and improved stains for mucin were all introduced in the 1980s,[56] after the increases in the incidence of AD were observed.

While the decreased incidence of SQ among Japanese and Americans is encouraging in terms of cancer prevention and control, it is counterbalanced by the increases in AD, especially among Japanese. As realization of the detrimental health effects of cigarette smoking initially grew, the tobacco industry strove to develop filtered cigarettes as less harmful cigarettes, but subsequent scientific evidence has failed to demonstrate any benefit from changes in cigarette design or manufacturing.[57] Despite the tobacco industry became well aware of the fact that filtered cigarettes were not less harmful, it has been advertised filtered or low-tar cigarettes to intend to reassure smokers and were meant to prevent smokers form quitting since the early 1950s in the United States[58] and later in Japan.[59] The false reassurances provided by market-

ing strategies of filtered/low-tar cigarettes might be related to the rising incidence of ADs of the lung.

The present results suggest that the shift from nonfilter to filter cigarettes may have had the result of replacing one cancer type with another. These findings emphasize the importance of tobacco control programs, namely programs that prevent the initiation of smoking, hasten the rate of smoking cessation or limit exposure to ETS, have been associated with a decrease in both cigarette consumption and smoking rates, and subsequently with a decrease in lung cancer incidence.[4,60]

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喫煙依存

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1 はじめに

わが国では2006年より健康保険を使った禁煙治療が開始され，喫煙行動は「ニコチン依存症」という疾患に位置づけられた．喫煙は継続することにより様々な疾患を誘発し，ひいては患者の生命予後を短縮させる．AHRQ（Agency for Healthcare Research and Quality，アメリカ医療研究品質局）の禁煙治療ガイドライン（Treating Tobacco Use And Dependence：2008 Update）[1]には，3分以内の簡易な禁煙アドバイスだけでも禁煙率は1.3倍増加するという医師の短時間介入の効果がレビューされており，患者の健康維持のためには，禁煙の専門外来だけでなく一般の医療現場における禁煙介入も重要である．そこで本稿では，どの医療現場でも遭遇する「ニコチン依存症」の患者に対して，一般内科医が短時間で実施することのできる効果的なアドバイスについて紹介する．

2 喫煙状況の確認

喫煙習慣を有する者は，程度の差こそあれ，ほぼ全員がニコチン依存症状態にあり，喫煙行動を継続することで心理的な安定感が得られる一方，禁煙することにより安定感が損なわれると感じている．本稿ではこのような状態を喫煙依存とよぶことにする．

初診患者に対しては，その患者が喫煙依存者であるか否かを識別するために，診察前の問診票や看護師・研修医が行う予診，あるいは診察中の問診により，喫煙状況を正確に把握する必要がある．その際に注意が必要なことは，現在の喫煙行動の把握に時間の幅をもたせて尋ねることである．なぜなら，最近の体調不良がきっかけで禁煙を余儀なくされたが，まだ喫煙依存状態から脱していない「みかけ禁煙者」が含まれているからである．これらの「みかけ禁煙者」も後述する禁煙支援の対象者と考えられることから，筆者はこれを真の禁煙支援の対象者と区別するため，「最近1か月間に1本以上タバコを吸いましたか？」という質問を用いている．

3 禁煙の必要度のアセスメント

次に，一般の医療現場における禁煙介入で優先順位の高い事項は，喫煙行動を現に有する患者にとっての禁煙の必要度をアセスメントすることである．喫煙を継続することにより，基礎疾患の悪化を引き起こしたり，治療の効果を著しく低下させる可能性が高い場合，担当医として患者に強く禁煙を指示する必要がある．以下に禁煙する必要がある疾患を提示する．

a．すぐに禁煙する必要がある疾患

1）虚血性心疾患・脳血管疾患などの循環器疾患

冠動脈疾患死亡リスクにおいて，血圧，コレステロールレベル，喫煙はいずれも独立した危険因子であり，その重複によりさらにリスクは

増加することが報告されている[2]．喫煙する者は血圧，コレステロールが最も低い群であっても，非喫煙者に比べてそのリスクは約3倍となる．また，脳卒中による死亡の相対リスクはヘビースモーカー（1日21本以上喫煙者）では男性で2.17倍，女性で3.91倍と有意に高まると報告されている[3]．循環器疾患の患者に対しては，患者の生命維持に直接かかわるため，担当医としてすぐに禁煙するよう強く指示する必要がある．

2）手術予定

手術予定の喫煙患者が術前に喫煙を継続することで，術後合併症の発生率は高まる．一方，中川らは，術後の呼吸器合併症の発生率は術前5～8週以上前に禁煙することで低下すると報告している[4]．また，術後創傷治癒合併症は術前3週間以上前に禁煙を開始することでリスクが低くなることが報告されており[5]，合併症予防の観点から手術予定のある患者はすぐに禁煙する必要がある．

3）慢性閉塞性肺疾患（COPD）

喫煙はCOPDのリスクの80～90%を占めるとされ，喫煙継続は患者の生命予後を短縮させる．COPD患者であっても早期に禁煙を開始することにより，呼吸機能の悪化を防ぐことが可能である[6]．COPDの治療では薬物療法とともに禁煙は必須であり，患者に強く禁煙を指示する必要がある．

b．禁煙の必要性が高い疾患

喫煙を維持することで，病期の進行が早まる，治療効果が減弱する，多重がんの罹患率や再発率が高まることなどの報告がある疾患として糖尿病，メタボリックシンドローム，消化管潰瘍，ピロリ菌除菌予定の患者，慢性肝炎・肝硬変，頭頸部がんや肺がん，食道がんなどの喫煙関連がん等があげられる．これらの疾患では禁煙することにより疾患の進行を抑えたり，合併症予防や治療効果の改善がみられるため，その疾患に合わせた禁煙の必要性を患者に伝える

ことが重要と考えられる．

c．その他の疾患

喫煙とは関連性の低いとされる疾患であっても，患者の今後の健康維持のために禁煙の介入は必要である．そのような患者に対しては，後述する患者の禁煙の準備性に応じた介入が推奨される．

4 禁煙の準備性に合わせた禁煙アプローチ

喫煙依存者に対して禁煙支援を行う際には，患者の禁煙の準備性を把握し，その準備性に応じた支援を実施することが効果的である．全く禁煙する気のない患者に対して禁煙の必要性を迫っても，多くの場合禁煙を開始するには至らない．James O. Prochaskaの提唱したステージ変容モデルでは，喫煙者を禁煙の準備性により「無関心期」「関心期」「準備期」「実行期」「維持期」の五つのステージに分類し，その準備性に合わせた指導を実施していくことが効果的とされている．

実際には，おもな疾患の治療が優先される医療現場において，ステージを聴取し細分化するだけの時間を費やすことは困難と思われる．そこで患者の禁煙の準備性を禁煙開始日が設定できるか否かによって2分類し，それぞれに合わせた指導を実施することが好ましいと考えられる．すなわち「みかけ禁煙（上記）」を除く喫煙依存者に対して，「禁煙を開始する日程を具体的に決めることができますか？」あるいは「○日から禁煙を開始できますか？」と尋ね，これに対する回答により，場合分けする．図1に医療現場における禁煙支援のフローチャートを示す．

a．禁煙開始日の設定できる患者に対して

健康保険を使った禁煙治療は，様々な禁煙介入のなかで最も禁煙の成功率が高く，準備性の高い患者に最も楽に禁煙を開始させる手段である．自施設に禁煙外来がある，もしくは患者の自宅の近くに禁煙治療を実施している医療機関

のある場合は，禁煙治療を紹介することが望ましい．同時に禁煙動機の強い準備期の患者には，禁煙によって現在の疾患にどんなメリットがあるかなどを一言伝え，禁煙を成功させる自信の強化を行う．

これに対し，禁煙治療を受診することができないと答えた患者に対しては，OTC（薬局での対面販売）の禁煙補助薬を紹介する．後述するが，OTC薬を用いた禁煙は，患者が自力で行う禁煙と比べて成功率が高い．特にニコチンパッチは現在一般用医薬品第1類に定められており，これを購入する際に薬剤師から指導を受けることが必須となる．医師による外来での指導が簡易であっても，これを補完する形で薬剤師が指導するため，患者の禁煙成功率は高まることが予想される．なお，具体的な禁煙方法については，薬剤師の指導以外にも外来診療のなかでパンフレット等を渡すことで，診察中の指導を最小限ですますことが可能である．
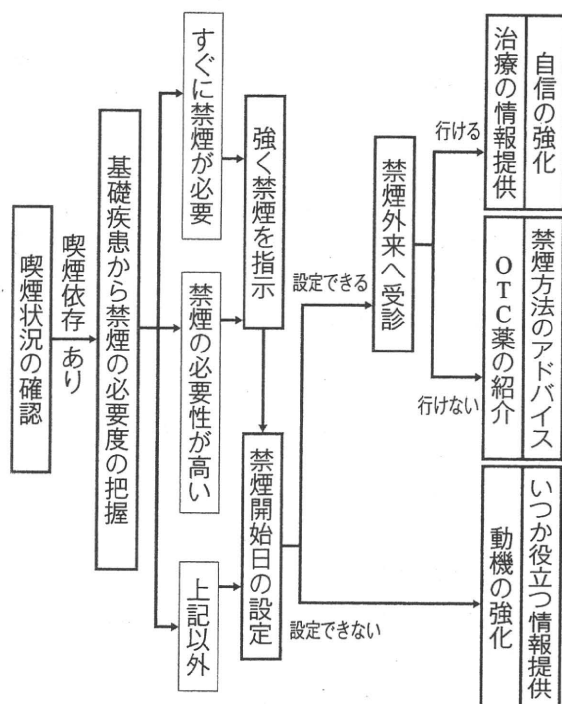
b. 禁煙開始日が設定できない患者に対して

禁煙開始日が設定できないと回答した患者に対しては，禁煙する動機の強化を行う．動機の強化は，患者の個別性に合わせ実施する．特に医師からの疾患を交えた動機付けは，一言であっても患者に強い印象を与え効果的である．疾患が喫煙に関連していない場合も，患者の今後の健康維持のために禁煙が重要であることを医師として伝えることが重要である．

また，一言で動機を強化したのち，いつか禁煙したくなった時に役立つ情報提供（禁煙補助薬の選択肢も増え，自力で行う禁煙と比べてずっと楽に禁煙できること等）を行うことが望ましい．

5 OTC薬を使った禁煙

従来，医療用医薬品であったニコチンガムやニコチンパッチは，その安全性からOTC化（薬局での対面販売）され，現在一般用医薬品として喫煙者が気軽に手に入れることのできる禁煙補助薬である．

患者が健康保険を使った禁煙治療を選択しない場合，患者の禁煙をスムーズに開始するためにニコチンを含む禁煙補助薬として情報提供をすることが望ましい．以下に，わが国で販売されるOTC薬について説明する．

a. ニコチンガム

ニコチンガムは，短時間作用型のガムタイプのニコチン製剤で，口腔粘膜からニコチンを吸収させ離脱症状を緩和させる．簡便かつ安全に禁煙をスタートできるニコチン製剤として，これまでに世界60か国で使用されてきた．2008年のCochrane reviewでは，ニコチンガムを使った禁煙は何もしない場合に比べて1.43倍禁煙成功率が高いとされている[7]．現在，一般用医薬品指定第2類に位置づけられている．

b. ニコチンパッチ

2008年にスイッチOTC化されたニコチンパッチは長時間作用型のニコチン製剤で，安定

図1 一般医療現場における禁煙指導のフローチャート

したニコチン補給が可能なニコチン製剤である．貼付薬という薬形から，仕事中や禁煙を知られたくない人でも使用可能である．前述のCochrane review では，ニコチンガムを使った禁煙は何もしない場合に比べて 1.66 倍禁煙の成功率が高いと報告されている[7]．

　OTC で販売されるニコチン製剤の禁忌は，重い循環器疾患(特に心筋梗塞 3 か月以内，急性期の脳梗塞など)，妊婦・授乳婦，うつの既往のある者等であり，ニコチン製剤を勧める際に注意を要する．前述のとおり，ニコチンパッチは一般用医薬品第 1 類に指定され，販売時に薬剤師の指導が必要となる．

6 保険を使った禁煙治療

　2006 年度より開始されたこの禁煙治療は，現在わが国で最も禁煙の効果が高く，最も患者が楽に禁煙するための近道である．薬物療法に加え，患者の個別性を踏まえた生活指導を実施する専門外来である．

a. 禁煙治療を受けることのできる患者の条件

　保険を使った禁煙治療には患者基準が設けられ，患者基準を満たした者のみが禁煙治療を保険で受けることが可能となる．以下に患者基準を示す．

　以下のすべての要件を満たす者であること

　①ニコチン依存症にかかわるスクリーニングテスト(TDS)(表1)でニコチン依存症(合計が 5 点以上)と判定された者であること．

　②ブリンクマン指数(＝1 日の喫煙本数×喫煙年数)が 200 以上の者であること．

　③直ちに禁煙することを希望し，「禁煙治療のための標準手順書」(日本循環器学会，日本肺癌学会および日本癌学会により作成)に則った禁煙治療プログラム(12 週間にわたり計 5 回の禁煙治療を行うプログラム)について説明を受け，当該プログラムへの参加について文書により同意している者であること．

　特に TDS 5 点以上の患者はニコチン依存症

と判定され，一般の医療現場において禁煙介入

表1 ニコチン依存症にかかわるスクリーニングテスト(TDS)

TDS	はい 1点	いいえ 0点
問1. 自分が吸うつもりよりも，ずっと多くタバコを吸ってしまうことがありましたか？		
問2. 禁煙や本数を減らそうと試みて，できなかったことがありましたか？		
問3. 禁煙したり本数を減らそうとしたときに，タバコが欲しくて欲しくてたまらなくなることがありましたか？		
問4. 禁煙したり本数を減らそうとしたときに，次のどれかがありましたか？(イライラ，神経質，落ちつかない，集中しにくい，憂うつ，頭痛，眠気，胃のむかつき，脈が遅い，手の震え，食欲または体重増加)		
問5. 問4でうかがった症状を消すために，またタバコを吸い始めることがありましたか？		
問6. 重い病気にかかったときに，タバコはよくないとわかっているのに吸うことがありましたか？		
問7. タバコのために自分に健康問題が起きているとわかっていても，吸うことがありましたか？		
問8. タバコのために自分に精神的問題(※)が起きているとわかっていても，吸うことがありましたか？		
問9. 自分はタバコに依存していると感じることがありましたか？		
問10. タバコが吸えないような仕事やつきあいを避けることが何度かありましたか？		
※(注)禁煙や本数を減らしたときに出現する離脱症状(いわゆる禁断症状)ではなく，喫煙することによって神経質になったり，不安や抑うつなどの症状が出現している状態．	合計	

合計 5 点以上でニコチン依存症と判定．

する際に，禁煙治療を勧めることで，患者の禁煙がスムーズに実行されやすい．

b. 治療プログラム

禁煙治療は12週間に5回の治療プログラムであり，初回230点，2〜4回184点，最終回180点の診療報酬が定められている．図2に禁煙治療のスケジュールを示す．なお，健康保険を使った禁煙治療には専任の看護師をおくことが要件となっており，医師と看護師の効果的な役割分担が診療の効率化と禁煙治療の効果を上げるために重要となっている[8]．

c. 禁煙治療での薬物療法

次に，保険を使った禁煙治療での薬物療法について紹介する．禁煙治療での薬物療法は，ニコチンパッチに加え，2008年に発売されたニコチンを含まない経口禁煙補助薬バレニクリンを用いる．バレニクリンは，中脳・腹側被蓋野にある$\alpha_4\beta_2$ニコチン性アセチルコリン受容体に選択的に結合することで，喫煙由来のニコチン

初診　2回目　3回目　　　　　4回目　　　　　5回目
診察　（2週間後）（4週間後）　（8週間後）　　（12週間後）

図2　健康保険を使った禁煙治療プログラムのスケジュール

*禁煙補助薬の処方.

が結合することを阻害するとともに，この刺激により側坐核から少量のドーパミンが放出される．これにより喫煙による満足感を抑制する拮抗作用と，禁煙に伴う離脱症状や切望感を軽減する作動薬作用の両方をもつ．バレニクリンを使った禁煙は，自力で禁煙する場合と比べ3.22倍禁煙成功率が増加することが報告されている[9]．ニコチン置換療法は重い循環器疾患など使用禁忌がみられたが，バレニクリンは使用禁忌がない点で使用しやすく，また服薬から1週間は喫煙を継続し，喫煙によって満足感が得られないという感覚を体験できる期間があることがユニークである．

禁煙補助薬の増加に伴い，禁煙治療には選択肢が生れ，患者背景に合わせた処方が可能となった．薬剤選択の基準や患者の個別性に合わせた効果的な支援法など，今後の治療の発展に注目が集まっている．

7 おわりに

多忙を極める一般の医療現場での禁煙支援は，優先順位が低くなりがちである．禁煙支援は様々な職種が一言ずつでも助言・情報提供していくことで，その効果は上がる[1]．一般医療現場におけるすべての医師が，患者の今後の健康維持や治療効果の向上のためにも，短時間でも患者に禁煙の重要性を伝えることの価値は，非常に高い．
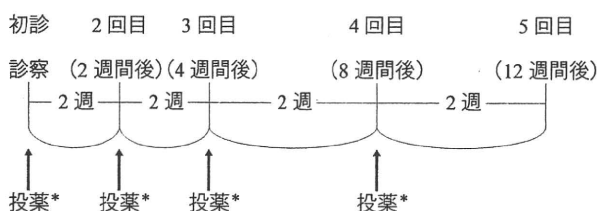
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田中英夫

症 例

ニコチンパッチ使用中に低ナトリウム血症を呈した肝硬変・糖尿病患者の 1 例*

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はじめに　2006 年の診療報酬の改定により，ニコチン依存症が新たな治療対象となり，一般医家の間でもニコチンパッチが広く処方されている[1]．他方，がん専門病院などで開設されている禁煙外来には，複数の基礎疾患を有する患者が訪れる機会が多いことから，禁煙治療中に予期せぬ健康障害が起きるかもしれない．今回われわれは，ニコチンパッチを用いた禁煙治療中に起こった低ナトリウム血症の 1 例を経験したので報告する．

症　　例

症　例：64 歳，男性．

主　訴：全身倦怠感，反応鈍．

既往歴：1978 年からアルコール依存症．1982年，胆石にて胆嚢摘出術．2003 年に糖尿病を指摘される．

喫煙歴：30 本/day×42 年間．

現病歴：2005 年，肝細胞癌（非 B，非 C 型）にて当センターを紹介受診，2006 年 1 月肝臓を部分切除（S2）した．2008 年 4 月，再発にて経皮経肝的門脈塞栓術施行，手術のためインスリン導入，術後強化インスリン療法となり退院となった．退院後の 4 月中旬に自分と家族の健康のため，当センターの禁煙外来を受診，ニコチン依存症の判定テ

ストである tobacco dependence screener (TDS) は 10 点と，保険を使った禁煙治療の適用基準 (TDS 5 点以上) を満たしていた．翌日よりニコチンパッチの貼付による治療を開始した．なお処方の際に，アルコール依存症の既往，および肝細胞癌に伴う肝機能低下を考慮し，ニコチンの過剰投与にならないよう，中等量のニコチンを含むニコチネル TTS20 から開始した．また就寝前に，同薬を剝がすことを指示した．禁煙治療開始から 7 日後の 4 月下旬，全身倦怠感が出現し，反応が鈍くなったため当院を受診し，血清ナトリウムの低下を認めたため緊急入院した．

入院時現症：意識は Japan Coma Scale I-1，動作，反応が鈍い．バイタル所見に異常を認めず．浮腫，脱水所見，黄疸なし．

入院時検査所見：血液一般検査は正常値で，生化学検査で肝胆道系酵素の軽度の上昇を認めた．NH_3 値の上昇なく，腎機能も正常値であった．Gluが軽度上昇しており，HbA_{1c} は 8.1% であった．電解質は Na 118 mEq/l と低ナトリウム血症を認めた．血清浸透圧は 261 mOsm/kg と軽度低下していた．腫瘍マーカーは正常範囲内で，ホルモン検査において TSH が 0.097 μU/ml と低下，ADH は 1.1 pg/ml と測定可能であった．尿検査所見ではNa 87.3 mEq/day とナトリウム利尿が起こっており，尿浸透圧は 447 mOsm/kg と高張尿であった (Table 1)．胸部 X 線，心電図，心エコーとも異常を認めなかった．腹部造影 CT で新たな病変を認めず，頭部 MRI において，異常所見を認めなかった．

入院後経過：本症例の治療として，細胞外液の

Table 1. 入院時検査所見

血算		GPT	42 IU/l	AFP	1.9 ng/ml
WBC	4,890/μl	γ-GTP	156 IU/l	PIVKA-II	31 mAU/ml
Neut	75.9%	ALP	359 IU/l	内分泌学的検査	
Lym	14.4%	T-Bil	0.5 mg/dl	ADH	1.1 pg/ml
Eos	0.2%	LDH	215 IU/l	aldosterone	78.7 pg/ml
Baso	0.8%	TC	144 mg/dl	cortisol	12.3 μg/dl
Mono	8.7%	ChE	127 IU/l	renin	0.4 pg/ml
RBC	384×10⁶/μl	NH₃	33 μg/l	TSH	0.097 μU/ml
Hb	13.0 g/dl	Na	118 mEq/l	FT₃	1.8 pg/ml
Ht	37.5%	K	5.1 mEq/l	FT₄	0.83 ng/dl
Plt	23.4×10⁴/μl	Cl	82 mEq/l	尿検査	
凝固		Ca	8.3 mg/dl	U-Na	43.0 mEq/l
PT	11.9 sec	BUN	9.0 mg/dl	U-Na	87.3 mEq/day
APTT	35.8 sec	Cr	0.69 mg/dl	U-Cl	64.4 mEq/day
Fib	180.9 mg/ml	Glu	215 mg/dl	U-K	87.3 mEq/day
生化学的検査		S-Osm	261 mOsm/kg	U-Osm	447 mOsm/kg
TP	7.6 g/dl	HbA₁c	8.1%	Ccr	89.8 ml/mim
Alb	4.2 g/dl	血清学的検査			
GOT	46 IU/l	CRP	0.22 mg/dl		

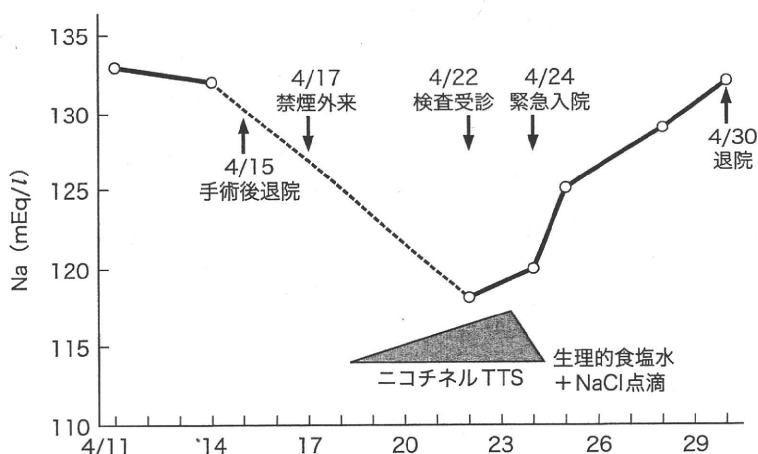**Fig. 1. 臨床経過**

増加のない低ナトリウム血症であると判断し，生理的食塩水の点滴をただちに開始した．ナトリウムの補正は1日に生理的食塩水500ml＋10%NaCl 20ml（Na 6.5 g/day，213 mEq/l/day）とし，これを第5病日まで投与したところ，血清ナトリウム値は改善した（Fig. 1）．治療後，禁煙治療開始後の状況を尋ねたところ，治療開始3日目あたりから発汗量が増加したこと，また，普段運動により約2lの真水を飲んでいたが，持続する口渇感によりその量がさらに増加したと答えた．また，ニコチンパッチは就寝中も貼った状態にしており，同薬を緊急入院となるまで使用していた．

考察

本症例は，肝細胞癌の再発治療の退院3日後に禁煙外来を受診し，翌日からニコチンパッチを連続装着し，外来受診から7日後に低ナトリウム血症のため緊急入院となり，生理的食塩水とナトリ
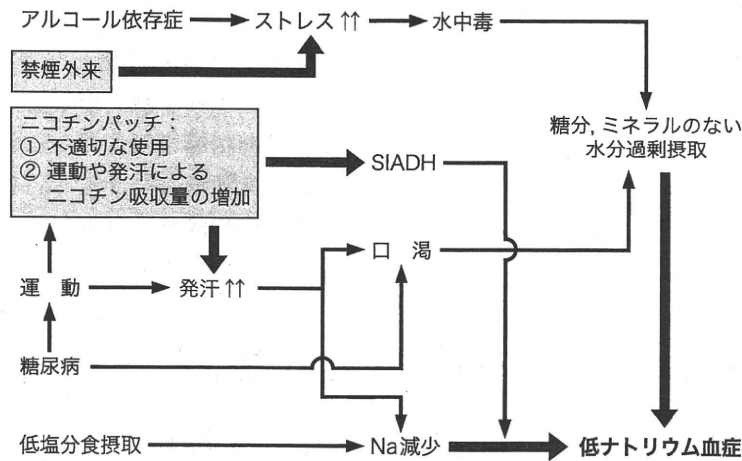
Fig. 2. 発生機序

ウムの点滴にて改善した．また，改善する前の低ナトリウム血症は，Table 1 に示すように血漿浸透圧 270 mOsm/kg 以下，尿浸透圧 300 mOsm/kg 以上，尿 Na 20 mEq/l 以上，腎機能正常，副腎皮質機能正常で，脱水所見も認めなかったことから，抗利尿ホルモン分泌異常症候群(SIADH)の診断基準を満たしていた[2]．

　低ナトリウム血症は，腎臓の排泄能によるものと水過剰摂取に分類され，さらに腎排泄能によるものでは①細胞外液不足，②細胞外液正常，③細胞外液過剰に分けられる[3]．③は，水とナトリウムが体内に貯留する場合で心不全，ネフローゼ症候群，肝硬変といった病態で起こる．②はサイアザイド系利尿薬服用，甲状腺機能低下症，癌や薬剤による SIADH などがある．①は体液の喪失が腎臓か腎臓外かでさらに分類する．腎性低ナトリウム血症は，尿細管障害や利尿薬の投与，副腎不全などで生じる．その他，高脂血症や高血糖，mannitol による偽性低ナトリウム血症も含む．一方腎外性低ナトリウム血症では，嘔吐や下痢，発汗過多など腎臓以外からのナトリウム喪失が生じる．

　本症例において，来院時脱水の徴候(turgor の低下，粘膜の乾燥)はなく，細胞外液量正常の低ナトリウム血症を推測するが，本症例患者ではさまざまな病態が重なっていたと推測される(Fig. 2)．糖尿病に対する運動療法で 1 日 15,000 から 20,000

歩(10〜13 km)歩行しており，この時点での発汗による細胞外液量低下は否定できず，腎外性の塩分喪失状態であった．

　ジョギングやマラソンによる脱水では低ナトリウム血症を伴うことが多く，その予防としては以前までいわれていた“渇く前の補給”から“発汗で失った分を補う”ことである[4]．しかし，本症例は，発汗で失った分を補う飲水ではなく，喉が渇く前に水分を多量摂取していた．加えて飲水量は禁煙治療開始後さらに増加したというが，その理由としては，基礎疾患である糖尿病による口渇症状のほかに，アルコール依存症に伴うストレス対処能力の低下，および禁煙の開始による心理的負担が重なり，これらが複合的に作用して心因性多飲による水中毒が惹起された可能性がある．スポーツ飲料水などの電解質の入った飲料は糖分が含まれているため控えており，飲水量は 1 日約 2l を超えていたという．また，妻が高血圧であるため，家庭では自身も塩分制限食を摂取していたことも入院後の聴取で判明した．

　さらに，禁煙治療開始後，医師の指示に反して就寝中もニコチンパッチを装着していたため，ニコチンによる発汗作用により持続的に発汗量が増大し腎外性の塩分喪失が起こったことも考えられた．加えてニコチンは薬剤による SIADH の原因の一つであり[3]，海外で喫煙者の精神科患者 10 例の血清ニコチンレベルの増加と衝動的な飲水と

SIADH の誘発の関連を示した報告があり[5]，また ニコチンパッチの使用中の SIADH の 1 症例も報告されている[6]．このことから，今回検査所見から判断された SIADH は，就寝中も連続して経皮吸収されたことによる可能性も否定できない．発汗による細胞外液減少に続き，細胞外液正常の低ナトリウム血症である SIADH，そして飲水過多による水中毒などの複数の条件が重なって低ナトリウム血症が出現したと考え，有害事象として報告した．

ニコチンパッチについて，サウナ使用時や運動時のニコチン経皮吸収薬の血漿中ニコチン濃度は，安静時に比べ有意に上昇するという報告がある[7,8]．経皮吸収貼付部位の血流量増加に関連しているものと考えられるので，処方の際はこれらの点に留意する必要があると思われる．また，ニコチンパッチの副作用として，口渇，ほてり，多汗といった自律神経症状が 0.1～5% 未満にみられること[9]を念頭に置き，糖尿病など自律神経障害のある患者へは，使用方法についての十分な説明と副作用等のチェックの必要がある．また，精神疾患の現病歴，既往歴を有する患者では，禁煙治療開始によって心理的ストレス負荷が増大し，これが精神疾患の悪化をきたすこともあることから，うつ指標等を用いた精神状態の経過観察を要するものと思われる．

ニコチンパッチは 2008 年 7 月から，医師の処方箋を要さずに全国の薬局で購入可能な over-the-counter(OTC)薬となった．このため，今回のような複数の基礎疾患を有する患者を含み，多くの禁煙希望者が手軽に本剤を入手できる状況になった．本剤を購入する際，薬剤師が服薬指導および禁煙指導を行うことになっているが，現病歴，既往歴を聴取したうえで，必要に応じ主治医に禁煙治療の相談を受けるよう，指導することが望ましいと思われる．

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ORIGINAL ARTICLE

Medical expenditures of men with hypertension and/or a smoking habit: a 10-year follow-up study of National Health Insurance in Shiga, Japan

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Hypertension and smoking are major causes of disability and death, especially in the Asia-Pacific region, where there is a high prevalence of a combination of these two risk factors. We attempted to measure the medical expenditures of a Japanese male population with hypertension and/or a smoking habit over a 10-year period of follow-up. A cohort study was conducted that investigated the medical expenditures due to a smoking habit and/or hypertension during the decade of the 1990s using existing data on physical status and medical expenditures. The participants included 1708 community-dwelling Japanese men, aged 40–69 years, who were classified into the following four categories: 'neither smoking habit nor hypertension', 'smoking habit alone', 'hypertension alone' or 'both smoking habit and hypertension.' Hypertension was defined as a systolic blood pressure of ≥140 mm Hg, a diastolic blood pressure of ≥90 mm Hg or taking antihypertensive medications. In the study cohort, 24.9% had both a smoking habit and hypertension. During the 10-year follow-up period, participants with a smoking habit alone (18 444 Japanese yen per month), those with hypertension alone (21 252 yen per month) and those with both a smoking habit and hypertension (31 037 yen per month) had increased personal medical expenditures compared with those without a smoking habit and hypertension (17 418 yen per month). Similar differences were observed even after adjustment for other confounding factors ($P < 0.01$). Japanese men with both a smoking habit and hypertension incurred higher medical expenditures compared with those without a smoking habit, hypertension or their combination.

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INTRODUCTION

Elevated blood pressure is the leading cause of death, as well as a major cause of disability in the world.[1,2] Approximately 13.5% of all deaths and 6.0% of all disability-adjusted life years among those aged ≥30 years are attributable to high blood pressure with systolic blood pressure of >115 mm Hg.[3] This is because of the strong effect of hypertension on the development of cardiovascular disease, including coronary heart disease and stroke.[4–7] Hypertension is a major contributor to cardiovascular diseases in the Asia-Pacific region.[3] Furthermore, cigarette smoking, which leads to cardiovascular disease as well as cancer and respiratory disease,[7–12] is also a major health burden in the Asia-Pacific region because of its popularity among men;[13] nearly two-thirds of the world's smokers live in 10 countries, and most of them are in that region.[14] Thus, both hypertension and a smoking

habit might be more important determinants of human health than other risk factors in the Asia-Pacific region.[15–22] For example, in Japan, hypertension and a smoking habit contribute to 20.8 and 20.5% of deaths among men, respectively, which is much greater than the mortality because of hypercholesterolemia (4.5%) or diabetes (5.0%).[15] In addition, 20–30% of Japanese men are estimated to have both hypertension and a smoking habit simultaneously,[16,23] and the risk of cardiovascular disease is higher in these individuals than in those with just one or neither of these two risk factors.[6,7,11,12,16]

The effect of hypertension and smoking should be considered from the viewpoint of medical expenditures, particularly in the Asia-Pacific region where there is a high prevalence of individuals with both of these two risk factors. However, the majority of previous epidemiological studies have only reported the association between a single risk

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factor and medical expenditures.[24–27] We hypothesized that hypertensive individuals with a smoking habit would incur higher future medical expenditures, especially in-patient expenditures, than those with just one or neither of these two risk factors because of a high incidence of cardiovascular and other serious diseases. To test this hypothesis, we attempted to measure the medical expenditures of individuals with hypertension and/or a smoking habit over a 10-year period in a community-based, male Japanese population.

METHODS
Medical expenditures
In Japan, many medical services are provided by the public medical insurance system,[28–30] which requires the enrollment of all Japanese residents ('health-insurance-for-all'). During the period when data were collected (from 1990 to 2001), public medical insurance consisted of two insurance systems. The eligibility for each insurance system was as follows: the first system, named Social Insurance, was for employees and their dependants and covered approximately two-thirds of the overall Japanese population; the other system, named National Health Insurance (NHI), was for those not covered by Social Insurance, for example, self-employed individuals such as farmers and fishermen, as well as retirees and their dependants, and covered the remaining one-third of the population. Prices were strictly controlled by a fee schedule set by the National Government and were determined on a 'fee-for-service' basis. The fee schedule was the same regardless of the insurance system. Furthermore, the same fee schedule applied to all the clinics and hospitals given approval to provide medical services under the public medical insurance system. However, some medical services including health check-ups for asymptomatic individuals and inoculations were not covered by medical insurance. The fee for these services was recorded in an insurance claim history file.

In this study, we used the insurance claim history files to obtain information on medical expenditures. Therefore, the medical expenditures in this study were confined to the range of the fee schedule used in the public medical insurance system in Japan. Total medical expenditures were divided into outpatient and in-patient medical expenditures.

Study design and participants
The present cohort comprised 4535 Japanese beneficiaries of NHI, the insurance system for self-employed individuals. The details of the present cohort have been reported previously.[25,31–33] In brief, the study participants, aged 40–69 years, lived in seven rural towns and a village in Shiga Prefecture, West Japan, and had a voluntary baseline survey in 1989–1991. In 1990, the study area had 82 155 residents, including 31 564 individuals aged 40–69 years, of whom 11 900 were NHI beneficiaries.[34] Therefore, the participants in this study represented approximately 38% of all NHI beneficiaries aged 40–69 years living in this area. The analysis was conducted only for men, because the prevalence of smokers is quite low among Japanese women;[8–10,16,23,35] our data showed that current smokers and former smokers accounted for 3.4% (n=87) and 0.5% (n=14), respectively, of 2596 female participants. Of the 1939 male participants, 231 were excluded because they were former smokers (n=229) or there was no information on smoking habit at the baseline survey (n=2). We excluded former smokers from the analysis because we wanted an exact measure of medical expenditures related to smoking at baseline. The remaining 1708 participants were included in the analysis. Monthly NHI claim history files of the Shiga NHI Organizations were linked with the baseline survey data files at the organizations. To protect the participants' privacy, their names were deleted from the linked data at the organizations. Therefore, the data were analyzed without knowledge of the participants' identity. This study was approved by the institutional review board of Shiga University of Medical Science for ethical issues (no. 16–15).

Data collection
The baseline survey was performed during the period 1989–1991 using standardized methods in accordance with the Manual for Health Check-ups under the Medical Service Law for the Aged, issued by the Japan Public Health Association in 1987.[36] Blood pressures were measured by well-trained public

health nurses in the right arm in the sitting position using a standard mercury sphygmomanometer after the participants had rested for at least 5 min. The use of antihypertensive medications and smoking habit were obtained from interviews conducted by well-trained public health nurses and medical doctors. Hypertension was defined as a systolic blood pressure of $\geqslant 140$ mm Hg, a diastolic blood pressure of $\geqslant 90$ mm Hg or taking antihypertensive medications. On the basis of this information, all eligible male participants were classified into the following four categories: 'neither smoking habit nor hypertension', 'smoking habit alone', 'hypertension alone' or 'both smoking habit and hypertension'. A drinking habit and a history of diabetes were also evaluated by the interviews. Body height and weight were measured and body mass index was calculated as body weight (kg) divided by the square of body height (m^2). Serum total cholesterol levels were measured by an enzymatic method.

We calculated medical expenditures per person in each of the four categories after a 10-year follow-up period. Information on medical expenditures for each participant and information on participants who withdrew from the NHI or those who died were obtained from the monthly NHI claim history files, beginning in April of the year after their initial health check-up and continuing until March 2001. Medical expenditures were expressed in Japanese yen, US dollars and euros (100 Japanese yen=1.08 US dollars or 0.76 euros, at the foreign exchange rate on 1 September 2009). Data on medical expenditures for each participant differed depending upon the period of subscription to the NHI. The medical expenditures for each participant were therefore divided by the period of subscription and expressed as expenditures per month of follow-up. If a beneficiary withdrew from the NHI or died, follow-up was terminated at that point. Follow-up was restarted for beneficiaries who withdrew and then re-enrolled in the NHI. Reasons for withdrawal from the NHI included moving to regions outside of Shiga Prefecture or transfer to the other insurance system.

Data analysis
Because the distribution of real medical expenditures was positively skewed, the data were logarithmically transformed to normalize the distribution and the results were expressed as geometric means. For participants with expenditures of 0 yen per month, the logarithmic transformations were performed by replacing 0 yen with 1 yen. There were four participants with total medical expenditures of 0 yen and five participants with outpatient medical expenditures of 0 yen. For comparison of total and outpatient medical expenditures per person in each category, we performed an analysis of covariance with the Bonferroni correction to adjust the P-value for multiple post hoc comparisons. The analysis of covariance incorporated the following variables as covariates: age (40–44, 45–49, 50–54, 55–59, 60–64 or 65–69 years old, using five dummy variables with 40–44 as a reference), body mass index, drinking habit (non-, current occasional or current daily drinker, using two dummy variables with non-drinkers as a reference), serum total cholesterol and a history of diabetes. Because 896 participants (52.5%) had in-patient medical expenditures of 0 yen, logarithmic transformations were not performed, and the Kruskal–Wallis test was used to compare in-patient medical expenditures among the four categories. A similar analysis was repeated after excluding participants who were taking antihypertensive medications at baseline.

In addition, to clarify whether medical expenditures associated with smoking and/or hypertension increase over time because of the occurrence of cardiovascular and other serious diseases, we calculated medical expenditures per person in each of the four categories for the overall follow-up period of 10 years and also stratified expenditures by the follow-up period (the first 5 years and the latter 5 years), using subgroups in which every participant was followed for >5 years.

Finally, we examined excess medical expenditures attributable to hypertension and/or a smoking habit in the study population using the arithmetic means of total medical costs in each category. The excess medical expenditures attributable to hypertension and/or a smoking habit were calculated as follows: (total medical expenditures in the 'smoking habit alone', 'hypertension alone', and 'both smoking habit and hypertension' category–total medical expenditures in the 'neither smoking habit nor hypertension' category) × number of participants in the 'smoking habit alone', 'hypertension alone' and 'both smoking habit and hypertension' category.

The statistical analysis was performed using SPSS 14.0J for Windows (SPSS Japan, Tokyo, Japan). The *P*-values were two sided and *P*-values of <0.05 were considered statistically significant.

RESULTS

Current smokers accounted for 68.1% of the 1708 male study participants, whereas hypertensive individuals accounted for 36.9% of the cohort. Table 1 summarizes the baseline risk characteristics of the male participants, grouped according to their smoking habit and hypertension status. Of the study population, 24.9% had both a smoking habit and hypertension, whereas 43.2% had smoking habit alone and 11.9% had hypertension alone. The 'both smoking habit and hypertension' group had the highest mean age. Only approximately 1% of the participants in each category had a history of cardiovascular disease, and no remarkable differences were observed among the four categories.

Total person-years were 15 508 and the mean follow-up time was 9.1 years. As shown in Table 2, during the 10-year follow-up period, total medical expenditures per person in the 'both smoking habit and hypertension' category (31 037 Japanese yen per month) tended to be higher than in the 'neither smoking habit nor hypertension' category (17 418 yen per month), in the 'smoking habit alone' category (18 444 yen per month) and in the 'hypertension alone' category (21 252 yen per month). For the multivariate-adjusted geometric means of total medical expenditures, the differences among the four categories were statistically significant (*P*<0.01). Similar statistically significant differences were also observed in outpatient medical expenditures (*P*<0.01). In addition, in-patient medical expenditures showed statistically significant differences among the four categories (*P*<0.01).

Subgroup analysis, in which participants taking antihypertensive medications at baseline were excluded (*n*=80), showed a broadly similar pattern; total medical expenditures per person were 19 084 yen per month for the 'hypertension alone' category (*n*=172) (outpatient, 11 108 yen; and in-patient, 7976 yen) and 31 263 yen per month for the 'both smoking habit and hypertension' category (*n*=378) (outpatient, 13 658 yen; and in-patient, 17 604 yen; data not shown in the table). However, the difference in medical expenditures, especially for outpatients, between the 'hypertension alone' category and the 'neither smoking habit nor hypertension' category was attenuated.

Table 3 shows medical expenditures per person grouped by smoking habit and hypertension status for the overall follow-up period of 10 years and also stratified by the follow-up period, which was derived from subgroups in which all participants had >5 years of follow-up (*n*=1491). The differences in medical expenditures, especially in-patient expenditures, among the four categories were much greater in the latter 5 years of follow-up than in the first 5 years.

Compared with the 'neither smoking habit nor hypertension' category, the excess medical expenditures attributable to a smoking habit alone were estimated to be 757 188 yen per month, and were calculated as follows: (18 444 yen–17 418 yen) × 738 participants with a smoking habit alone. Accordingly, the excess medical expenditures attributable to a smoking habit alone represented 2.0% of the total medical expenditures for the 1708 participants (37 090 403 yen), and were calculated as follows: 757 188 yen/37 090 403 yen. Using similar methods, the excess medical expenditures attributable to hypertension alone and both a smoking habit and hypertension were estimated to be 782 136 yen and 5 801 694 yen, respectively, which represented 2.1 and 15.6% of the total medical expenditures for the study cohort.

DISCUSSION

We carried out a 10-year follow-up study between 1990 and 2001 and showed that Japanese men with a smoking habit alone, hypertension alone or both a smoking habit and hypertension had increased personal medical expenditures compared with those without a smoking habit and hypertension. The coexistence of these two risk factors further increased medical expenditures in comparison with the existence of just one of these two risk factors. The increments in the expenditures associated with both or just one of these two risk factors were prominent in the latter period of follow-up. The sum of excess medical expenditures attributable to hypertension and/or a smoking habit represented approximately 20% of the total medical expenditures of the study cohort. An important strength of our study was that the participants consisted of community-based individuals who were beneficiaries of one of the public medical insurance systems on the basis of 'health-insurance-for-all' in Japan. Therefore, our data can probably be generalized to the Japanese male population. An additional strength of our study was that the 10-year follow-up period was long enough to provide an accurate evaluation of medical expenditures associated with serious conditions caused by smoking and hypertension. This allowed the calculation of medical expenditures stratified by the follow-up period.

Table 1 Baseline risk characteristics in 1989–1991 of 1708 male National Health Insurance beneficiaries in Shiga, Japan, grouped by smoking habit and hypertension status

	Smoking habit and hypertension category				
	Neither	*Smoking alone*	*Hypertension alone*	*Both*	*P-value*
Number of participants (distribution (%))	340 (19.9)	738 (43.2)	204 (11.9)	426 (24.9)	
Age (years)[a]	52.0±7.5	52.8±8.5	54.4±7.3	56.3±7.9	<0.01
Body mass index (kg m^{-2})[a]	22.6±2.3	22.0±2.5	24.0±3.0	23.0±2.8	<0.01
Drinking habit[b]					<0.01
Occasional drinker (%)	30.9	19.3	25.6	14.4	
Daily drinker (%)	43.8	59.2	51.2	67.5	
Serum total cholesterol (mmol l^{-1})[a]	4.83±0.81	4.79±0.90	5.05±0.83	4.82±1.01	<0.01
History of diabetes (%)[b]	4.4	4.6	3.9	4.5	0.98
Medication for hypertension (%)[b]	0	0	15.7	11.3	0.12
History of cardiovascular disease (%)[b]	0.3	0.4	1.0	1.4	0.17

[a]Values show the mean ± s.d.; groups were compared by one-way analysis of variance.
[b]The χ^2-test; medication for hypertension was compared only between the 'hypertension-alone' group and the 'both' group.

Table 2 Medical expenditures per person grouped by smoking habit and hypertension status, after a 10-year follow-up from 1990 to 2001, based on National Health Insurance in Shiga, Japan

| | Medical expenditures per person per month | | | | |
| | Total | | Outpatient | | In-patient |
Smoking habit and hypertension category	Arithmetic mean	Adjusted geometric mean	Arithmetic mean	Adjusted geometric mean	Arithmetic mean
Neither (n=340)	17 418 yen (187.51 dollars) (131.82 euros)	6782 yen	8508 yen (91.59 dollars) (64.39 euros)	4994 yen	8910 yen (95.92 dollars) (67.43 euros)
Smoking alone (n=738)	18 444 yen (198.55 dollars) (139.59 euros)	7066 yen	8606 yen (92.65 dollars) (65.13 euros)	4713 yen	9852 yen (106.06 dollars) (74.56 euros)
Hypertension alone (n=204)	21 252 yen (228.79 dollars) (160.84 euros)	9072 yen	13 276 yen (142.92 dollars) (100.48 euros)	6674 yen[†‡]	7976 yen (85.87 dollars) (60.37 euros)
Both (n=426)	31 037 yen (334.12 dollars) (234.89 euros)	10 721yen[†‡]	14 235 yen (153.25 dollars) (107.74 euros)	6981 yen[†‡]	16 801 yen (180.87 dollars) (127.16 euros)
		$P<0.01^a$		$P<0.01^a$	$P<0.01^b$

At the foreign exchange rate on 1 September 2009, 100 Japanese yen=1.08 US dollars or 0.76 euros.
[a]Analysis of covariance adjusted for age, body mass index, drinking habit, serum total cholesterol and a history of diabetes.
[b]Kruskal–Wallis test.
[†]$P<0.05$ vs. neither, for multiple *post hoc* comparisons with Bonferroni correction.
[‡]$P<0.05$ vs. smoking alone, for multiple *post hoc* comparisons with Bonferroni correction.

Table 3 Medical expenditures per person grouped by smoking habit and hypertension status, after a 10-year follow-up from 1990 to 2001, based on National Health Insurance in Shiga, Japan

| | Medical expenditures per person per month (arithmetic mean) | | | | | |
| | Total | | Outpatient | | In-patient | |
Smoking habit and hypertension category	10 years	First 5 years / latter 5 years	10 years	First 5 years / latter 5 years	10 years	First 5 years / latter 5 years
Neither (n=301)	12 311 yen	10 162 yen 15 583 yen	7945 yen	6742 yen 9467 yen	4366 yen	3420 yen 6116 yen
Smoking alone (n=649)	14 810 yen	11 133 yen 23 717 yen	8345 yen	7105 yen 10 395 yen	6482 yen	4028 yen 13 353 yen
Hypertension alone (n=172)	20 929 yen	16 725 yen 25 941 yen	14 345 yen	11 424 yen 17 159 yen	6584 yen	5301 yen 8783 yen
Both (n=369)	26 693 yen	16 339 yen 51 715 yen	13 920 yen	10 819 yen 18 427 yen	12 773 yen	5520 yen 33 288 yen

The data were derived from subgroups in which every participant was followed for >5 years, and are presented for the overall follow-up period of 10 years and also stratified by the follow-up period.
At the foreign exchange rate on 1 September 2009, 100 Japanese yen =1.08 US dollars or 0.76 euros.

Our data showed that hypertension alone or a smoking habit alone increased total medical expenditures by 3834 yen and 1026 yen, respectively, which represented a 22 and 6% increment compared with the expenditures of individuals without either risk factor. Medical expenditures in the participants with hypertension alone tended to be higher than in those with a smoking habit alone. This may be reasonable, because the treatment of hypertension usually requires antihypertensive medications, and this directly increases medical expenditures, especially for outpatients. The results from our subgroup analysis after excluding participants with antihypertensive medications at baseline support this explanation. At the time of our study, any medical services for smoking cessation, including nicotine replacement therapy, were not provided by the public medical insurance system in Japan. However, the analysis stratified by the follow-up period showed a further increment in expenditures, especially in-patient expenditures, of participants with smoking alone in the latter 5 years of follow-up. These results suggest that smoking increases medical expenditures later because of the occurrence of serious diseases. A similar explanation may be applicable to increased medical expenditures of participants with hypertension alone in the later period, which may be because of the use of antihypertensive medications as well as the occurrence of cardiovascular disease. However, we could not identify the particular disease or event that directly increased medical expenditures among participants with either hypertension or smoking.

The coexistence of a smoking habit and hypertension was identified in approximately 25% of the study cohort and increased total medical expenditures by 13 619 yen. This represented a 78% increment

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compared with the expenditures of individuals with neither risk factor. NIPPON DATA80[16] and the Hisayama study[11] reported that Japanese who had both hypertension and a smoking habit were at increased risk of cardiovascular disease compared with those who had either risk factor alone or neither risk factor. These previous reports provide one possible explanation for our findings of increased medical expenditures of hypertensives with a smoking habit compared with the other three categories. Alternatively, the effect of smoking on cancer and respiratory disease[8,9] might have contributed to the increased medical expenditures among hypertensives with a smoking habit. Our data on the time-related changes of medical expenditures during the follow-up period support these possible explanations, as there was a 232% increment in future expenditures of individuals with both risk factors compared with individuals with neither risk factor.

The mean level of blood pressure is higher in Japan than in Western countries,[17,35,37-41] despite a substantial decline in blood pressure during the past four decades.[42] In addition, the prevalence of smoking among Japanese men remains much higher compared with men in the West,[8-10,17,35,37,41,43] although there has been a trend for a decline in smoking.[42] As a result, approximately 70–80% of Japanese men have hypertension and/or a smoking habit,[16,23] which would directly contribute to as much as 20% of the entire medical expenditures in this population. Individuals with the coexistence of both these two risk factors comprise approximately 20–30% of the Japanese male population.[16,23] It should be noted that the combination of hypertension and smoking would contribute to approximately 15% of total medical expenditures, not only because of the substantially high value of medical expenditures but also because of the high prevalence of individuals with the coexistence of both risk factors. As the relative importance of hypertension and smoking on human health is likely to be similar among Japan and other Asia-Pacific countries such as China and Korea,[17-22] a broadly similar pattern of increased medical expenditure may be observed in these countries as well.

This study has several limitations. First, although the participants were selected from a community-based population whose health status was relatively typical of the overall Japanese population,[28] the participants were limited to NHI beneficiaries belonging to self-employed occupational groups in one area of Shiga prefecture. The socio-economic status and lifestyle of these beneficiaries may have had an effect on their health. In addition, the study participants may have been concerned about their heath status, because they voluntarily underwent the survey. Moreover, no information on a history of serious disease other than cardiovascular diseases was available at baseline. However, the study participants consisted of healthy community-dwelling individuals who participated in the baseline survey without the need of assistance. We therefore believe that most of the participants were free of serious disease at baseline, as a history of cardiovascular disease was identified at baseline in only 0.7% of the participants. Second, the public medical insurance system in Japan differs from that in other countries. Therefore, absolute values of medical expenditures estimated in this study should not be directly comparable to other populations, and our results cannot necessarily be extrapolated to other populations. Third, blood pressure was measured only once in each participant, and classification of participants based on this single measurement may have overestimated the prevalence of hypertension. This misclassification may consequently have led to the underestimation of differences in medical expenditures between the hypertensive and non-hypertensive groups. In addition, we had no serial data on smoking habit and hypertension after the baseline survey. Despite the lack of serial data, we believe that our results, based on a single baseline survey and 10-year follow-up,

support our conclusion that hypertensive individuals with a smoking habit incur higher medical expenditures in the future. Fourth, our analysis did not account for the severity of hypertension or the amount of tobacco smoking because the number of eligible participants was not large enough to stratify hypertension and smoking status. Finally, the details of the medical diagnoses, medical treatment status (for example, prescriptions), clinical condition and cause of mortality were not available in this study. Thus, further studies are needed to clarify the effect of these variables. However, our subgroup analysis provided important evidence that antihypertensive medications significantly increase medical expenditures, especially outpatient expenditures.

In conclusion, hypertensive individuals with a smoking habit incur higher medical expenditures in the Japanese male population. Attention should be paid to such individuals, especially in countries where both hypertension and a smoking habit are prevalent. To reduce the economic burden on the health-care system because of hypertension and smoking, efforts should be made to prevent and treat hypertension and to encourage individuals not to smoke, especially before the occurrence of serious diseases that increase medical expenditures.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

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APPENDIX

The Health Promotion Research Committee of the Shiga National Health Insurance Organizations

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