麻疹、腮腺炎及德國麻疹三種混合疫苗注射劑

M-M-R® II (Measles, Mumps and Rubella Virus Vaccine Live, MSD)

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本藥須由醫師處方使用

麻疹、腮腺炎及德國麻疹三種混合疫苗注射劑(M-M-R® II; Measles, Mumps and Rubella Virus Vaccine Live, MSD)為活性病毒疫苗，用於預防麻疹、腮腺炎及德國麻疹之預防接種。

M-M-R II為減菌之凍晶乾燥劑，含有(1)ATTENUVAX® (活性麻疹病毒疫苗，MSD)，乃毒性減弱之麻疹病毒，衍生自Enders氏之減毒Edmonston菌株並增殖於雞胚胎細胞培養基中；(2)MUMPSVAX® (活性腮腺炎病毒疫苗，MSD)，為Jeryl Lynn™ (B級)腮腺炎病毒菌株，增殖於雞胚胎細胞培養基中；(3)MERUVAX® II (活性德國麻疹病毒疫苗，MSD)，為減毒之活性德國麻疹病毒衍生自Wistar RA 27/3菌株，並增殖於WI-38人類具雙套染色體的肺纖維組織母細胞(human diploid lung fibroblasts)培養基中。

混合稀釋液後的疫苗採皮下注射。若按指示混合稀釋液，注射劑量為0.5毫升。其中所含病毒數目至少為1,000 CCID$_{50}$(50%細胞感染劑量，cell culture infectious dose)之麻疹病毒，12,500 CCID$_{50}$之腮腺炎病毒及1,000 CCID$_{50}$之德國麻疹病毒。每劑量經計算含有14.5毫克的山梨醇(sorbitol)，磷酸鈉(sodium phosphate)，1.9毫克的蔗糖(sucrose)，氯化鈉(sodium chloride)，14.5毫克的水解膠(hydrolyzed gelatin)，少於或等於0.3毫克的重組人類白蛋白(recombinant human albumin)，少於1 ppm的牛血清，其他的緩衝劑和培養基成分及大約25微克的新霉素(neomycin)。此產品不含防腐劑。

適應症

適應症：預防麻疹、腮腺炎及德國麻疹。

說明：

M-M-R II適用於12個月大或12個月大以上的人，用以同時預防麻疹、腮腺炎及德國麻疹(見用量及用法)。

有證據顯示，感染野生種麻疹的母親所生之嬰兒，在小於1歲時接種此疫苗，之後再追加接種時有可能產生不足的抗體。因此對於提早注射所得之保護與可能發生抵抗力不足之優缺點，應加以衡量。

由於仍保有來自母體的殘留麻疹病毒抗體，年紀小於15個月的嬰兒有可能對此疫苗的麻疹病毒沒有反應。年紀愈小，血清轉換(seroconversion)的可能性愈低。但對於在偏遠地區或其它相當難以接觸的族群中，預防接種計畫較困難執行，以及在某些族群中，大部分的嬰兒在15個月大以前可能會感染野生種麻疹，因此對於這類族群預防接種應提早進行。在此情況下嬰兒在12個月大前即接種，15個月大時必須再接種。

用法及用量

供皮下注射。不可血管內注射。

注射M-M-R II時，不可同時給予免疫球蛋白(immune globulin, IG)(見藥物交互作用)。對任何年紀的皮下注射劑量都是0.5毫升，最好注射位置是上臂的外側。

注意：稀釋及注射此疫苗時所使用的無菌注射器須不含防腐劑、消毒劑及清潔劑。因為這些物質會使此活性病毒疫苗失去活性。建議使用的注射器規格是25號規格(gauge)及5/8英吋針頭。

稀釋時，只使用與疫苗同時提供的稀釋液。因其不含防腐劑及其它會使疫苗失去活性的物質。

在溶液及容器合適的情況下，任何注射劑在使用前皆須目測是否含有任何微粒及顏色改變。在稀釋前，凍乾的M-M-R II錠成黃色晶體狀。稀釋後呈澄清黃色。

預防接種的建議時間表

在12個月或更大時接種此疫苗者，須在4至6歲或11至12歲時再次接種。再接種的原因是因為有些人對第一劑無抗體的反應。

(注意：各國政府有可能使用適用於當地的接種時間表取代以上的建議。)

麻疹爆發流行時的預防接種時間表

6至12個月大的嬰兒

在麻疹爆發流行時，當地的衛生機關可能建議預防接種6至12個月大的嬰兒。此年齡層的嬰兒有可能對疫苗無法產生抗體反應。腮腺炎及德國麻疹疫苗對小於12個月大的嬰兒的安全性及有效性尚未被評估。年紀越小，血清轉換的可能性越低。這些嬰兒在15個月大時應接種第二劑，並於4至6歲或11至12歲大時再次接種。

接種疫苗的其他考量

未懷孕的青春期及成年女性

在某些注意事項被遵守後(見注意事項)，達生育年齡而尚未懷孕的青春期及成年女性應接種活性減毒的德國麻疹疫苗。接種後的女性，可保護自己於懷孕時免於感染德國麻疹，並且保護胎兒不被感染而造成先天性德國麻疹引起的缺陷。

達生育年齡之婦女應被告知，避免於接種後3個月內懷孕，避免懷孕的理由也應被告知(見注意事項，懷孕一欄)。

當可責信賴的檢驗服務切符實際使用時，達生育年齡之婦女可做血清檢驗以決定其對德國麻疹的易感度。然而，除了對婚前及生育前婦女的篩檢外，例行性地對所有生育年齡的女性做此檢驗是十分昂貴的。雖然此檢驗可有效地對只有可能感染的女性做預防注射。另外，此法需婦女至門診二次：一次為篩檢，另一次為預防注射。因此，已知未懷孕且未曾接種之婦女應毋需做血清檢驗，而可直接接種德國麻疹疫苗。特別是血清檢驗的價格不菲，且其不能確保可能感染的婦女皆接種此疫苗。

青春期後女性應被告知，接種疫苗後2-4個星期後常有可能產生自限性關節疼痛及關節炎(見副作用)。

分娩後女性

很多例子中發現，分娩後立即對有可能感染的女性做德國麻疹預防注射是相當方便的(見注意事項，授乳母親)。

其他族群

大於12個月且未接種疫苗的小孩，若會接觸可能感染德國麻疹的孕婦時，應接種活性減毒的德國麻疹疫苗(如單一病毒的德國麻疹疫苗或M-M-R II)以降低其對孕婦暴露於此病毒的風險。

計劃到國外旅遊的人，假如沒有免疫力，有可能感染到麻疹、腮腺炎或德國麻疹，並將此疾病帶回自己的國家。因此，在國際旅遊前，易受一種或多種這些疾病感染的人應接種單一或混合病毒的疫苗。然而，M-M-R II較適於有可能感染腮腺炎及德國麻疹的人。如果單一麻疹病毒的疫苗無法立即取得，旅遊者應接種M-M-R II，無須考慮其對腮腺炎或德國麻疹的免疫情形。

對於有可能感染的高危險群例如大學生，醫護人員及軍事人員，預防接種是被建議的。

接觸病毒後的預防接種

在接觸野生種麻疹後，72小時內給予預防接種可以提供某些程度的保護力。但若是在接觸之前幾天即給予預防接種，可產生足夠的保護力。目前尚未有足夠證據顯示接觸於野生種腮腺炎或德國麻疹後，立即做預防接種會產生任何保護力。

與其它疫苗併用

M-M-R II必須在其它活性病毒疫苗使用之前或之後一個月才可接種。

M-M-R II曾與活性減毒水痘病毒疫苗及去活性嗜血桿菌b型結合疫苗(使用不同的注射器與注射部位)併用。對個別疫苗抗原的免疫反應並未減弱。對M-M-R II所產生的不良反應之種類、發生頻率及嚴重性與其他只含單一成份之疫苗相類似。

例行性的併用DTP(白喉、破傷風、百日咳疫苗)和／或OPV(口服小兒麻痺疫苗)與麻疹、腮腺炎及德國麻疹疫苗並不被建議，原因是併用這些抗原的數據並不多。

然而其它的接種時間表曾被使用。已發表的研究資料顯示併用全部建議的疫苗(白喉、破傷風、百日咳疫苗，口服小兒麻痺疫苗，和嗜血桿菌b型疫苗，有或無B型肝炎疫苗，及水痘疫苗)，並無發生這些小兒疫苗間的干擾情形(活性、減毒或非活性)。

單一劑量小瓶

假如預防偶發性的麻疹是唯一目標，則可考慮使用含有麻疹病毒的疫苗(詳看適當的產品仿單)。假如也同時考慮腮腺炎和德國麻疹的免疫狀況，於查閱適當的產品仿單後，應考慮使用合適的腮腺炎疫苗或德國麻疹疫苗再接種。

首先將所有的稀釋液抽至注射器中以備稀釋使用。將注射器中所有稀釋液注入含有凍晶乾燥疫苗之小瓶，輕輕搖動使之完全混合。假如此凍晶疫苗無法全部溶解，此疫苗並應棄置不用。用注射器抽出瓶中所有液體並對病人進行皮下注射。

每個病人皆須使用不同的無菌注射器及針頭，以避免彼此傳染B型肝炎病毒或其他感染物質。

禁忌症

對此疫苗之任何成份包括動物膠有過敏者。

孕婦勿接種M-M-R II；此疫苗對胎兒發展的可能影響在此階段尚未知曉。青春期後女性接種此疫苗之後三個月內必須避免懷孕(見注意事項，懷孕)。

對neomycin會產生過敏或類過敏反應者(稀釋後每劑量疫苗內約含25微克之neomycin)。

任何發燒的呼吸道疾病或其它活動性發燒感染。

活動性未治療的肺結核。

接受免疫抑制療法患者不可接種，但使用皮質類固醇作為置換療法如愛迪生氏病(Addison's disease)之患者，不在此限。

惡血質病、白血病、任何類型的淋巴瘤，其它影響骨髓或淋巴系統的惡性腫瘤患者。

原發性及後天性免疫缺乏情況，包括因AIDS或其他人類免疫缺乏病毒感染之免疫抑制患者細胞性免疫缺乏；及低丙種球蛋白血症(hypogammaglobulinemic)與血中兩種球蛋白功能不良症(dysgammaglobulinemic)。有報告指出，當含麻疹病毒的疫苗不慎被使用於嚴重的免疫力妥協病人時，此疫苗中散佈的麻疹病毒直接造成麻疹包含性腦炎(measles inclusion body encephalitis, MIBE)，肺炎及死亡。有先天性或遺傳性免疫缺乏家族史的個人，在其免疫能力被確定前。

注意事項

一般性

適當的治療裝備必須包括epinephrine注射劑(1:1000)，以便過敏性或類過敏性反應發生時立即使用。

患有個人或家族性癲癇病史者，使用M-M-R II必須小心，曾有腦損傷病史或其它任何因發燒而導致的壓力情況，應避免使用之。醫師應警覺預防接種後可能導致的體溫上升(見副作用)。

對蛋過敏

活性麻疹及腮腺炎疫苗是於雞胚胎細胞培養基中製得。曾因吃蛋產生過敏性、類過敏性反應或其它立即反應(如荨麻疹、口及喉嚨腫大、呼吸困難、低血壓或休克)的人，注射此含微量雞胚胎抗原的疫苗有極大可能產生立即過敏反應的危險性。在此情況下，預防注射的危險及益處應被仔細衡量以決定是否接種。注射此疫苗於此類接種者須極度小心，一旦過敏反應發生，應立即做適當的處理。

血小板減少症(Thrombocytopenia)

有血小板減少症的人在預防接種後可能會症狀加重。另外接種第一劑M-M-R II(或其單、雙價成份的疫苗)會產生血小板減少的人，再次接受此疫苗時症狀可能會再出現。可以分析血清檢驗的結果以決定再接種是否必要。在此情況下，預防注射的危險性及益處應被仔細衡量以決定是否接種(見副作用)。

懷孕

當孕婦接種M-M-R II時，是否對胎兒造成傷害或影響孕婦之生殖能力，目前尚未知曉。因此，懷孕女性不應使用M-M-R II。另外，婦女於接種此疫苗後三個月內應避免懷孕(見禁忌症)。

在輔導那些懷孕時不小心接種此疫苗或接種三個月內懷孕的婦女時，醫師本身應如曉下列事項(1)在一個十年的研究中，調查超過700位於懷孕前後三個月內接種德國麻疹疫苗(其中189位接種 Wistar RA 27/3型菌株)的婦女，沒有一位新生兒有先天性德國麻疹症候群之異常；(2)在懷孕的前三個月感染腮腺炎會增加自然流產的機率。雖然腮腺炎疫苗之病毒被發現會感染胎盤及胎兒，但沒有證據證明其會導致人類先天性畸形；及(3)報告指出懷孕期間感染野生種麻疹會增加胎兒危險。自然流產、死胎、先天性缺陷及早產的機率都會增加。減毒的麻疹疫苗病毒對懷孕之影響，尚未有足夠的研究。然而，最好小心假設這些疫苗病毒菌株也會對胎兒造成不良影響。

授乳母親

是否麻疹或腮腺炎疫苗病毒會從人類乳汁中分泌出來尚未知曉。最近研究顯示，產後婦女接種活性減毒德國麻疹疫苗後，哺乳時會分泌病毒於乳汁中且會傳給體乳的嬰兒。經血清證明感染德國麻疹病毒的嬰兒，沒有一個產生嚴重症狀；但有一個呈現輕微的典型後天性德國麻疹臨床症狀。授乳母親接種M-M-R II時必須小心。

嬰幼兒

麻疹疫苗對小於6個月大的嬰兒之安全性及有效性資料尚未被建立。腮腺炎及德國麻疹疫苗對小於12個月大的嬰兒的安全性及有效性資料也尚未被建立。

其它

已知感染人類免疫缺乏病毒的小孩或年輕成年人，若無免疫抑制症狀者可以接受接種；然而，應嚴密監測這些接種者是否感染疫苗可預防的疾病，因為其免疫力產生的效率較沒感染人類免疫缺乏病毒者低(見禁忌症)。

大部份的易感染個體接種後7-28天，會出鼻子或喉嚨分泌出少量活性減毒德國麻疹病毒，沒有證實證據可顯示這些病毒會傳染給與接種者有接觸的易感染者身上。因此，親密的個人接觸所造成的傳染，雖然理論上可能，但是並不認為是一重要危險。然而，經哺乳將德國麻疹疫苗病毒傳給嬰兒之報告確有證據存在(見授乳母親)。

沒有自接種疫苗者傳染活性減毒麻疹或腮腺炎病毒給易感染者之報告。

具報告指出活性減毒麻疹、腮腺炎及德國麻疹病毒疫苗若分開接種時，會暫時降低皮膚對結核菌素的敏感度。因此，結核菌素試驗須於M-M-R II接種前或同時行之。正接受結核病治療的小孩接種活性麻疹病毒疫苗後，病情不會因之惡化。迄今，尚無報告研究麻疹病毒疫苗對有結核病但尚未治療之兒童的影響。

如同其他疫苗，接受M-M -R II接種並不能使全部的接種者都產生保護力。

藥物交互作用

在接種M-M-R II之時，同時給予免疫蛋白可能不會產生預期的免疫效果。給予免疫球蛋白(人類)和輸血後三個月或更久始可接種疫苗。

副作用

與M-M-R II相關的副作用是來於使用單價或組合的疫苗。

一般發生

注射部位有短時間的灼熱感和／或刺痛感。

偶而發生

全身

發燒(101°F [38.3°C]或更高)

皮膚

發疹或似麻疹樣的疹，通常是小範圍，但也可能是全身性。

大體上，發燒、發疹，或二者出現在接種後第5天及第12天之間。

很少發生

全身

輕微局部反應如紅斑、硬塊及觸痛；喉嚨痛，身體不適，異常麻疹，暈厥，暈躁。

心血管

血管炎

消化方面

腮腺炎，噁心，嘔吐，腹瀉。

血液／淋巴系統方面

局部淋巴腺病變(lymphadenopathy)，血小板減少，紫斑(purpura)。

過敏性

過敏反應如注射部位出現風疹塊及紅腫，過敏性及類過敏性反應，相關的現象如血管神經疾病所引起的水腫(包括末梢或臉部水腫)和支氣管的痙攣，蕁麻疹發生於不論是否有過敏病史的病人。

肌肉骨骼方面

關節痛及／或關節炎(通常為暫時性且很少為慢性[詳參下述])，肌肉痛。

神經／精神方面

小孩發燒性痙攣，非發燒性痙攣或癲癇發作，頭痛，頭昏，感覺異常，多發性神經炎polyneuritis多神經病polyneuropathy，Guillain-Barre症候群，運動失調，無菌性腦膜炎[詳參下述]，麻疹包含性腦炎(meales inclusion body encephalitis-MIBE，見禁忌症)，約每三百萬劑中會出現一次腮炎併發病變之病例報告，但無證據顯示該病變確實由疫苗引起。接種活性麻疹病毒疫苗所產生此類嚴重的神經失調之危險性仍遠低於野生種麻疹所引起的(佔病例報告的二千分之一)。

呼吸系統

感染性肺炎，肺炎(見禁忌症)，咳嗽，鼻炎。

皮膚

多形紅斑(erythema multiforme)，Stevens-Johnson症候群。注射部位發痘，腫脹，搔癢。

特殊感覺

多種視神經炎，包括眼球後神經炎(retrobulbar neuritis)，視神經乳頭炎(papillitis)及網膜炎；眼麻痺，中耳炎，神經性耳聾，結膜炎。

泌尿生殖器

副睪丸炎(Epididymitis)，睪丸炎(orchitis)

其他

在接種麻疹、腮腺炎及德國麻疹疫苗後，極罕見因為各種原因或不明原因而導致的死亡。然而，在健康成人身上(參見禁忌症)此種死亡的因果關係尚未充分明瞭。

在已發表的研究報告指出，於1982-1993年M-M-R II上市後在芬蘭所接種的150萬小孩及大人中，不曾出現任何因疫苗所引起的死亡或永久性的癲發症。

關節痛和／或關節炎(通常為暫時性且很少慢性)及多發性神經炎為野生種德國麻疹之特徵，其發生率及嚴重程度關年齡及性別而異，成年女性最高，青春期前孩童最低。

慢性關節炎與自然性德國麻疹感染有關，也與持續從身體組織分離出之病毒及／或病毒抗原有關。只有極少數疫苗接種者發展成慢性關節病狀。

小孩接種後很少發生關節反應，且一般為短期性。成年婦女接種疫苗後關節炎及關節痛的發生率一般比小孩為高(小孩：0-3%；婦女：12-20%)，且該反應更明顯及時間更長。病狀可能持續數月，偶而數年。對青春期女性，該反應發生率介於小孩與成年婦女之間。甚至一般年長婦女(35-45歲)對這些反應之耐受力尚佳且很少影響到正常活動。

在25年(1971-1996)上市監視期間，全世界超過2億劑量的M-M-R和M-M-R II被使用過。嚴重的不良反應像腦炎及腦病一直極為罕見。

在未曾有野生種麻疹病史，但的確接種過麻疹疫苗的孩童中，曾發生發急性硬化泛腦炎(subacute sclerosing panencephalitis, SSPE)之報告。其中有些病例可能是導致於一歲前未發現的麻疹感染，或可能因麻疹疫苗引起。根據全美國使用麻疹疫苗分佈的估計，在一百萬次接種麻疹疫苗中約有一例與SSPE有關的病例。此機率遠低於因感染野生種麻疹而致的SSPE(一百萬個麻疹病例中有6-22例)。於疾病管制中心所做之追溯性病例管制研究結果指出，自然性麻疹具有較高危險性導致SSPE。故整體而言，麻疹疫苗可預防SSPE。

接種麻疹、腮腺炎及德國麻疹三種混合疫苗注射劑後，曾有報告發生無菌性腦膜炎之案例。雖然使用Urabe株之腮腺炎疫苗和無菌性腦膜炎發生有因果關係，但並無證據顯示Jeryl Lynn™之腮腺炎疫苗和無菌性腦膜炎有關連。

注射麻疹疫苗後罕有產生脂膜炎(panniculitis)之報告。

用藥過量

用藥過量極少發生，且其與嚴重的不良反應並無關聯。

包裝

每盒1支單一劑量小瓶的凍晶乾燥疫苗及1小瓶稀釋液。

每盒10支單一劑量小瓶的凍晶乾燥疫苗及分開盒裝10小瓶稀釋液。

每盒10支10劑量小瓶的凍晶乾燥疫苗及分開盒裝10瓶(7mL／瓶)稀釋液。

貯存

為確保疫苗之效價，於運輸過程中，本疫苗必須貯存在10°C (50°F)以下，運輸過程若經冷凍不會影響其效價。

因為光照可能使疫苗失去活性，故本疫苗須隨時避免光線照射。

稀釋前之凍晶乾燥疫苗請保存於2-8°C (36-46°F)以下。稀釋液可與疫苗一起貯存在冰箱中或將其單獨置放於室溫中，切勿冷凍。

含有凍晶乾燥疫苗與稀釋液的組合包裝須貯存於2-8°C (36-46°F)。疫苗稀釋後請儘快使用。若須貯存，則將此稀釋後的疫苗置於其原來小瓶中，貯存於2-8°C(36-46°F)黑暗處。若於8小時內未使用完即須丟棄。

製造廠：Merck Sharp & Dohme Corp., 美國默克藥廠
廠　址：770 Sumneytown Pike, West Point, PA 19486, U.S.A.
包裝廠：Merck Sharp & Dohme (Australia) Pty. Limited 澳洲默沙東藥廠
廠　址：54-68 Ferndell St., S. Granville, N.S.W.2142 Australia
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IPC-MMR-I-122007

MMR-HK/TAI-20090837
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Injection

M-M-R® II

(MEASLES, MUMPS, and RUBELLA VIRUS VACCINE LIVE, MSD)

M-M-R® II (Measles, Mumps, and Rubella Virus Vaccine Live, MSD) is a live virus vaccine for vaccination against measles (rubeola), mumps, and rubella (German measles).

M-M-R II is a sterile lyophilized preparation of (1) ATTENUVAX® (Measles Virus Vaccine Live, MSD), a more attenuated line of measles virus, derived from Enders' attenuated Edmonston strain and propagated in chick embryo cell culture; (2) MUMPSVAX® (Mumps Virus Vaccine Live, MSD), the Jeryl Lynn™ (B level) strain of mumps virus propagated in chick embryo cell culture; and (3) MERUVAX® II (Rubella Virus Vaccine Live, MSD), the Wistar RA 27/3 strain of live attenuated rubella virus propagated in WI-38 human diploid lung fibroblasts.

The reconstituted vaccine is for subcutaneous administration. When reconstituted as directed, the dose for injection is 0.5 mL and contains not less than 1,000 $CCID_{50}$ (50% cell culture infectious dose) of measles virus; 12,500 $CCID_{50}$ of mumps virus; and 1,000 $CCID_{50}$ of rubella virus. Each dose of the vaccine is calculated to contain sorbitol (14.5 mg), sodium phosphate, sucrose (1.9 mg), sodium chloride, hydrolyzed gelatin (14.5 mg), recombinant human albumin (≤0.3 mg), fetal bovine serum (< 1 ppm), other buffer and media ingredients and approximately 25 mcg of neomycin. The product contains no preservative.

INDICATIONS

M-M-R II is indicated for simultaneous vaccination against measles, mumps, and rubella in individuals 12 months of age or older (see also DOSAGE AND ADMINISTRATION).

There is some evidence to suggest that infants who are born to mothers who had wild-type measles and who are vaccinated at less than one year of age may not develop sustained antibody levels when later revaccinated. The advantage of early protection must be weighed against the chance for failure to respond adequately on reimmunization.

Infants who are less than 15 months of age may fail to respond to the measles component of the vaccine due to presence in the circulation of residual measles antibody of maternal origin; the younger the infant, the lower the likelihood of seroconversion. In geographically isolated or other relatively inaccessible populations for whom immunization programs are logistically difficult, and in population groups in which wild-type measles infection may occur in a significant proportion of infants before 15 months of age, it may be desirable to give the vaccine to infants at an earlier age. Infants vaccinated under these conditions at less than 12 months of age should be revaccinated after reaching 15 months of age.

DOSAGE AND ADMINISTRATION

FOR SUBCUTANEOUS ADMINISTRATION *Do not inject intravascularly.*

Do not give immune globulin (IG) concurrently with M M R II. (See DRUG INTERACTIONS.)

The dose for any age is 0.5 mL administered subcutaneously, preferably into the outer aspect of the upper arm.

CAUTION: A sterile syringe free of preservatives, antiseptics, and detergents should be used for each injection and/or reconstitution of the vaccine because these substances may inactivate the live virus vaccine. A 25 gauge, 5/8" needle is recommended.

To reconstitute, use only the diluent supplied, since it is free of preservatives or other antiviral substances which might inactivate the vaccine.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Before reconstitution, the lyophilized vaccine is a light yellow compact crystalline plug. M-M-R II, when reconstituted, is clear yellow.

RECOMMENDED VACCINATION SCHEDULE

Individuals first vaccinated at 12 months of age or older should be revaccinated at 4 to 6 years of age or 11 to 12 years of age. Revaccination is intended to seroconvert those who do not respond to the first dose. *[Note: Local vaccination schedules may be substituted for the above recommendations as dictated by local authorities.]*

MEASLES OUTBREAK SCHEDULE

Infants Between 6 to 12 Months of Age

Local health authorities may recommend measles vaccination of infants between 6 to 12 months of age in outbreak situations. This population may fail to respond to the components of the vaccine. Safety and effectiveness of mumps and rubella vaccine in infants less than 12 months of age have not been established. The younger the infant, the lower the likelihood of seroconversion. Such infants should receive a second dose of M M R II at 15 months of age followed by revaccination at 4 to 6 years of age or 11 to 12 years of age.

OTHER VACCINATION CONSIDERATIONS

Non-Pregnant Adolescent and Adult Females

Immunization of susceptible non-pregnant adolescent and adult females of childbearing age with live attenuated rubella virus vaccine is indicated if certain precautions are observed (see PRECAUTIONS). Vaccinating susceptible postpubertal females confers individual protection against subsequently acquiring rubella infection during pregnancy, which in turn prevents infection of the fetus and consequent congenital rubella injury.

Women of childbearing age should be advised not to become pregnant for three months after vaccination and should be informed of the reasons for this precaution (see PRECAUTIONS, Pregnancy).

If it is practical and if reliable laboratory services are available, women of childbearing age who are potential candidates for vaccination can have serologic tests to determine susceptibility to rubella. However, with the exception of premarital and prenatal screening, routinely performing serologic tests for all women of childbearing age to determine susceptibility (so that vaccine is given only to proven susceptible women) can be effective but is expensive. Also, 2 visits to the health-care provider would be necessary - one for screening and one for vaccination. Accordingly, rubella vaccination of a woman who is not known to be pregnant and has no history of vaccination is justifiable without serologic testing - and may be preferable, particularly when costs of serology are high and follow-up of identified susceptible women for vaccination is not assured.

Postpubertal females should be informed of the frequent occurrence of generally self-limited arthralgia and/or arthritis beginning 2 to 4 weeks after vaccination (see SIDE EFFECTS).

Postpartum Women

It has been found convenient in many instances to vaccinate rubella-susceptible women in the immediate postpartum period (see PRECAUTIONS, Nursing Mothers).

OTHER POPULATIONS

Previously unvaccinated children older than 12 months who are in contact with susceptible pregnant women should receive live attenuated rubella vaccine (such as that contained in monovalent rubella vaccine or in M-M-R II) to reduce the risk of exposure of the pregnant woman.

Individuals planning travel abroad, if not immune, can acquire measles, mumps, or rubella and import these diseases to their country. Therefore, prior to international travel, individuals known to be susceptible to one or more of these diseases can receive either a monovalent vaccine (measles, mumps, or rubella), or a combination vaccine as appropriate. However, M-M-R II is preferred for persons likely to be susceptible to mumps and rubella; and if monovalent measles vaccine is not readily available, travelers should receive M-M-R II regardless of their immune status to mumps or rubella.

Vaccination has been recommended for susceptible individuals in high-risk groups such as college students, health-care workers, and military personnel.

POST-EXPOSURE VACCINATION

Vaccination of individuals exposed to wild-type measles may provide some protection if the vaccine can be administered within 72 hours of exposure. If, however, vaccine is given a few days before exposure, substantial protection may be afforded. There is no conclusive evidence that vaccination of individuals recently exposed to wild-type mumps or wild-type rubella will provide protection.

USE WITH OTHER VACCINES

M-M-R II should be given one month before or after administration of other live viral vaccines.

M-M-R II has been administered concurrently with live attenuated varicella and inactivated *Haemophilus influenzae* type b (Hib) conjugate vaccines using separate injection sites and syringes. No impairment of immune response to individually tested vaccine antigens was demonstrated. The type, frequency, and severity of adverse experiences observed with M-M-R II were similar to those seen when each vaccine was given alone.

Routine administration of DTP (diphtheria, tetanus, pertussis) and/or OPV (oral poliovirus vaccine) concurrently with measles, mumps, and rubella vaccines is not recommended because there are limited data relating to the simultaneous administration of these antigens.

However, other schedules have been used. Data from published studies concerning the simultaneous administration of the entire recommended vaccine series (i.e., DTaP [or DTwP], IPV [or OPV], Hib with or without Hepatitis B vaccine, and varicella vaccine), indicate no interference between routinely recommended childhood vaccines (either live, attenuated, or killed).

SINGLE DOSE VIAL

If the prevention of sporadic measles outbreaks is the sole objective, revaccination with a measles-containing vaccine should be considered (see appropriate product circular). If concern also exists about immune status regarding mumps or rubella, revaccination with appropriate mumps- or rubella-containing vaccine should be considered after consulting the appropriate product circulars.

First withdraw the entire volume of diluent into the syringe to be used for reconstitution. Inject all the diluent in the syringe into the vial of lyophilized vaccine, and agitate to mix thoroughly. If the lyophilized vaccine cannot be dissolved, discard. Withdraw the entire contents into a syringe and inject the total volume of reconstituted vaccine subcutaneously.

It is important to use a separate sterile syringe and needle for each individual patient to prevent transmission of hepatitis B and other infectious agents from one person to another.

CONTRAINDICATIONS

Hypersensitivity to any component of the vaccine, including gelatin.

Do not give M-M-R II to pregnant females; the possible effects of the vaccine on fetal development are unknown at this time. If vaccination of postpubertal females is undertaken, pregnancy should be avoided for three months following vaccination (see PRECAUTIONS, Pregnancy).

Anaphylactic or anaphylactoid reactions to neomycin (each dose of reconstituted vaccine contains approximately 25 mcg of neomycin).

Any febrile respiratory illness or other active febrile infection.

Active untreated tuberculosis.

Patients receiving immunosuppressive therapy. This contraindication does not apply to patients who are receiving corticosteroids as replacement therapy, e.g., for Addison's disease.

Individuals with blood dyscrasias, leukemia, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic systems.

Primary and acquired immunodeficiency states, including patients who are immunosuppressed in association with AIDS or other clinical manifestations of infection with human immunodeficiency viruses; cellular immune deficiencies; and hypogammaglobulinemic and dysgammaglobulinemic states. Measles inclusion body encephalitis (MIBE), pneumonitis and death as a direct consequence of disseminated measles vaccine virus infection have been reported in severely immunocompromised individuals inadvertently vaccinated with measles-containing vaccine.

Individuals with a family history of congenital or hereditary immunodeficiency, until the immune competence of the potential vaccine recipient is demonstrated.

PRECAUTIONS

GENERAL

Adequate treatment provisions including epinephrine injection (1:1000) should be available for immediate use should an anaphylactic or anaphylactoid reaction occur.

Due caution should be employed in administration of M-M-R II to persons with individual or family histories of convulsions, a history of cerebral injury or any other condition in which stress due to fever should be avoided. The physician should be alert to the temperature elevation which may occur following vaccination (see SIDE EFFECTS).

HYPERSENSITIVITY TO EGGS

Live measles vaccine and live mumps vaccine are produced in chick embryo cell culture. Persons with a history of anaphylactic, anaphylactoid, or other immediate reactions (e.g., hives, swelling of the mouth and throat, difficulty breathing, hypotension, or shock) subsequent to egg ingestion may be at an enhanced risk of immediate-type hypersensitivity reactions after receiving vaccines containing traces of chick embryo antigen. The potential risk to benefit ratio should be carefully evaluated before considering vaccination in such cases. Such individuals may be vaccinated with extreme caution, having adequate treatment on hand should a reaction occur.

THROMBOCYTOPENIA

Individuals with current thrombocytopenia may develop more severe thrombocytopenia following vaccination. In addition, individuals who experienced thrombocytopenia with the first dose of M-M-R II (or its component vaccines) may develop thrombocytopenia with repeat doses. Serologic status may be evaluated to determine whether or not additional doses of vaccine are needed. The potential risk to benefit ratio should be carefully evaluated before considering vaccination in such cases (see SIDE EFFECTS).

PREGNANCY

It is not known whether M-M-R II can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Therefore, the vaccine should not be administered to pregnant females; furthermore, pregnancy should be avoided for three months following vaccination (see CONTRAINDICATIONS).

In counseling women who are inadvertently vaccinated when pregnant or who become pregnant within 3 months of vaccination, the physician should be aware of the following: (1) In a 10-year survey involving over 700 pregnant women who received rubella vaccine within 3 months before or after conception (of whom 189 received the Wistar RA 27/3 strain), none of the newborns had abnormalities compatible with congenital rubella syndrome; (2) Mumps infection during the first trimester of pregnancy may increase the rate of spontaneous abortion. Although mumps vaccine virus has been shown to infect the placenta and fetus, there is no evidence that it causes congenital malformations in humans; and (3) Reports have indicated that contracting of wild-type measles during pregnancy enhances fetal risk. Increased rates of spontaneous abortion, stillbirth, congenital defects and prematurity have been observed subsequent to infection with wild-type measles during pregnancy. There are no adequate studies of the attenuated (vaccine) strain of measles virus in pregnancy. However, it would be prudent to assume that the vaccine strain of virus is also capable of inducing adverse fetal effects.

NURSING MOTHERS

It is not known whether measles or mumps vaccine virus is secreted in human milk. Recent studies have shown that lactating postpartum women immunized with live attenuated rubella vaccine may secrete the virus in breast milk and transmit it to breast-fed infants. In the infants with serological evidence of rubella infection, none exhibited severe disease; however, one exhibited mild clinical illness typical of acquired rubella. Caution should be exercised when M-M-R II is administered to a nursing woman.

PEDIATRIC USE

Safety and effectiveness of measles vaccine in infants below the age of 6 months have not been established. Safety and effectiveness of mumps and rubella vaccine in infants less than 12 months of age have not been established.

OTHER

Children and young adults who are known to be infected with human immunodeficiency viruses and are not immunosuppressed may be vaccinated. However, the vaccinees who are infected with HIV should be monitored closely for vaccine-preventable diseases because immunization may be less effective than for uninfected persons (see CONTRAINDICATIONS).

Excretion of small amounts of the live attenuated rubella virus from the nose or throat has occurred in the majority of susceptible individuals 7 to 28 days after vaccination. There is no confirmed evidence to indicate that such virus is transmitted to susceptible persons who are in contact with the vaccinated individuals. Consequently, transmission through close personal contact, while accepted as a theoretical possibility, is not regarded as a significant risk. However, transmission of the rubella vaccine virus to infants via breast milk has been documented (see Nursing Mothers).

There are no reports of transmission of live attenuated measles or mumps viruses from vaccinees to susceptible contacts.

It has been reported that live attenuated measles, mumps, and rubella virus vaccines given individually may result in a temporary depression of tuberculin skin sensitivity. Therefore, if a tuberculin test is to be done, it should be administered either before or simultaneously with M-M-R II.

Children under treatment for tuberculosis have not experienced exacerbation of the disease when immunized with live measles virus vaccine; no studies have been reported to date of the effect of measles virus vaccines on untreated tuberculous children.

As for any vaccine, vaccination with M-M-R II may not result in protection in 100% of vaccinees.

DRUG INTERACTIONS

Administration of immune globulins concurrently with M-M-R II may interfere with the expected immune response. Vaccination should be deferred for 3 months or longer following administration of immune globulin (human) and blood or plasma transfusions.

SIDE EFFECTS

The adverse reactions associated with the use of M-M-R II are those which have been reported following administration of the monovalent or combination vaccines.

COMMON

Burning and/or stinging of short duration at the injection site.

OCCASIONAL

Body as a whole

Fever (101°F [38.3°C] or higher)

Skin

Rash, or measles-like rash, usually minimal but may be generalized

Generally, fever, rash, or both appear between the 5th and the 12th days.

RARE

Body as a whole

Mild local reactions such as erythema, induration and tenderness; sore throat, malaise, atypical measles, syncope, irritability

Cardiovascular

Vasculitis

Digestive

Parotitis, nausea, vomiting, diarrhea

Hemetologic/Lymphatic

Regional lymphadenopathy, thrombocytopenia, purpura

Hypersensitivity

Allergic reactions such as wheal and flare at injection site, anaphylaxis and anaphylactoid reactions, as well as related phenomena such as angioneurotic edema (including peripheral or facial edema) and bronchial spasm, urticaria in individuals with or without an allergic history

Musculoskeletal

Arthralgia and/or arthritis (usually transient and rarely chronic [see below]), myalgia

Nervous/Psychiatric

Febrile convulsions in children, afebrile convulsions or seizures, headache, dizziness, paresthesia, polyneuritis, polyneuropathy, Guillain-Barre syndrome, ataxia, aseptic meningitis (see below), measles inclusion body encephalitis (MIBE) (see CONTRAINDICATIONS). Encephalitis/encephalopathy have been reported approximately once for every 3 million doses. In no case has it been shown that reactions were actually caused by vaccine. The risk of such serious neurological disorders following live measles virus vaccine administration remains far less than that for encephalitis and encephalopathy with wild-type measles (one per two thousand reported cases).

Respiratory System

Pneumonia, Pneumonitis (see CONTRAINDICATIONS), cough, rhinitis

Skin

Erythema multiforme, Stevens-Johnson syndrome, vesiculation at injection site, swelling, pruritis

Special senses

Forms of optic neuritis, including retrobulbar neuritis, papillitis, and retinitis; ocular palsies, otitis media, nerve deafness, conjunctivitis

Urogenital

Epididymitis, Orchitis

Other

Death from various, and in some cases unknown, causes has been reported rarely following vaccination with measles, mumps, and rubella vaccines; however, a causal relationship has not been established in healthy individuals (see CONTRAINDICATIONS). No deaths or permanent sequelae were reported in a published post-marketing surveillance study in Finland involving 1.5 million children and adults who were vaccinated with M-M-R II during 1982 to 1993.

Arthralgia and/or arthritis (usually transient and rarely chronic), and polyneuritis are features of infection with wild-type rubella and vary in frequency and severity with age and sex, being greatest in adult females and least in prepubertal children.

Chronic arthritis has been associated with wild-type rubella infection and has been related to persistent virus and/or viral antigen isolated from body tissues. Only rarely have vaccine recipients developed chronic joint symptoms.

Following vaccination in children, reactions in joints are uncommon and generally of brief duration. In women, incidence rates for arthritis and arthralgia are generally higher than those seen in children (children: 0-3%; women: 12-20%), and the reactions tend to be more marked and of longer duration. Symptoms may persist for a matter of months or on rare occasions for years. In adolescent girls, the reactions appear to be intermediate in incidence between those seen in children and adult women. Even in older women (35 to 45 years), these reactions are generally well tolerated and rarely interfere with normal activities.

Post-marketing surveillance of the more than 200 million doses of M-M-R and M-M-R II that have been distributed worldwide over 25 years (1971 to 1996) indicates that serious adverse events such as encephalitis and encephalopathy continue to be rarely reported.

There have been reports of subacute sclerosing panencephalitis (SSPE) in children who did not have a history of infection with wild-type measles but did receive measles vaccine. Some of these cases may have resulted from unrecognized measles in the first year of life or possibly from the measles vaccination. Based on estimated nationwide measles vaccine distribution, the association of SSPE cases to measles vaccination is about one case per million vaccine doses distributed. This is far less than the association with infection with wild-type measles, 6-22 cases of SSPE per million cases of measles. The results of a retrospective case-controlled study conducted by the Centers for Disease Control and Prevention suggest that the overall effect of measles vaccine has been to protect against SSPE by preventing measles with its inherent higher risk of SSPE.

Cases of aseptic meningitis have been reported following measles, mumps, and rubella vaccination. Although a causal relationship between the Urabe strain of mumps vaccine and aseptic meningitis has been shown, there is no evidence to link Jeryl Lynn™ mumps vaccine to aseptic meningitis.

Panniculitis has been reported rarely following administration of measles vaccine.

OVERDOSAGE

Overdose has been reported rarely and was not associated with any serious adverse events.

AVAILABILITY

To be filled in locally.

STORAGE

During shipment, to ensure that there is no loss of potency, the vaccine must be maintained at a temperature of 10°C (50°F) or colder. Freezing during shipment will not affect potency of the vaccine. Protect the vaccine from light at all times, since such exposure may inactivate the viruses.

Before reconstitution, store the vial of lyophilized vaccine at 2 to 8°C (36 to 46°F) or colder. The diluent may be stored in the refrigerator with the lyophilized vaccine or separately at room temperature. **Do not freeze the diluent.**

Combination pack containing lyophilized vaccine and diluent together should be stored at 2 to 8°C (36 to 46°F).

It is recommended that the vaccine be used as soon as possible after reconstitution. Store reconstituted vaccine in the vaccine vial in a dark place at 2 to 8°C (36 to 46°F) and discard if not used within 8 hours.