) twice daily; maximum 840 mcg/day. Pediatric: Safety and efficacy not established in children under age 5 or 168 mcg twice daily; maximum 420 mcg/day.
- Fluticasone : Adults (12 years and older): Oral inhalation, 2 puffs (110-220 mcg each) twice daily.
- BOS : combination therapy with Fluticasone, montelukast and azithromycin in stabilizing the manifestations of BOS⁶.
- Montelukast: : Adults (> 15 y/o): 10 mg po daily. Children ages 12 mo to 5 years 4 mg daily (granules or chewable tablets available); children 6-14 years 5 mg po daily (chewable tablets).
- Azithromycin: (Adults and children > 6 years) : 250 mg po three times per week

補充 7 - 神經系統的具體用藥說明

神經病變 (Neuropathy):

- Amitriptyline : Adults: start at 25 mg orally at bedtime (increase dose by 25mg weekly, max : 150 mg daily.)
- Paroxetine : 10 mg orally qd and increase by 10 mg weekly to maximum dose : 50 mg daily.(兒童的安全性與有效性尚未建立)
- Pregabalin : 50 mg orally tid (150 mg/day) and may be increased to MAX dose 100 mg orally three times a day (300 mg/day) within 1 week based on efficacy and tolerability. pediatric patients : 5-15 mg/kg/day ⁷.

肌肉痙攣(Muscle Cramps):

- Baclofen (Oral Tablet: 10 mg) : Adults 5-10 mg orally tid as needed for cramps. Children 12 years and older 10-15 mg per day in 2-3 divided doses as needed.
- Clonazepam : 0.25 – 1 mg orally at bedtime.
- Diazepam : Adults 2-10 mg orally at bedtime; Children 1-2.5 mg orally at bedtime.
- Vitamin B complex (including fursulthiamine 50 mg, hydroxocobalamin 250 µg, pyridoxal phosphate 30 mg, and riboflavin 5 mg) can be taken three times per day.

補充 8 - 感染染病的具體用藥說明

PCP 預防：	<p>Sulfamethoxazole(400mg)/Trimethoprim(80mg), 480 mg/tab (單劑量)、960 mg/tab (雙劑量)</p>	<ul style="list-style-type: none"> ● 成人：一星期給 6 天 (480mg)/week，可以以多種方式給藥，例如：每天兩次，每次服用 960mg，一星期給 2 天。960mg 一周給三天或 480mg 每天。 ● 兒童（口服混懸劑 200 mg/40 mg/5 ml）：$< 20 \text{ kg}$，5 mg TMP/kg 2 divided doses 每周兩天。 ● 20-40 公斤的兒童，480mg /tab bid 每周兩天。 ● 對於 > 40 公斤的兒童，請遵循成人劑量。
	<p>Dapsone (口服片劑 25、100 毫克)</p> <ul style="list-style-type: none"> - 不建議 G6PD 缺乏症 - 對磺胺過敏的患者禁用 - 監測高鐵血紅蛋白血症 (methemoglobinemia) 的發生 (定期脈搏血氧儀) 	<ul style="list-style-type: none"> ● 成人：每天兩次口服 50 毫克或每天一次 100 毫克。 ● 兒童：1 mg/kg/天，分 2 次口服 (最高 100 mg/天)。
	<p>Pentamidine (300 毫克溶液用吸入粉末)</p>	<p>成人和兒童 > 5 歲：300 毫克。每 4 週吸入一次。也可以每 14-21 天靜脈注射 4 mg/kg。</p>
Encapsulated Organism prophylaxis	<p>Penicillin VK (口服片劑：250 mg、500 mg；口服混懸劑：125 mg/5 ml、250 mg/5 ml)</p>	<ul style="list-style-type: none"> ● 成人：每天兩次口服 750 mg (體重 > 60 公斤)，每天兩次口服 500 mg (體重 < 60 公斤)。 ● 兒童：每天兩次口服 250 mg (體重 20-40 公斤)，每天兩次口服 125 mg。

		mg (體重 < 20 公斤)
VZV 預防	Acyclovir : (口服膠囊：200 mg；口服片劑 400 mg；口服混懸劑 200 mg/5 ml) :	成人：每天兩次口服 400 毫克，< 6 歲的兒童每天兩次口服 200 毫克。
	Valacyclovir (500 毫克和 1 克錠劑)	成人：每天口服 500 毫克一次至兩次。兒童和體重 < 40 公斤的成人：每天兩次口服 250 毫克
真菌預防 (Fungal Prophylaxis)： 對於那些被認為有黴菌感染高風險的人 (使用 > 0.5mg/kg prednisone)。	Voriconazole (口服：50 mg、200 mg；口服懸浮劑：40 mg/ml)	成人：口服 200 mg 每天兩次。 兒童：4 mg/kg/天，每日兩次，分次服用。(進行血中濃度監測，建議在給藥後 5 天進行低谷濃度監測，建議濃度落於 2-6 mcg/ml 之間。
	Posaconazole (口服錠劑：100 毫克；口服懸浮劑 40 mg/ml)。值得注意的是，由於懸浮液吸收不一致，一般不推薦。	對於 13 歲及以上的人，確定了每天 300 mg。 10-20 kg：每日 100 mg 20-40 公斤：每日 200 mg >40 公斤：每日 300 mg 進行血中濃度監測建議預防低谷濃度 >0.75 mcg/ml 和 < 3 mcg/ml 之間。

補充 9 – 肌肉骨骼系統的具體用藥說明

- Calcium replacement : 1000-1500 mg of elemental calcium oral daily.
- Vitamin D replacement (25000 IU oral capsule, 50,000 IU oral capsule, liquid filled, 8000 IU/ml oral liquid, 400 IU, 50000 IU oral tablet): 400-800 IU orally daily.
- Bisphosphonates: (e.g. alendronate 5, 10, 35, 40, 70 mg oral tablets and 70 mg/75ml oral solution)
- Treatment of osteoporosis= 10 mg orally daily (in corticosteroid-induced osteoporosis, post-menopausal women), 5 mg orally daily (in corticosteroid-induced osteoporosis, males) or 70 mg orally weekly.
- Prevention of osteoporosis= 35 mg orally weekly.
- Calcitonin : 100 IU intramuscular/subcutaneous daily or 200 IU intranasally daily.

補充 10 - 兒科神經精神病學評估

- 評估智力功能 Wechsler Intelligence Scales: Block Design, Vocabulary subtests (15 minutes). 評估工作記憶/處理速度, Wechsler Intelligence Scales: Digit span, Coding, Symbol Search subtests (15 minutes).
- 評估記憶力, Children's Memory Scale: Stories, Faces, Dots subtests (15 minutes) plus California Verbal Learning Test (15 minutes).
- 另外家長測量報告可當作行為/情緒/社會問題(Behavior Assessment System for Children – 2nd Edition; 20 minutes), 執行功能 (Behavior Rating Inventory of Executive Function; 5 minutes) 的篩選器。

¹Children's Oncology Group, ALTE07C1 Neuropsychological, Social, Emotional, and

Behavioral Outcomes in Children with Cancer

<https://kidscancer.uchicago.edu/sites/pedscancer.uchicago.edu/files/uploads/ALTE07C1DOC.pdf>

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