ported for cells derived from A-T patients and was later found in NBS, A-TLD, and FA patients as well *(266,269)*. Moreover, cells derived from tumors with mutated *BRCA1 (272)* and *CHK2 (202)* genes also undergo RDS when they are irradiated. It has been proposed that in combination with defects in other cell cycle checkpoints, RDS may contribute to the destabilization of the genome, thereby predisposing individuals bearing these genetic aberrations to cancer.

Patients with the rare genetic disease Bloom's syndrome (BS) are predisposed to developing all the cancers that affect the general population. BS arises through mutations in both alleles of the BLM (Bloom's syndrome mutated) gene, which encodes a 3'-5' DNA helicase, a member of the RecQ family. Cells derived from BS patients exhibit marked genetic instability, and BLM protein is known to contribute to the cellular response to IR by acting as a downstream ATM kinase effector *(273)*. Notably, BLM-deficient cells exhibit a normal p53 response to IR, as well as an intact G1/S cell cycle checkpoint, which indicates that the ATM and p53 pathways are functional in BS cells *(273)*. BLM-deficient cells also exhibit an intact S-phase arrest, proper recovery from S-phase arrest, and intact p53 and p21 responses after HU treatment. However, BLM-deficient cells show a reduction in the number of replicative cells and a partial escape from the G2/M cell cycle checkpoint, and have an altered p21 response *(274)*.

Many tumors display numerical and structural centrosome aberrations. Recent evidence shows that the centrosome plays an active role not only in the regulation of microtubule nucleation activity, but also in the coordination of centrosome duplication with cell cycle progression, in the stress response, and in cell cycle checkpoint control *(275)*. The single centrosome in G1 phase is duplicated during S phase. The two centrosomes then set up the poles of the mitotic spindle, and each incipient daughter cell receives one centrosome *(276)*. Note that centrosome aberrations can give rise to chromosomal instability, and cells that lack a functional p53 pathway are proposed to acquire multiple centrosomes through the failure of a G1-phase checkpoint *(277)*. p53 controls centrosome duplication by either direct physical binding to the centrosomes or by enhancing $p21^{WAF1}$ expression, which regulates the timely activation of CDK2/cyclin E and ensures the coordinated initiation of centrosome and DNA duplication *(277)*. Thus, loss or mutational inactivation of p53 leads to abnormal amplification of centrosomes due to the deregulation of the centrosome duplication cycle, which increases the frequency of mitotic defects and unbalanced chromosome transmission to daughter cells.

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TODAY'S THERAPY 2004

今日の治療指針

私はこう治療している

［ポケット判］

総編集

山口　徹　北原　光夫

責任編集

相澤　好治　飯田　三雄
飯塚　一　井廻　道夫
内山　聖　大友　弘士
押味　和夫　鎌谷　直之
河野　茂　郡　健二郎
小林　祥泰　島田　和幸
白川　洋一　杉本　壽
武谷　雄二　田野　保雄
富野康日己　永井　厚志
中谷　壽男　中村　利孝
堀内　勁　前沢　政次
松本　俊夫　八木　聰明
柳澤　繁孝　山田　信博
山脇　成人

〈五十音順〉

医学書院

原発性SSは一般に10-20年の長期にわたって症状はあまり進行することはないが，約5%に悪性リンパ腫を合併することがあり，経過観察を十分に行う必要がある．

診断は，1999年に新しく採択された厚生労働省のSSの改訂診断基準が用いられる．①生検病理組織検査，②口腔検査，③眼科検査，④血清検査の4項目からなり，いずれか2項目以上を満たせばSSと診断する．

治療方針

本症は病型によって治療方針が異なる．一般に乾燥症状のみの症例（腺型）は非ステロイド抗炎症薬（NSAIDs）やステロイド薬の適応とはならない．腺外症状を呈する症例（腺外型）に対してNSAIDsやステロイド薬が使用される．

A. 眼乾燥症状のある症例

℞処方例　1），2）のいずれかに3），4）を適宜組み合わせて用いる

人工涙液の点眼

1) ヒアレインミニ点眼薬（0.1%・0.3%），またはヒアレイン点眼薬（0.1%）　1回1-2滴　1日4-5回

2) マイティア点眼薬　1回1-2滴　1日4-5回

ヒアレインミニ点眼薬には防腐剤が含まれないため，角結膜炎の強い症例に適している．

3) モイスチャーエイド（ドライアイ用保護用眼鏡）

4) プラークによる涙点閉鎖

B. 口腔乾燥症状のある症例

℞処方例　1）に2)-7）のいずれかを適宜組み合わせて用いる

1) サリベートエアゾル（50 mL）　1回1-2秒　1日4-5回　口腔内噴霧

2) イソジンガーグル（30 mL）　20倍に希釈し1日数回うがい

3) サリグレンカプセル（30 mg）　1-3カプセル　分1-3　食後

4) フェルビテン錠（12.5 mg）　6錠　分3　食後

5) ピソルボン錠（4 mg）　3-6錠　分3　食後（保険適用外）

6) ツムラ麦門冬湯　9.0 g　分2-3　食前または食間（保険適用外）

7) ツムラ六参養栄湯　9.0 g　分2-3　食前または食間（保険適用外）

C. 活動性の低い腺外臓器病変

1. 発熱，関節症状，反復性唾液腺腫脹，リンパ節腫脹など

℞処方例　下記のいずれかを用いる

1) ロキソニン錠（60 mg）　3錠　分3　食後

サイトテック錠（200 μg）　3錠　分4　毎食後および就寝前

2) プレドニン錠（5 mg）　1-3錠　分1-2　食後

2. レイノー現象に対して

℞処方例　下記のいずれかを用いる

1) ユベラNソフトカプセル（200 mg）　3カプセル　分3　食後

2) プレタール錠（100 mg）　2錠　分2　朝・夕食後

3) プロサイリン錠（20 μg）　6錠　分3　食後

D. 活動性の高い腺外臓器病変

①進行性間質性肺炎，間質性腎炎，自己免疫性肝疾患，神経障害（中枢性，末梢性），②高ガンマグロブリン血症やクリオグロブリン血症に伴う高粘稠度症候群．

℞処方例　下記のいずれかを用いる

1) プレドニン錠（5 mg）　4-8錠　分2-3　食後

2) ソル・メドロール注（1,000 mg）　1日1,000 mg　1日1回　点滴静注　3日連続（保険適用外）

E. その他

悪性リンパ腫，尿細管性アシドーシス，自己免疫性甲状腺疾患，リウマチ・膠原病などが合併している場合では，それに対する個々の治療を行う．

■患者説明のポイント

・自己免疫疾患でかつ慢性疾患であることから病気と上手に付き合う決心をさせる．
・乾燥症状のみの場合は対症療法で十分である．
・予後は比較的良好であるが，腺外病変，他のリウマチ・自己免疫疾患が合併することがあり，それに対する治療が必要である．
・悪性リンパ腫の合併は，一般人口の40倍と高く，本症の予後を左右する．悪性リンパ腫を含めて腺外病変の合併は定期的に通院して，早期診断および早期治療をすることが大切である．

■服薬指導上の注意

・防腐剤入りの点眼薬を使用した場合，角結膜炎を増悪させることがある．
・薬に対して薬剤アレルギーを起こしやすいことを説明しておく．
・ステロイド服薬者には，骨粗鬆症の合併に注意する．

■看護・介護のポイント

・室内の加湿を十分に保つ．
・疲れやすい，頭痛，集中力低下，気分がよく変わる，などの不定愁訴が多く，将来に対する不安が強い．病気と共存する心構えと，病気を正しく理解して不安を除くこと．前向きの積極的な生活を指導する．
・レイノー現象のある患者には保温に注意させる．
・感染症に罹患しやすく，上気道感染の予防にうがいを励行させる．
・う歯を生じやすく，歯磨きを励行させる．
・個々の症例により違いが大きいので，対応はきめ細かに行う．

成人発症スチル病
Adult-Onset Still Disease

廣畑俊成　帝京大学助教授・内科

病態と診断

成人発症スチル病は小児の全身型若年性関節リウマチ（スチル病）の成人型と考えられる．不明熱の原因となることが多く，その病態形成にあたっては，高サイトカイン血症（IFN-γ，TNF-α，IL-6など）が重要な役割をはたすと考えられている．本症では，39°C以上におよぶ弛張熱・関節痛・サーモンピンク色の丘疹状紅斑（リウマトイド疹）の3主徴に加えて，咽頭痛・リンパ節腫脹などがみられる．検査所見では好中球主体の白血球数増加，血沈の促進，CRPの上昇が必発で，さらに肝機能異常，血清フェリチン値の著明な上昇（正常上限の5倍以上）を認めることが多い．抗核抗体やリウマトイド因子は通常陰性である．

本症の診断は上記の臨床・検査所見の組み合わせによりなされるが，感染症・悪性腫瘍・膠原病などの除外診断を的確に行うことが重要である．成人スチル病研究班による分類基準（Yamaguchi M, et al. 1992）もよく用いられている．

本症の合併症として血球貪食症候群，DIC，アミロイドーシスがまれにみられる．

治療方針

成人発症スチル病と診断した場合は，まず中等量から大量の副腎皮質ステロイドの投与を行う．効果が不十分の場合は，ステロイドパルス療法や免疫抑制剤の併用を考慮する．免疫抑制剤の中ではメトトレキサートがよく用いられる．初期治療により炎症が十分に鎮静化したあと，副腎皮質ステロイドをゆっくりと減量する．急激な減量により再燃をきたしやすいので，2週ごとに総投与量の10%程度の減量を目安にする．

A. 基本治療

℞処方例　下記の1）を単独，もしくは2），3）のいずれかと組み合わせて用いる

1) プレドニン錠（5 mg）　6-12錠　分3　毎食後

2) ソル・メドロール注　1回500-1,000 mg　1日1回　点滴静注　3日間連続（保険適用外）

投与中は高血圧，高血糖，胃潰瘍の発生などに注意する．

3) メソトレキセート錠（2.5 mg）　3-4錠　分2-3　週1回　食後（保険適用外）

B. 血球貪食症候群を合併した場合の治療

℞処方例

ネオーラルカプセル（25 mg）　6カプセル　分2（保険適用外）

血中トラフ値を50-100 ng/mLに保つよう投与量を適宜調節する．

■患者説明のポイント

・本症の診断には他疾患の除外が重要であることを説明する．
・原則として生命予後は良好だが，時に血球貪食症候群・DIC・アミロイドーシスなど重篤な合併症をきたすことがある．
・寛解する例がある反面，慢性関節炎に移行したり，また長期寛解のあと再発する場合もある．

■服薬指導上の注意

・ステロイド治療による副作用（特に骨粗鬆症・動脈硬化）とその対策についてよく説明する．
・ステロイド内服中は決してむやみに減量あるいは中断しないように十分説明しておく．

■看護・介護のポイント

・リウマトイド疹は発熱時に一過性に出現することが多いので，注意深く観察する．
・薬剤アレルギーが現れやすいので注意する．
・大量のステロイドや免疫抑制療法中には易感染性に注意を払う．

フェルティ症候群
Felty Syndrome

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病態と診断

フェルティ症候群は，脾腫と好中球減少症（2,000/μL以下）を伴う関節リウマチ（RA：rheumatoid arthritis）の一亜型である．本症はRAの1%以下にみられ，その95%はHLA-DR4陽性である．RAの発症後10-20年して発生する例が多い．50-70歳の女性に多く，男女比は1：2-4である．脾腫の程度はさまざまであるが，脾臓の大きさと好中球減少の程度は相関しない．本症の関節症状は一般のRAに比して関節変形や骨破壊