Table 3: FDA Contact Information

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[原著]

事前検査におけるヘモグロビン測定の導入

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Implementation of measuring hemoglobin concentration at pre-donation test

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抄 録

　香川県赤十字血液センターでは2003年10月に, 事前検査として血液比重にかわって, ヘモグロビン(Hb)測定法を導入した。Hb法の最大の利点はその定量性にあり, 献血者にHb値を数字として提示することができ, Hb低値者, 高値者に対する対応を明確にし得た。また, 懸念されていたHb不足による献血不適格者数, VVR発症率も比重法施行時と大差がなかった。今回の検討で, Hb12.5g/dL以上がほぼ比重1.053以上に, 12.0g/dL以上が1.052以上に相当すること, Hbと赤血球指数との関係から, 赤血球が正色素性から小球性低色素性に変わるHb値が12.5～12.0g/dLであることから現行の採血基準は妥当であると考えられた。Hb法は測定装置がHbの表示まで時間を要すること, 温度差による配慮が必要であるなどの欠点はあるが, 定量性, 均一性を重視するGMPからみても従来の比重法より優れていると結論した。

Key words: Pre-donation examination, Hemoglobin determination
Blood donation criteria, HemoCue hemoglobin analyzer

はじめに

　香川県赤十字血液センターでは, 2003年10月より, 事前検査として硫酸銅法による比重測定にかわって, 簡易ヘモグロビン(Hb)測定装置, ヘモキュウヘモグロビンシステム(以下Hb法)による方法に変更した。採血基準は, 血液事業の根幹の一つであり, その判定には定量的なHb法が最も妥当と考えられるゆえである。自動血球算定装置がルーチン化したわが国において, 貧血の診断はすべてHb, ヘマトクリット, 赤血球数によっており, 目視による比色法(ザーリ法)や比重法(硫酸銅法)は赤十字血液センターを除いて用いられていない。最近の献血の適否に関する世界の論文は, すべてがHb法を用いて判断しており[1-3], 比重法は

検査法として教科書の記載すらない現状である[4]。

今回，比重法とHb法の比較，変更前後の献血不適格者の比率，副作用，とくに血管迷走神経反応(Vasovagal Reflex：以下VVR)の比率，また，200mL献血12.0g/dL以上，400mL献血12.5g/dL以上とされている採血基準の妥当性についても検討した。さらに，Hb法の有用性を生かして，不適格者のHb濃度別による個人指導のありかたについても検討したので，これらの成績を報告する。

方　法

簡易Hb法（ヘモキュウ）によるヘモグロビン測定は，あらかじめ試薬が充填された専用マイクロキュベットに10μLの末梢血をサンプリングしアナライザーにセットして，表示されるHb量を読み取る。Hb測定はアザイドメトヘモグロビン法により570nmと880nmからなる2波長様式によっている。

200mL献血申込者63名，400mL献血申込者62名において，血液比重測定と同時に自動血球計数装置(STKS)によるHb測定を行い両法の比較を行った。次に，平成14年4月1日から15年3月31日の間に比重法によって判定した献血者と平成16年4月1日から17年3月31日の間にHb法で判定した献血者において，本社採血基準による献血不適格者の比率，VVRの発症比率を比較検討した。また，献血申込者男性1,472名，女性771名のHb法によるHb濃度別度数分布を作成した。次に，STKSによって得られたMCV，MCH，MCHCとHb値の関係をみることにより，Hb法採用時の採血基準の妥当性を検討した。

Hb法（ヘモキュウ）を導入して1年6カ月経過した時点で，献血バスで実際に使用している看護師17名にアンケート調査を行った。

結　果

1．比重法とHb法の関係

400mL献血申込者のうち，血液比重1.053以上を示した献血者62名のHb値は12.6～17.3g/dLの範囲になり，その平均値±1SDは14.96±1.12g/dLであった。同様に比重1.052以上の200mL献血申込者63名は12.1～16.4の範囲で平均

値は13.64±1.16g/dLであった。以上から，400mLの採血基準1.053以上またはHb12.5g/dL以上，200mLの採血基準1.052以上または12.0g/dL以上は両者ともcut off値として妥当であると考えられた。また，比重法の結果はHb値で幅広い範囲に分布し，定量性がないことも明らかとなった。

2．簡易Hb法と自動血球計算装置との相関

簡易Hb法（ヘモキュウ）と自動血球算定装置(Coulter STKS)によって測定した結果の相関を図1に示した。相関係数0.951（Y＝0.8893X＋1.59)の高い相関がみられた。

3．Hb法による献血者ヘモグロビンの度数分布

Hb測定の定量性を生かして献血者ヘモグロビンの度数分布が得られた（図2）。献血申込者の男性1,472名，女性771名の解析で最も頻度が高いのは，男性15.0～15.5g/dL，女性12.5～13.0g/dLであった。

4．比重法およびHb法による献血不適格者の比較

表1に比重法(平成14年4月1日～15年3月31日)とHb法(16年4月1日～17年3月31日)で判定した比重あるいはHb不足による献血不適格者の比率を示す。両者の年齢区分毎不適格率で大きな差異は認めなかった。200mL，400mLの合計において比重法の男性申込者は23,985名，うち不適格者数(率)151名(0.6％)，女性申込者は21,715名，うち不適格者4,404名(20.3％)，Hb法の男性申込者22,749名，不適格者数(率)151(0.6％)，女性申込者20,504名，不適格者数3,958名(19.3％)で，いずれも差異を認めなかった。400mL申込女性で40歳代では，多数の(26～30％)不適格者がみられた。また，400mL申込女性でHb12.5g/dL未満431名のうち10.0g/dL未満が43名(10.0％)，8g/dL未満も4名みられ，治療を必要とすると考えられた。

5．献血時副作用の比較

輸血副作用のうち採血基準が関係すると思われるvaso-vagal reaction(VVR)の発症率を比較した。ヘモキュウが用いられる献血バス200mL，400mL採血のVVRはHb法で男性が減少していたが，女性での頻度の差は認められなかった（表2）。いずれにしてもHb法を導入してVVRが増加することはなかった。
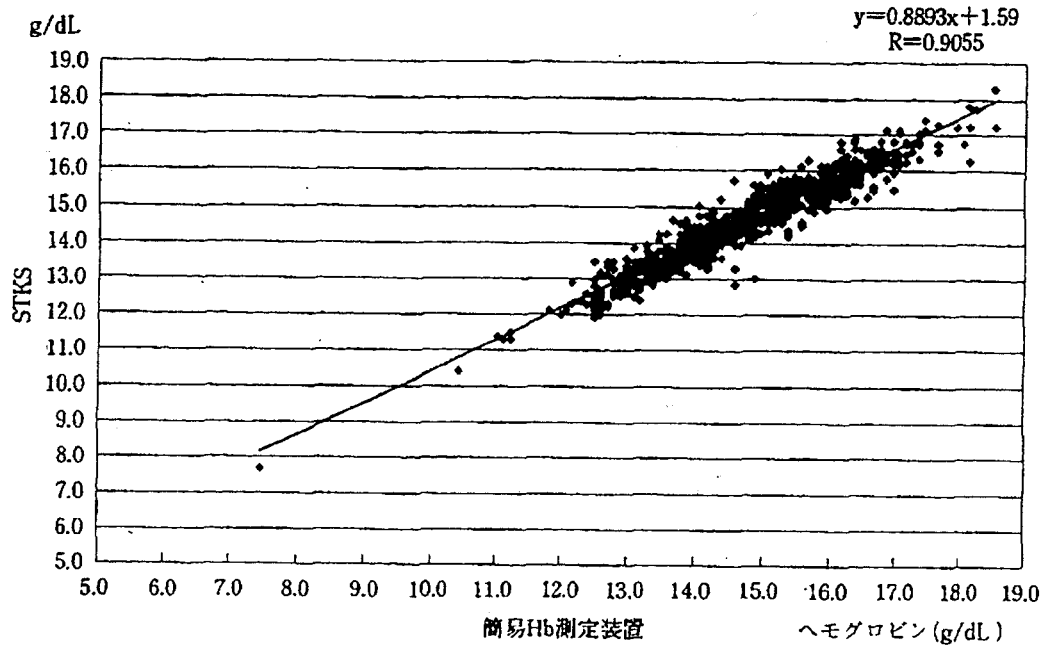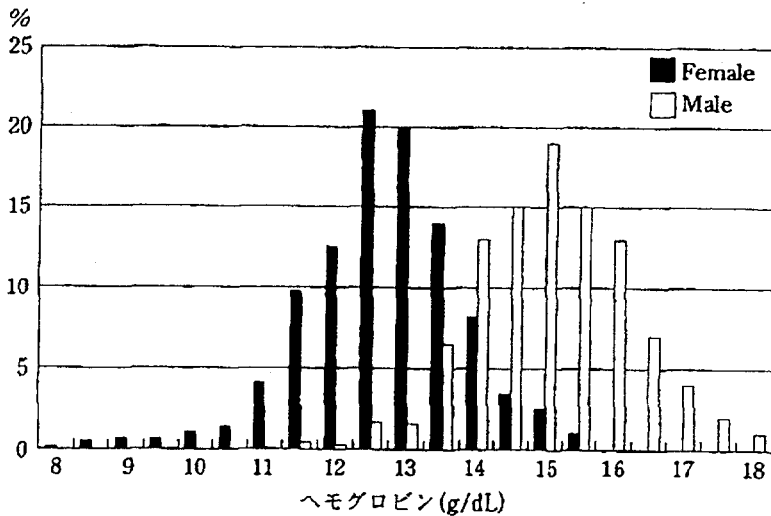
$$y=0.8893x+1.59$$
$$R=0.9055$$

図1　簡易Hb測定装置(ヘモキュウ)と自動血球算定装置(STKS)との比較

献血申込者，男性1,472名，女性771名の
ヘモグロビン分布。男性で最も多いの
は15.0〜15.5g/dL，女性で最も多いのは
12.5〜13.0g/dLであった。

図2　献血申込者のヘモグロビン値の分布

6．ヘモグロビンと赤血球指数の関係

　Hb値と赤血球指数(MCV，MCH，MCHC)の平均値の関係を表3に示す。Hbの低下に伴って赤血球指数も低下してくる。低下傾向が認められるのは男性で，MCV，MVH，MCHCともHb12.5g/dL未満から，女性12.0g/dL未満からであり，小球性低色素性の傾向が認められるのは男

性が0.5g/dL高かった。以上から，Hbの低下にともなって赤血球は12.5〜12.0g/dLで正色素性から小球性低色素性に変わることが判明した。

7．Hb低値による献血不適格者への対応

　Hb測定の定量性を生かして献血者のHb値に応じた指導を行うこととした。Hb値10g/dL未満の献血者には医療機関を受診し治療を受けるよう医

表1　比重法およびHb法による献血不適格者の比較

			年齢区分	19~19	20~29	30~39	40~49	50~59	60~69	計
比重法	男性	200	申込数	1,091	286	346	550	517	210	3,000
			不適数	8	0	5	5	15	1	34
			不適率	0.7	0	1.4	0.9	2.9	0.5	1.1
		400	申込数	1,040	4,464	5,683	5,198	3,659	941	20,985
			不適数	5	14	21	29	30	18	117
			不適率	0.5	0.3	0.4	0.6	0.8	1.9	0.6
	女性	200	申込数	2,240	3,139	2,938	1,976	1,904	689	12,877
			不適数	399	602	689	448	239	67	2,444
			不適率	17.8	19.2	23.5	22.8	12.6	9.7	19.0
		400	申込数	601	1,923	2,097	1,923	1,771	523	8,838
			不適数	110	446	588	582	198	36	1960
			不適率	18.3	23.2	28.0	30.3	11.2	6.9	22.2
Hb法	男性	200	申込数	1,050	298	340	421	448	224	2,781
			不適数	7	1	1	4	5	8	26
			不適率	0.7	0.3	0.3	1.0	1.1	3.6	0.9
		400	申込数	1,147	4,183	5,510	4,832	3,373	923	19,968
			不適数	2	9	17	24	31	18	101
			不適率	0.2	0.2	0.3	0.5	0.9	2.0	0.5
	女性	200	申込数	2,422	2,579	2,825	1,762	1,510	612	11,710
			不適数	461	425	593	386	140	64	2,069
			不適率	19.0	16.5	21.0	21.9	9.3	10.5	17.7
		400	申込数	601	2,038	2,286	1,786	1,584	499	8,794
			不適数	176	454	596	467	163	33	1,889
			不適率	29.3	22.3	26.1	26.1	10.3	6.6	21.5

表2　比重法およびHb法によるVVR発症率の比較

		男 性	女 性
比重法	軽症	83	53
	重症	1	1
	計	84	54
	発症率（%）	0.44	0.43
Hb法	軽症	44	50
	重症	3	2
	計	47	52
	発症率（%）	0.27	0.44

師が指導し，12g/dL未満，10g/dL以上の献血者には食事指導用のパンフレットを作成し配布すると同時に，月に1度栄養士会による個別栄養指導も開設した。

8．Hb高値の献血者の頻度

採血可能であった男性1,472名，女性771名について（図2），Hb17.0g/dL以上の比率は，17.5＞Hb≧17.0：30例（3.0%），18.0＞Hb≧17.5：3例（0.3%），18.5＞Hb≧18.0：3例（0.3%），19.0＞Hb≧18.5：1例（0.1%）の計37例で，いずれも男性で女性にはみられなかった。また，赤血球指数は正常であった。

9．ヘモキュウ使用者のアンケート結果

ヘモキュウを使用している看護師のアンケート結果は以下のとおりであった。まず，利点としては①感染性廃棄物としての後始末が簡単になった（100%），②測定法が簡単である（74%），③献血者にHb値を示すことで説得力がある（63%），などであった。欠点としては①外気温や光線の影響

表3　Hbと赤血球指数の関係

Hb(g/dL)	男　性			女　性		
	MCV (fl)	MCH (pg)	MCHC (g/dL)	MCV (fl)	MCH (pg)	MCHC (g/dL)
16.0＞Hb≧15.5	93±4	32±2	34±0			
15.5＞Hb≧15.0	93±5	32±2	34±1	93±4	32±2	35±1
15.0＞Hb≧14.5	92±3	32±2	34±1	92±3	32±1	35±0
14.5＞Hb≧14.0	92±5	32±2	34±1	91±3	31±1	35±0
14.0＞Hb≧13.5	92±4	32±2	35±1	91±1	32±1	35±0
13.5＞Hb≧13.0	92±6	32±2	34±0	90±4	31±2	35±1
13.0＞Hb≧12.5	92±5	32±2	34±1	90±3	31±1	34±0
12.5＞Hb≧12.0	84±6	28±3	34±1	91±6	31±2	34±0
12.0＞Hb≧11.5	83±5	28±2	34±0	87±5	30±2	34±1
11.5＞Hb≧11.0*	77±0	25±0	33±0	83±5	28±2	34±0
11.0＞Hb≧10.5				83±6	27±2	34±1

n＝20　(*n＝2)

を受けやすい(94％)，②測定に時間がかかる(94％)，③新たに精度管理が必要になった(69％)，などであった。

考　案

　従来から採血基準として用いられている硫酸銅法による血液比重は，献血者を1.052未満，1.052以上(200mL)，1.053以上(400mL)と3区分して可否を判定するもので，各区分内に様々なヘモグロビン濃度が含まれる定性法であり，血液事業が始まって以来半世紀あまりずっと用いられている。しかしながら，比重法は測定者により±0.001程度のバラツキがあることが指摘されている[5]。一般に，赤血球沈降速度は，高温で促進，低温で遅延し補正が必要とされている[6]。佐野らの検討では，10℃で20℃に比し，0.001～0.002低い値，30℃で0.001～0.002高い値が得られるとしている[5]。また，James ら[7]は比重法の方がHb法よりも偽の適判定(false-pass)が多いことを証明した。以上から，現在のGMPに準拠した血液事業の理念からすれば，いつ，誰が，どう行っても一定した数値が得られるHb法の方が理想的であることは明白である。今回，簡易ヘモグロビン測定装置(ヘモキュウ)を導入して2年あまりになるので，従来の比重法との比較を様々な面から試みた。

　ヘモキュウによるHb測定は，自動血球計算装置との相関で高い相関があり，とくに問題がない

ことが示された。これは過去の報告のとおりである[8]～[10]。また，比重法とHb法で献血不適格者の比率が異なるか否かを検討した。比重法とHb法の比較検討では，時期が異なるため厳密な比較ではないが，献血不適格者の増減はなく，現行の採血基準で有意の差はないと思われた。男性のVVRは，軽症でHb法の方が少なくヘモグロビン値以外の原因が考えられる。

　Hb法の利点は，献血者のHb値を数字として表示できることであり，度数分布を知ることができる。この度数分布によって，女性献血申込者の中に，10g/dL未満の要加療者が不適格者の10％近くみられることが判明した。従来の比重法では，低比重以外の情報がなくそのまま放置されるわけであるが，Hb法ではHb値を提示できるので医療機関への受診を勧めることができた。また，10.0～12.5g/dLの方には栄養指導や食事のアドバイスができた。すなわち，貧血の予防と治療の双方を区別して指導することが可能である。

　採血基準では，真性赤血球増加症(多血症)は採血しないことになっているが，比重法ではHb高値者を除外することができない。Hbを測定することによって，17g/dL以上は男性で3.7％にみられ，女性にはみられなかった。また，これらは白血球数，血小板数，赤血球指数が正常で，相対的(ストレス)赤血球増加症と考えられた。真性赤血

球増加症は白血球増加，血小板増加，小球性低色素性赤血球の傾向を示すことから，今回の検討で，Hb19.0g/dL未満で白血球数，血小板数，赤血球指数が正常であれば，採血可能と判断した．

今回Hb測定の定量性を生かして，従来の採血基準の妥当性を検討した．まず，比重法とHb法の比較で，1.052以上はHb12.1g/dL以上を，1.053以上はHb12.6g/dL以上を示した．また，Hb値の低下に伴って赤血球指数が低下してくるが，平均値の低下開始に相当するHb値は，小球性低色素性赤血球に移行する点で，女性の成分採血の際の可否判定に用いられているところである．低下開始点は男性12.5g/dL，女性12.0g/dLで，男性が0.5g/dL高かった．また，12.5g/dL以下の男性献血申込者の比率は0.6％と少なく，あえて男性の採血基準を引き上げる必要はないと考えられる．以上および米国FDAの基準[11]を勘案して，私たちはHb法の判定に男女差を設けず，従来の採血基準を用いることで問題がないと考えた．

今回用いたヘモキュウによるHb測定法は，英国のNational Quality Assessment Schemeの精度管理で正確性の保証が得られている[11]．また，静脈血採血と耳朶あるいは指尖毛細血管穿刺との間に差異があるとの議論がある．これは，サンプリングが不適切な場合で，血流が十分保たれ，穿刺が正確に行われた場合は有意の差がないとの見解が一般的である[12]．また，指尖穿刺の方が，静脈穿刺より正確性を欠くとの報告もある[13]．

献血の可否を決定する検査は，大別して，血液学的検査，生化学検査，感染症関連検査が行われている．生化学，感染症関連検査は1953年血液事業が開始されて以来，次々と改良，改善が加えられ，NAT検査の導入によって世界的水準を保つにいたっている．一方，採血基準の根幹である貧血の有無判定については，当初の硫酸銅による比重法が現在にいたるも用いられ，一向に改良の気

配がない．その間，比重不足による献血不適格者は増加の一途であり，女性の400mL献血で本社の調査で，1990年 9.9％，2000年 18.1％，2003年 21.3％である[14, 15]．輸血によるウイルス性肝炎が激減したのと極めて対照的である．いうまでもなく比重法は測定者の目視による定性的判定法であり，温度・湿度の影響，使用滴下回数や蒸発，観察者の主観を無視できない．臨床の場においても，かつては比重法や比色法（ザーリ法）が用いられたが，現在はHb，ヘマトクリットに統一され，比重，比色によっている医療機関は皆無である．したがって，血液センターと医療機関の間で貧血に関するかぎり整合した議論が全くできていない．国は献血者の確保の推進として，献血の検査結果を健康診査，人間ドック，職場検診で活用するとともに，地域の保健指導に用いるよう求めているが[16]，比重で表示される献血不適格者の成績は利用し得ない状況である．以上から，血液センターにおいてもHb法を早急に導入し，定量的な評価によって献血者の健康を守る配慮をすべきである．

結　論

1．献血の可否判定にHb法を導入した．従来の比重法に比して，不適格者率，副作用発症率とも差異はなかった．

2．Hbおよび赤血球指数の度数分布から，従来の採血基準（400mL：12.5g/dL以上，200mL：12.0mg/dL以上）を用いて差し支えないことが判明した．

3．Hb低値の献血申込者に対して，Hb値に応じた栄養指導，医療機関への受診指導を行うことができた．

4．Hb法は定量性，客観性において比重法に優っており，Hb法に統一すべきであることを提言した．

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Statistical analysis of inappropriate results from current Hb screening methods for blood donors

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BACKGROUND: The objective was to apply statistical analysis to the false passes and fails that occur with the primary and secondary Hb-screening methods used at blood-donor sessions.

STUDY DESIGN AND METHODS: Venous samples from 1513 potential donors who had undergone primary $CuSO_4$ screening using capillary blood (Hb cut-offs: women, 125 g/L; men, 135 g/L) were tested at the session by a secondary method (HemoCue; cut-offs: women, 120 g/L; men, 130 g/L) and again at the base laboratory using another system (Beckman Coulter General S system), which generated the "true" Hb value.

RESULTS: False-pass and -fail rates for women and men, respectively, were 11.2 and 6.3 percent (women) and 5.2 and 1.8 percent (men) for $CuSO_4$; 1.9 and 3.7 percent (women) and 1.5 and 0.4 percent (men) for HemoCue; and 2.7 and 2.4 percent (women) and 1.8 and 0.2 percent (men) for a combined procedure that mimicked current practice of only testing $CuSO_4$ fails by HemoCue.

CONCLUSION: $CuSO_4$ Hb screening gives large numbers of false passes, particularly in women. Using venous samples, the majority correctly pass at the lower HemoCue cut-offs. The current dual-testing policy appears convenient for donor sessions, but because small percentages of false passes and fails represent large numbers of donors, every effort should be made to improve the accuracy of Hb screening.

Potential blood donors who attend donor sessions in the Trent Region (situated in the East Midlands, UK) initially undergo a health-screening survey. After passed this survey, they are subjected to primary Hb screening by the $CuSO_4$ gravimetric method carried out on finger-prick capillary blood, the cut-off levels for donation being set to correspond to Hb values of 125 g per L for women and 135 g per L for men.[1-3] To optimize blood-collection rates, UK regulations allow individuals who fail the primary $CuSO_4$ test to continue with the donation process if they pass the secondary Hb screening performed on a predonation venous sample using the HemoCue system.[2,4,5] With this method, donor acceptance or rejection is set at lower Hb levels: 120 g per L for women and 130 g per L for men.

We have recently become concerned that some donors are being bled inappropriately with these screening methods, whilst others with an acceptable Hb level are failing the tests. The purpose of this study is to determine whether this is the case and how to quantitate the problem by applying statistical analysis to the primary and secondary Hb-screening procedures used at our donor sessions, comparing them with a standard Hb measurement.

MATERIALS AND METHODS

Studies were carried out on potential volunteer blood donors attending routine donor sessions held throughout the Trent Region. All participants were fully informed of the purpose of the project and gave signed consent. The

study had been formally approved by the Trent Multicentre Research Ethics Committee.

To avoid bias when selecting individual subjects for the study, a simple systematic sampling scheme was used at each donor session. Before screening, every n^{th} potential donor was approached for consent to enroll in the trial. If an individual declined, each subsequent person was approached until one consented. Subsequently, the next n^{th} individual was approached and so on. The value of n was controlled by the transfusion service staff at the screening station.

During quiet periods, n could be set at 1 so that every potential donor could be approached. During busier periods a larger value of n could be set, and at exceptionally busy times, sampling could be discontinued completely to avoid delaying the session.

Venous blood samples were collected from 730 women and 783 men who were potential donors who had undergone the primary $CuSO_4$ gravimetric Hb-screening test. All the venous samples, which included those from individuals who passed and failed $CuSO_4$ screening, were taken before any blood donation and tested at the donor session by the HemoCue method. These machines are calibrated to the International Council for Standardization in Haematology standard. The HemoCue results were used to construct a hypothetical screening test and were expressed as either a pass or fail in respect to cut-off Hb values of 120 g per L for women and 130 g per L for men.

A combined procedure that followed current practice was also applied. Thus, respondents were initially screened on the standard $CuSO_4$ test; those who passed were deemed to have passed the combined procedure. Those who failed the $CuSO_4$ test were considered to have passed the combined procedure if a subsequent HemoCue result was at least 120 g per L for women and 130 g per L for men.

The venous samples were tested again at the base laboratory with the Beckman Coulter General-S system (Beckman Coulter, High Wycombe, UK). These results were deemed to be the "true" Hb values against which the results of the $CuSO_4$, HemoCue and combined procedures could be compared.

Statistical methodology

In view of the known differences in Hb levels between men and women, data for the different sexes were analyzed separately. Because donor characteristics would be likely to vary considerably between individual donor sessions, any sampling biases with respect to donor age were adjusted by stratifying data for both men and women into quinquen-

nial age bands and then testing to determine whether reweighting of the age-stratified data was necessary. This was achieved by chi-squared tests, comparing test and whole donor population data, and by a one-way ANOVA conducted for each of the women and men data sets with various Hb counts as the dependent variable and age category as the factor of interest.

The need to reweight was confirmed by both tests. A chi-squared value of 54.88 ($p < 0.0001$, $df = 10$) in respect to age distribution for women indicated that the test sample was severely under-represented in the 17 to 30 years age range, whereas for the age distribution for men, a chi-squared value of 18.60 ($p < 0.046$, $df = 10$) showed the test sample was under-represented in the 20-and-under ages. For the ANOVA, F values of 3.00 ($df = 10,724$, $p = 0.001$) for women and 2.23 ($df = 10,782$, $p = 0.015$) for men confirmed that in each case, Hb varied with age.

Reweighting to give reasonable donor population estimates was therefore carried out by calculating the stratified sample proportion of individuals possessing the appropriate attribute, together with its SE. This proportion is an unbiased estimator of the true population proportion possessing the desired attribute.[6,7] All values and standard errors were obtained using a statistical software package (SAS, SAS Institute, Cary, NC), and all proportions and standard errors were converted to percentages by multiplying them by 100.

The results of each screening test were compared to baseline Beckman Coulter Hb values of 125 g per L (women) and 135 g per L (men) for the $CuSO_4$ test and 120 g per L (women) and 130 g per L (men) for the HemoCue and combined procedures. The "false-pass" rates (i.e., the percentages of potential donors who would pass the relevant screening test but would fail the baseline Beckman Coulter test) were of particular interest.

RESULTS

Table 1 shows the results of the $CuSO_4$ Hb screening compared with the baseline Beckman Coulter values of 125 g per L (women) and 135 g per L (men). Table 2 (women)

TABLE 1. Results of $CuSO_4$ screening test compared with Beckman Coulter baseline at Hb levels of 125 and 135 g per L for women and men, respectively: population percentage estimates, stratum weighted by age

$CuSO_4$ result	Beckman Coulter result	Women Estimated percentage	Women SE	Men Estimated percentage	Men SE
Fail	Fail	12.4	1.3	3.9	0.7
Fail	Pass	6.3	0.9	1.8	0.5
Pass	Fail	11.2	1.3	5.2	0.8
Pass	Pass	70.1	1.8	89.0	1.1
Correct classification (%)		82.5		93.0	

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TABLE 2. Results of screening tests for women compared with Beckman Coulter baseline Hb level of 120 g per L: population percentage estimates, stratum weighted by age

Screening test result	Beckman Coulter test result	CuSO$_4$ Estimated percentage	SE	HemoCue Estimated percentage	SE	Combined Estimated percentage	SE
Fail	Fail	6.0	1.0	6.0	0.9	5.3	0.9
Fail	Pass	12.7	1.3	3.7	0.7	2.4	0.6
Pass	Fail	1.9	0.6	1.9	0.6	2.7	0.7
Pass	Pass	79.4	1.6	88.4	1.3	89.6	1.2
Correct classification (%)		85.4		94.4		94.9	

TABLE 3. Results of screening tests for men compared with Beckman Coulter baseline Hb level of 130 g per L: population percentage estimates, stratum weighted by age

Screening test result	Beckman Coulter test result	CuSO$_4$ Estimated percentage	SE	HemoCue Estimated percentage	SE	Combined Estimated percentage	SE
Fail	Fail	2.2	0.5	2.0	0.5	1.7	0.5
Fail	Pass	3.6	0.6	0.4	0.2	0.2	0.2
Pass	Fail	1.3	0.4	1.5	0.4	1.8	0.5
Pass	Pass	93.0	0.9	96.2	0.7	96.3	0.7
Correct classification (%)		95.3		98.2		98.0	

and Table 3 (men) give the results of the individual CuSO$_4$ and HemoCue screening tests and of the combined procedures, comparing them with Beckman Coulter baseline values of 120 g per L for women and 130 g per L for men.

DISCUSSION

The UK requires a predonation Hb screening to be carried out on all potential donors, and only individuals with an Hb level at or greater than 120 g per L for women or 130 g per L for men proceed to donate.[8,9] However, accuracy of Hb-screening procedures at blood-donor sessions may be a problem, and our study, by quantitating this, provides data for informed debate (Tables 1-3). It also shows how such studies may be approached in the future. In the present case, statistical analysis without the need to reweight would have required an even larger sample size. This would have been impractical because the length of time it took to obtain the informed consent required by the Ethics Committee had a deleterious effect on the efficient running of many donor sessions, particularly busy ones. As a result, the test sample was not representative of the donor population as a whole. This, and because of clustering of sessions, made it important to reweight the data so that the test population truly reflected the whole donor population with regard to factors that affect screening outcomes, such as age and sex. Reweighting necessitated expressing the results in proportions (percentages) rather than as raw figures.

The primary purpose of Hb screening is donor protection, preventing an anemic individual from exacerbating their condition with potential ill effects. The secondary purpose is to ensure the patient receives a minimum infused Hb dose per RBC transfusion. Screening also acts as a nonspecific measure of the general health of the donor and may identify some conditions which could potentially be harmful to the recipient.[2]

Protocols with set cut-offs are not without problems: they cause administration and quality control costs, donor inconvenience, expense and anxiety as a result of medical follow-up of deferrals, as well as permanent loss of donors. Additionally, cut-offs need to be set to maximize donor safety but be balanced against the system's ability to collect an adequate blood supply, a particular concern when trying to exclude women with iron deficiency. Hb reference ranges vary with age, race, and sex, and are affected by altitude, smoking, and the site from which the sample is taken.[2,10] It has been suggested that, rather than having set cut-off values, a standard should be established whereby blood donations contain a "minimum Hb dose" of 50 g; this would allow individual blood centers to evaluate the appropriate safe Hb cut-off for their donors.[2]

The CuSO$_4$ gravimetric test has been the method of choice in the UK for primary Hb screening of potential blood donors for many years. It is fast, inexpensive, does not require a venous sample, and, although rigorous training and constant monitoring of session staff is necessary, does not need trained laboratory personnel. It does not, however, give a quantitative result, has a subjective endpoint, is difficult to quality control, and presents problems with the disposal of biohazardous material.[2] Although very anemic donors can, on occasion, pass the CuSO$_4$ test,[11] early reports suggested that the CuSO$_4$ method tended to give inappropriate failures, and thus significant numbers of such failed donors could be recovered with a revised Hb range or if an alternative screening method was applied.[2]

This is the rationale for the primary and secondary Hb-screening tests used in the UK. It is supported by several studies that show that many units of blood can be collected that would otherwise be lost. Figures of between 11 and approximately 50 percent recovery of donations with secondary screening are quoted.[2,12-14] The lowering of the cut-off Hb values for the secondary screening also helps. In one study, 29 percent of failed

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donors passed the secondary test (HemoCue) at Hb cut-offs of 125 and 135 g per L (women and men, respectively); but with the cut-offs reduced to 120 and 130 g per L, this figure increased to over 44 percent.[14]

Initially there was concern that such a high proportion of donors, 11.2 percent of women and 5.2 percent of men in the present study, inappropriately pass the $CuSO_4$ screening test (Table 1); and, it should be noted that at these higher baselines, a HemoCue screening test would have considerably reduced the false-pass rates. Thus, the high false-pass rates in Table 1 do not mean that there is a similar proportion of donors being bled inappropriately. Examination of Tables 2 and 3 show that at baselines of 120 and 130 g per L, the $CuSO_4$ screening tests exhibit conservative false-pass rates similar in magnitude to the HemoCue procedure; only 1.9 percent of women and 1.3 percent of men who pass the $CuSO_4$ test have Hb levels less than 120 and 130 g per L, respectively, and should have been rejected as donors, indicating that, in practice, the current $CuSO_4$ cut-off levels can be tolerated. (The higher false-fail rates with the $CuSO_4$ test in Tables 2 and 3 are due to the higher cut-off settings.)

Tables 2 and 3 show that, had it been used in isolation, the HemoCue procedure would have classified 94.4 percent of women and 98.2 percent of men correctly at Hb levels of 120 and 130 g per L, respectively. Although this would appear to offer an improvement on the $CuSO_4$ test (set at 125 and 135 g/L for women and men, respectively), at present, the HemoCue procedure would be difficult to apply as a primary screening test on every potential donor because venous samples are preferred at our sessions. (HemoCue can be used on finger-prick blood, but capillary samples are known to give unreliable results[12,15] with all technologies and are thus unsuitable for secondary screening of blood donors.) Taking a venous sample from each person before donation could prove unacceptable to donors, slow down the donation process, as well as increase costs. Many studies have shown the excellent correlation between HemoCue and standard photometric methods in the laboratory,[14-18] and indeed we found the same in a prestudy evaluation of the analyzers used in this project. (In addition, HemoCue has a theoretic advantage over other photometric methods in that it incorporates a turbidity control, allowing more accurate results on lipemic samples.[2]) However, previous work has shown that accurate measurement of Hb level using the HemoCue system is difficult to achieve in the field.[19,20] There are several possible reasons for this; they include inadequate mixing of specimens,[19] sampling techniques, and operator performance,[20] rather than problems inherent to the methodology, and studies have shown that meticulous attention to sample mixing, mode of filling the cuvette, and continuous monitoring and training of staff can help to improve performance.[20]

Tables 1 through 3 show that the $CuSO_4$ and Hemo-Cue screening tests are less accurate, compared with Beckman Coulter values, for women than men, with false-pass and -fail rates being higher for women than males. This has been recognized previously, and it was suggested that such differences in screening-test performance can be explained by the distribution of women and men donor Hb levels relative to the cut-off values for acceptance.[21] A comforting factor in our study, in spite of its relatively small sample size, is that the lowest false-pass levels were 109 g per L for women and 123 g per L for men. Although it was inappropriate to collect blood from such individuals by our current guidelines, these figures are not alarming; there were no clinical sequelae, as far as we are aware, in the donors, and the recipients would have obtained an adequate amount of Hb. The donors who had been inappropriately bled were contacted and informed.

The results of the "combined" screening procedures (Tables 2 and 3), which mimic current practice at donor sessions, respectively, show false-pass and false-fail rates of 2.7 and 2.4 percent, respectively, for women and 1.8 and 0.2 percent, respectively, for men. The false-pass rates for the combined procedure slightly exceed those for the HemoCue alone: 95-percent CIs for these differences in rate are approximately 1.6 and 0.8 percent for women and men, respectively. On the other hand, the false-fail rates on the combined procedures are slightly smaller than for HemoCue alone, with 95-percent CIs for these differences in rate of approximately 2.3 and 0.6 percent for women and men, respectively. It should be noted here that any false pass on HemoCue alone would also pass the combined procedure, regardless of the $CuSO_4$ test result. Consequently, the false-pass rate for the combined procedure must be at least as great as that for HemoCue alone.

In summary, compared with HemoCue alone, current practice trades off a slightly higher false-pass rate against a slightly lower false-fail rate, and so is still reasonable in spite of the error rates in the initial $CuSO_4$ screen, and they need not be changed until the problems of accurately measuring Hb in the field can be reduced or eliminated. Because approximately 2 million donations are collected annually in the UK, even small percentages of false passes and false fails at the Hb-screening stage represent a large number of individuals, and, consequently, any improvement in accuracy of Hb screening will be welcome.

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