Recommendations for changes to acceptance criteria for UK whole blood and component donors

These recommendations have been produced by a project group, at the request of the UK Blood Transfusion Services' Forum.

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1 Remit

The remit of the project was:

- to evaluate the rationale of key non-microbiological donor selection criteria with respect to published evidence and relevant expert professional opinion
- to make recommendations for changes and for studies to evaluate proposed changes.

2 Summary of recommendations

2.1 Donors with a diagnosis of hypertension

The guideline (DSG 2005 Appendix 6) stated:

Donors who have been diagnosed with high blood pressure may donate provided that:

1. *They have not suffered any adverse effects of raised blood pressure (BP) such as heart disease (angina, heart attack or heart failure), stroke, transient ischaemic attack (TIA or mini-stroke), or peripheral vascular disease (intermittent claudication, gangrene).*

2. *They are taking only a Beta(β)-blocker and/or diuretic as their treatment for the raised BP. The list below shows the proper and trade names of allowed drugs. It is important to note that this list is not exclusive and that these drugs may be used to treat other conditions such as heart failure and abnormal heart rhythms (arrhythmia); both of which would mean the donor must not donate. Other medication should be assessed independently.*

3. *Treatment is stable. This requires:*
   That the donor is well and not having any problems with feeling faint, fainting or giddiness.
   They have been on the same dose of medication for at least a month.
   They are not undergoing tests to find out the underlying cause of their raised BP.

We **recommend** that donors with stable treated hypertension should be accepted as blood and component donors, regardless of the medication being taken to control hypertension, provided anti-hypertensive medication has not been altered within the 4 weeks prior to donation, and the donor has no history suggestive of cardiovascular or cerebrovascular, disease, renal impairment or peripheral vascular disease

Donors may self-report that their hypertension is well controlled; communication with the GP is not necessary. In accordance with advice previously received by the SAC we **do not** recommend blood pressure measurement at sessions.

2.2 Type 2 diabetes

The guideline (DSG 2005 Appendix 6) stated:

Obligatory	**Must not donate if:** Requires medication.	
	Discretionary	If controlled by diet alone, accept.
	See if relevant	Infection – General

We **recommend** that individuals with non-insulin dependent diabetes should be accepted as whole blood or component donors, provided that treatment is stable

(i.e. not altered within the past 4 weeks) and the donor is well, with no history suggestive of cardiovascular or cerebrovascular, disease, renal impairment or peripheral vascular disease.

The Blood Safety and Quality Regulations 2005 require permanent exclusion of diabetics if being treated with insulin. We do not at present propose to challenge this. The regulations do not require diabetics on oral medication to be excluded.

2.3 Implementation of changes to acceptance criteria

2.3.1 Training

Implementation of changes will need to be supported by a programme of training of all staff involved in donor selection and in providing advice to donors. In addition to training in the new acceptance criteria and relevant questions, the importance of recording donor adverse events should be re-emphasised.

2.3.2 Communication strategy

If maximum benefits are to be gained from changes in acceptance criteria, these should be carefully communicated to previously excluded donors, and made known to potential new donors who fall into the newly accepted category, and to their medical advisers (e.g. via patient groups and professional organisations).

2.3.3 Monitoring of adverse events

Acceptance of previously excluded donors must be kept under careful review to detect any increase in donor adverse events using agreed definitions. For example, in NBS this could be done by applying a flag to the donor's medical history record in PULSE. A standard query could then be written, that would extract the records of these donors and cross-check against records of adverse events (advice from Barbara Stearn and Ursula Everson). This should be run at regular intervals and reviewed by a designated member of the donor clinical team.

3 Rationale for recommendations

3.1 The decision to review the guidelines on donors with stable treated hypertension and well controlled type 2 diabetes on oral medication was arrived at for the following reasons;

3.1.1 these are chronic conditions with a high prevalence in the population eligible to donate blood. The prevalence of both conditions is increasing, in part because of increasing obesity in the general population.

3.1.2 available donor deferral data, though of limited usefulness, suggest that hypertension is a frequent reason for deferral.

3.1.3 other blood services accept donors with these conditions

3.1.4 preliminary scoping of literature suggested that acceptance of such donors is safe; this has been confirmed by a literature review (see Appendix 1).

3.1.5 the Blood Safety and Quality Regulations do not exclude these donors

3.2 In assessing the advisability or otherwise of accepting donors with these conditions, the following questions were considered;

3.2.1 How many potential donors might be reinstated or recruited?

3.2.2 Would the change in acceptance criteria put donors at an increased risk of adverse reactions?

3.2.3 What are the possible risks to the recipient of blood as a direct effect of medication taken by the donor?

3.2.4 Is there a possible teratogenic effect of medication taken by the donor if blood is transfused to a pregnant female?

3.3 Methods used

3.3.1 Review of available data on

3.3.1.1 donor deferrals

3.3.1.2 epidemiology of disease

3.3.1.3 adverse reactions

3.3.2 Review of literature

3.3.3 Advice from clinical experts

3.3.4 Information obtained from other blood services

4 Results: Donors with stable treated hypertension

4.1 Assessment of number of donors that might be reinstated or recruited

4.1.1 Donor deferral data

Data are available from NBS and SNBTS on the number of donors deferred at sessions because of hypertension treated with medication other than beta-blockers or diuretics. These should be interpreted with caution as they are calculated differently, and do not include donors previously permanently deferred, or those who self-defer following advice from the blood services.

Data source	Time period	Deferral code	Number of deferrals	% age of total deferrals (excluding low Hb)
NBS	Jul 2006-Jun 07	HBP	3960	2.1
SNBTS	2005-2007	C30X	1503	1.7
SNBTS	2005-2007	C02J	1363	1.6

4.1.2 Disease epidemiology.

Data on the prevalence of treated hypertension in the population were obtained from the 2003 Health Survey for England. The following table shows the percentage of population categorised as 'normotensive, treated'; defined as having SBP<140mmHg and DBP<90mmHg **and** currently taking drugs specifically prescribed to treat high blood pressure. These individuals would be eligible for re-instatement or recruitment as blood donors.

Age range	Men	Women
16-24	-	0.2%
25-34	0.1%	0.3%
35-44	1.6%	1.4%
45-54	5.5%	4.9%
55-64	11.0%	11.4%
65-74	16.1%	16.1%
75+	10.4%	12.3%
Total	5.4%	6.0%

Adapted from Table 7.7 Health Survey for England 2003 Vol 2
http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsStatistics/DH_4098712

4.2 Risk of an adverse reaction to blood donation in a 'normotensive treated' donor

The UK blood services do not have data on adverse reactions in donors with treated hypertension.

A review of literature (see Appendix 1), expert advice (see Appendix 2), and experience from other blood services (see Appendix 3) all indicate that such donors are not at increased risk of vasovagal reactions.

4.3 Risks to the recipient of blood as a direct effect of medication taken by the donor

Expert advice (see Appendix 2) is that the small quantity of drug contained in donated blood would be unlikely to cause an adverse reaction in a recipient. The experts were not specifically asked to consider the risk to a neonate, however the acceptance criteria for US apheresis plasma donors include anti-hypertensive medication, thus the UK blood services are already using plasma from donors taking these drugs for MB treatment and transfusion to neonates and children up to 16 years (Gordon Nicholson NBS, personal communication).

Only one paper was found relating to drugs in donated blood [17]. This suggested that, for non-teratogenic drugs, donor medication may be disregarded in relation to blood components containing 50ml or less plasma from a single donor; for blood components with a high plasma content (250ml) a safety level will be achieved by deferring for 5 plasma half-lives.

4.4 Possible teratogenic effect of medication taken by the donor if blood is transfused to a pregnant female. See Section 6 below.

5 Results: Donors with well controlled non-insulin dependent Type 2 diabetes

5.1 Assessment of number of potential donors that might be reinstated or recruited?

5.1.1 Donor deferral data

No data on deferrals of diabetics are available from NBS.
SNBTS data 2005-2007 indicates that 171 donors were deferred because of code E03X (diabetes mellitus); 0.2% of all deferrals excluding low Hb. These data do not include donors previously permanently deferred, or those who self-defer following advice from the blood services.

5.1.2 Disease epidemiology.

Data on the prevalence of non-insulin dependent diabetes are not readily obtainable. An analysis of volume, expenditure and trends published by the NHS Information Centre and Yorkshire and Humber Public Health Observatory gives an overall prevalence of diabetes in the population of 4.75% (2.4 million) and predicted a prevalence of 5.05% (2.6 million) by 2010.
http://www.library.nhs.uk/diabetes/viewresource.aspx?resid=61024
http://www.yhpho.org.uk/Download/Public/356/1/Diabetes_key_facts.pdf

The National Diabetes Audit Report for 2004/05 contains information on more than 500,000 patients collected from primary and secondary care organisations, representing 28% of the 1.8 million registered diabetic population at that time. The audit found that 9% had type 1 diabetes, 82% type 2 and 9% unspecified.

http://www.ic.nhs.uk/our-services/improving-patient-care/the-national-clinical-audit-support-programme-ncasp/audit-reports/diabetes

5.2 Risk of an adverse reaction to blood donation in diabetics.

Autonomic neuropathy is a common complication of diabetes, occurring in 20-40% of adult diabetics (types 1 and 2). 12% suffer from symptomatic postural hypotension. The risk increases with increasing duration of diabetes.
Figures from NHS Highland Diabetes Managed Clinical Network (MCN) Website
http://www.diabetes-highland.scot.nhs.uk/Guidelines/22Neuropathy/22_1.htm

It might therefore be expected that diabetics are less able to tolerate phlebotomy; however this is not supported by available data on adverse events, nor by published evidence.

5.2.1 NBS data on adverse events

Review of records of NBS active donors with diet-controlled diabetes showed no excess of adverse reactions; uncomplicated diabetes *per se* does not appear to pose an increased risk.

All donors on the NBS PULSE database with diet-controlled diabetes are flagged with a DIA medical code on their medical history record. A list was obtained of all active donors with DIA flag from all three datacentres. Each individual PULSE record was checked for confirmation of diagnosis. For all active donors who had

donated blood since the DIA code was added to the medical history, the following were recorded: sex, age, date diabetes recorded on PULSE, number of donations and number of adverse events since DIA code added.

Adverse events recorded in donors coded DIA

102 donors; 62 male, 40 female
432 donations

Adverse events:	VV1 = 3	1 in 144 donations
	UVP = 3	1 in 144 donations

No moderate or severe vasovagal events. No serious vascular complications.

National NBS data for comparison

3 months: November 07, December 07 and January 08, 523,206 venepunctures

Adverse Event	**UVP**	**BR1**	**BR2**	**BR3**	**VV1**	**VV2**	**VV3**
Number	16252	126	145	13	6497	533	242
incidence	1:32	1:4152	1:3608	1:40,246	1:81	1:982	1:2162
%	3.1	0.02	0.03	0.0025	1.24	0.1	0.05

UVP = unsatisfactory venepuncture
BR1
BR2
BR3
VV1 = felt faint
VV2 = simple faint
VV3 = complicated faint

5.2.2 Published data

There is no published evidence in literature to suggest that donors with diabetes are at increased risk of vasovagal episodes or other adverse events following blood donation, and some evidence of possible benefits (see Appendix 1)

5.3 Risks to the recipient of blood from diabetic donors or as a direct effect of medication taken by the donor.

Expert advice (Dr Simon Thomas) is that a unit of whole blood from a donor taking oral hypoglycaemic medication might contain 10-100 fold less than a single therapeutic dose and is very unlikely to produce hypoglycaemia in the recipient.

Acceptance criteria for US apheresis plasma donors include diabetes on oral medication, thus the UK blood services are already using plasma from these donors for MB treatment and transfusion to neonates and children up to 16 years (Gordon Nicholson NBS, personal communication).

5.4 Possible teratogenic effect of medication taken by the donor if blood is transfused to a pregnant female. See Section 6 below.

6 Risk of transfusing a known or possibly teratogenic drug

There is a theoretical risk that a fetal abnormality may result if blood containing a teratogenic drug is given to a woman in early pregnancy. Dr Thomas' initial advice when considering ACE inhibitors was that we should adopt a precautionary approach, however if we reject ACE inhibitors for this reason, then to be consistent we should also exclude donors taking other known or likely teratogens. This approach would have the certain and serious outcome of reducing the availability of blood.

It is our view that, in terms of likelihood and impact, the risk of producing a fetal abnormality is far outweighed by the risk of jeopardising the supply.
We suggest that further advice is required regarding the current policy of exclusion of donors taking drugs regarded as highly teratogenic. We do **not** consider that donors taking ACE inhibitors should be excluded because of a risk of teratogenicy, and we do **not** recommend any additional drug exclusions. The rationale for these recommendations is outlined below.

6.1 Inconsistency of current guidelines

Currently a small number of drugs are specifically excluded by the DSG because of concerns regarding fetal abnormality. These are the retinoids (permanent deferral of donors who have taken Etretinate, 12 month deferral for Acitretin and 4 weeks for Isoretinoin), Clomiphene and Tamoxifen, (12 weeks), Dutasteride, (6 months) and Finasteride (4 weeks). However donors taking other known or likely teratogens (Lithium, tetracyclines, anticonvulsants, statins, progestagens) are currently accepted, provided that the condition for which they are prescribed is not an exclusion criterion. Statins are a particular concern as they are widely and increasingly prescribed to donors who are otherwise eligible.

6.2 Lack of evidence of risk

It is unlikely that an unexpected fetal abnormality would ever be recognised as transfusion related; a formal literature search has not been conducted. The risk must therefore remain a theoretical one.

6.3 Transfusion in early pregnancy is uncommon

Available data on the use of blood in pregnancy are limited, however data from the EASTR Study, (Dr Angus Wells, personal communication) suggest that <0.1% of red cells are given to pregnant women before the peripartum period.

The 2007 'Better Blood Transfusion' HSC strongly advised avoiding transfusion in pregnancy unless absolutely necessary.

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Appendix 1

Review of literature relevant to the safety of blood donation by individuals with

a) Treated hypertension
b) Type 2 diabetes controlled by oral medication

Background

This review was undertaken as part of a project to support proposed modification of selection criteria for whole blood and component donors in the UK, to allow acceptance of donors with treated hypertension or type 2 diabetes controlled by oral medication.

Objective

To assess the evidence for safety of blood donation in individuals with controlled hypertension or type 2 diabetes controlled by oral medication.

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Methods

The overall approach to this review was based on the literature searching and analysis plan undertaken for selected common transfusion queries for recipients, e.g. 1 vs 2 checking pre-transfusion at the bedside.

Search strategy

The following sources were searched to identify papers relevant to this review; *The Cochrane Library* 2008, Issue 1, MEDLINE (1950 onwards), EMBASE (1974 onwards), CINAHL (1982 onwards), BNID (1994 onwards), the NHSBT SRI Handsearching Databases and the Web of Science (all years) to February 2008. Conference abstracts of British Blood Transfusion Society 2001-2007, International Society of Blood Transfusion Biennial 2004 & 2006, Regional 2005-2007, European Haematology Association 2002-2007, Association of American Blood Banks 2002-2007, American Society of Haematology 2004-2007 were also searched. Details of the search strategy are attached as Appendix 1.

As we anticipated that there would be a paucity of literature of direct relevance, no publication type, date or language restrictions were applied.

Eligibility criteria

Papers were eligible for inclusion if they addressed the safety to the donor of volunteer or autologous blood donation with specific reference to blood pressure or diabetes in the donor, including possible effects of medication taken for either condition. Studies of the haemodynamic effects of phlebotomy on subjects with hypertension or diabetes were also included.

Papers investigating possible predictive factors for adverse events in volunteer donors were selected for inclusion only if they included blood pressure or diabetes as a variable.

Foreign language papers were included if an English abstract/full text translation was available.

Selection for inclusion

One reviewer (DS) screened all titles and abstracts identified by the search for relevance to the review questions, and excluded clearly irrelevant papers.

Remaining papers were selected for review of their full content and were assessed for eligibility by two reviewers (DS & CEC), one of whom (CEC) is an expert in donor clinical care.

Data extraction

One reviewer (DS) extracted data from the eligible papers onto a study specific spreadsheet. The details extracted were the year and place of publication, objectives of the paper, type of study, study population, relevant observations and results.

Analysis of data

In view of the heterogeneity of the studies and lack of standard definitions of types and severity of adverse events, analysis of results was largely descriptive. Patterns of adverse event reporting were a key feature of presentation of results; all recorded adverse events were included. In particular we were interested in the incidence of vasovagal reactions, cardiovascular or cerebrovascular events and symptomatic haemodynamic changes during and following phlebotomy in donors with hypertension or diabetes compared to control subjects.

Results

Characteristics of included studies

The search yielded 2009 references and 10 conference abstracts.

Initial screening reduced the number of potentially eligible papers to 130. Full text screening reduced the number of eligible papers to 16 (see Fig 1). None of the conference abstracts was eligible for inclusion.

Data from the 16 included papers are summarised in Table 1. The included studies were undertaken between 1961 and 2006. There were no randomised controlled trials, 10 of the included papers[1,2,5,8,9,10,11,12,13,14,] reported on observational studies, 6[3,4,6,7,15,16] were case controlled studies, of

which only one[4] used matched controls and was thus able to determine the contributory role of individual variables in vasovagal reactions.

Eight papers studied vaso-vagal reactions in volunteer blood donors[1-8]. In six of these studies[1-6], blood pressure was investigated as a possible predictive factor, none reported on findings in diabetic donors. One study[7] investigated the effect on donor adverse reactions of modifying the acceptable limits for pre-donation blood pressure; one study[8] investigated the incidence of adverse reactions in donors taking anti-hypertensive medication.

Four papers reported studies of the safety of pre-operative autologous donation in patients with various risk factors including hypertension or diabetes[9-12]. These included one study using haemodynamic monitoring[10] and one using continuous ambulatory BP monitoring[12].

One paper reported a study of the haemodynamic response to venesection in normal subjects and patients with coronary heart disease or hypertension[13], and one reported the outcomes of treatment of resistant hypertension by repeated phlebotomy[14].

Two studies described the effect of phlebotomy on diabetic subjects[15,16].

Studies of vaso-vagal reactions in volunteer blood donors

Trouern-Trend *et al*[4] reported a large retrospective case-controlled multicentre study designed to determine the contributory role of sex, age, blood pressure and pulse as independent risk factors for syncopal reactions. 1013 donors suffering an adverse reaction (from 1,250,000 donations) were compared with non-reacting controls matched by age, sex and donation status. The authors found that a high systolic blood pressure (>150mmHg) was protective against syncope and observed that donors with low pre-donation blood pressure had higher reaction rates, but when adjusted for other variables, this finding was not significant and blood pressure overall was not considered to be a predictor.

Two further studies[1,6] found no correlation between pre-donation blood pressure and syncope. Three studies[2,3,5] (2 observational studies and one using random unmatched controls) found that pre-donation blood pressure was slightly but significantly lower in donors with syncope when compared to non-reactors, or all donors.

Tomasolu *et al*[7] investigated the effects on donor adverse reactions of adopting more liberal criteria for donor acceptance, including relaxing the limits for pre-donation blood pressure from 90-180/50-100 to <200/100, with no lower limit, and no restriction on medication. They estimated that 40-60 donors presented with a systolic blood pressure of 180-200; none had an adverse reaction. The reaction rate in 787 donors with systolic blood pressure <100 was 3.7% c.f. an overall rate of 2.3-3.3%.

Pisciotto *et al*[8] investigated the incidence of adverse reactions in donors taking anti-hypertensive medications, excluding β-blockers. Of 16,424 donors attending mobile collection units, 212 had a history of hypertension controlled by medication including reserpine, methyldopa and hydrallazine. The frequency of reactions in repeat donors taking medication was lower but not significantly different from repeat donors not taking medication. All adverse reactions in donors on anti-hypertensives were mild.

Studies of pre-operative autologous donation (PAD) in patients with hypertension or diabetes.

Data from these papers are of limited relevance as many autologous donors do not meet the usual criteria for volunteer donors, many are first-time donors and the conditions and methods of phlebotomy may differ from homologous donations. Nevertheless they provide useful information regarding the safety of phlebotomy in subjects with hypertension and diabetes.

Aubuchon & Popovsky[9] analysed data on adverse reactions in 5660 PADs from 25 centres over 2 months. Sixteen percent of patients (886) did not meet the usual homologous donor health criteria, including 57 with hypertension, 21 with type 1 diabetes and 416 taking various cardiac medications. The overall reaction rate in patients not meeting homologous donor criteria was higher than in those that did (4.3% c.f. 2.7%, $p<0.0001$), and reactions were twice as common in first donations compared to subsequent donations. Reaction rates in donors with hypertension (1/57; 1.8%), type 1 diabetes (1/21; 4.8%) and donors taking cardiac drugs (15/416; 3.6%) were not significantly increased. Only 4 severe reactions occurred, all in patients with a previous history of cardiac or cerebrovascular disease.

Similar data were reported by Hillyer *et al*[11] in a retrospective observational study of 1393 consecutive donations, of which 207 were classified as 'high risk autologous', including 23 insulin dependent diabetics and 101 patients with hypertension on 2 or more drugs. 665/1393 donors were classified as 'non-high risk autologous' and 521/1393 were homologous donors. Donor characteristics and parameters were evaluated including pre- and post-donation mean arterial pressure and heart rate. The number and severity of adverse reactions were recorded, and the 3 groups compared. Eight (3.9%) of the 207 high-risk autologous donors had an adverse reaction (7 mild, 1 moderate, 0 severe) , c.f. 3.3% of non-high risk autologous donors and 4.4% of homologous donors. None of the medical risk factors evaluated, including diabetes and hypertension on 2 or more drugs, was predictive of an adverse reaction.

Spiess *et al*[10] described a pilot study of haemodynamic changes during phlebotomy in a cohort of 123 high-risk patients donating 224 units of blood, compared to a control group of 8 healthy volunteers. The study group included 58 patients with hypertension requiring 2 or more drugs and 10 patients with diabetes (type unspecified). Blood pressure, pulse oximetry and modified 2-lead electrocardiogram were measured at baseline, then following removal of approximately 7mL/kg blood (with volume replacement in 174 donations), then at 5-min intervals therafter, sitting and standing. A wide variation in individual haemodynamic responses was observed; 49/224 (22%) patients had a 20% decrease in blood pressure from baseline, however syncope occurred in only 5/224 (2.2%). Additionally, dysrhythmia with syncope occurred in 7/224 (3.1%); but the authors do not report on the previous medical history of these patients.

Wiesbach *et al*[12] undertook continuous ambulatory monitoring of blood pressure in the 24 hours after PAD with fluid replacements, in a small cohort of 20 patients, 11 with known hypertension on treatment (3 also had ischaemic heart disease), 2 with previously undiagnosed hypertension and 7 with normal blood pressure. Changes in blood pressure post-phlebotomy were demonstrated in 25% of patients, but there were no significant differences between hypertensive and non-hypertensive patients.

Haemodynamic study of the effects of venesection

Thomas *et al*[13] studied the haemodynamic response to venesection in a study group of 18 patients with cardiovascular disease and a control group of 14 subjects. The study group were undergoing phlebotomy for later autologous donation, or for treatment of co-existing polycythaemia, and included 5 patients with hypertension, 11 taking β-blocking drugs, 11 taking vasodilators and 3 taking diuretics. The control group included healthy volunteers and patients with polycythaemia without cardiac or lung disease, and taking no medication. Blood pressure, stroke volume and cardiac index fell in both groups during venesection, but there were no significant differences observed between the two groups.

Treatment of resistant hypertension by phlebotomy

Zidek *et al*[14] reported an observational study in which fifteen patients with essential hypertension resistant to a triple drug regime (usually a diuretic, β-blocker, vasodilator or Ca antagonist) were treated by removal of 500 ml blood at monthly intervals x 3, and the effects observed. Repeated phlebotomies resulted in sustained reduction of blood pressure in all but one patient, and it is relevant to our study that no side effects were noted, in particular no signs of cerebral or cardiac ischaemia following phlebotomy.

Effect of phlebotomy in patients with diabetes

Two papers addressed the effects of phlebotomy in patients with diabetes. Though neither was primarily concerned with safety, both reported that phlebotomy was well tolerated and that some beneficial biochemical changes were observed.

Bofill *at al*[15] undertook a study to determine whether the presence of diabetes mellitus influences the erythropoietin response to repeated phlebotomies compared with non diabetic age and sex matched controls. They included 22 consecutive diabetic patients scheduled for major surgery in whom clinical and metabolic complications had been excluded and renal and liver function were considered unaffected (2 were on no treatment for diabetes, 10 were controlled by diet alone, 6 by diet and oral hypoglycaemics and 4 by diet and insulin). Each subject donated several units of blood in a 12 to 29 day period. A total of 5 reactions occurred, 2 in diabetic patients and 3 in controls; all were minor vasovagal episodes. Bleeding produced a significant decrease in serum glucose, cholesterol, triglyceride, apoprotein β concentration in the diabetic patients. Except for glucose, this effect was not observed in controls. The decrease in haemoglobin concentration did not produce clinical symptoms in either group and recovery was regarded as normal.

A randomised controlled trial to evaluate the effect of blood letting on insulin sensitivity and insulin secretion, in 28 male patients with high ferritin type 2 diabetes[16] randomised to phlebotomy or observation, found that patients who had three 500ml phlebotomies at 3 week intervals had improved insulin sensitivity and HbA1c levels compared with controls. No adverse events were recorded.

Discussion

The purpose of this systematic review was to ascertain the evidence for safety or otherwise of blood donation by individuals with treated hypertension or type 2 diabetes. It was disappointing that,

despite the large amount of accumulated data on adverse reactions to blood donation, only a single study was found[4] that investigated blood pressure as an independent risk factor for adverse events. It was however very reassuring that no study was found that reported an excess of adverse reactions in either volunteer or autologous donors with hypertension or diabetes, despite the inclusion in some studies of patients with significant cardiac disease.

BLOOD DONOR PROJECT – SEARCH STRATEGIES

THE COCHRANE LIBRARY

#1 BLOOD DONORS single term (MeSH)
#2 BLOOD NEXT DONOR* OR BLOOD NEXT DONATION OR DONAT* NEXT BLOOD
#3 (ALLOGENEIC NEXT DONOR* OR AUTOLOGOUS NEXT DONOR* OR BLOOD NEXT COLLECT* OR BLOOD NEXT LETTING OR PHLEBOTOM* OR VENEPUNCTUR* OR VENIPUNCTUR* OR VENESECTION OR VENISECTION):ti
#4. #1 OR #2 OR #3
#5. (BLOOD AND DONOR* AND (SELECT* OR ACCEPT* OR ELIGIB* OR INELIGIB* OR DEFERRAL OR DEFERRED OR RECRUIT* OR REINSTAT* OR RETENTION OR RETAINING OR RETURN* OR CARE OR HEALTH OR CRITERIA OR SCREEN* OR REJECT* OR EXCLUD* OR INCLUD*)):ti
#6. (BLOOD AND (DONATION* OR DONOR*) AND (REACTION* OR SAFETY OR COMPLICATION* OR SIDE NEXT EFFECT* OR ADVERSE NEXT EFFECT* OR ADVERSE NEXT EVENT* OR FAINT* OR VASO NEXT VAGAL OR VASOVAGAL OR RISK*)):ti
#7. (HEMOVIGILAN* OR HAEMOVIGILAN*) AND (DONOR* OR DONATION*)
#8. #5 OR #6 OR #7
#9. HYPERTENSION explode all trees (MeSH)
#10. HYPERTENSI* OR HIGH NEXT BLOOD NEXT PRESSURE* OR ANTIHYPERTENSI* OR ANTI NEXT HYPERTENSI*
#11. ACE NEXT INHIBITOR* OR CALCIUM NEXT CHANNEL NEXT BLOCKER* OR NORMOTENSIVE OR MEDICATION OR DRUG*
#12. #9 OR #10 OR #11
#13. DIABETES MELLITUS explode all trees (MeSH)
#14. DIABET*
#15. #13 OR #14
#16. #12 OR #15
#17. #4 AND #16
#18. #8 OR #17

MEDLINE (Dialog DataStar)

1. BLOOD-DONORS.DE.
2. (BLOOD ADJ DONOR$1 OR BLOOD ADJ DONATION OR DONAT$3 ADJ BLOOD).TI,AB.
3. (ALLOGENEIC ADJ DONOR$1 OR AUTOLOGOUS ADJ DONOR$1 OR BLOOD ADJ COLLECT$3 OR BLOOD ADJ LETTING OR PHLEBOTOM$3 OR VENEPUNCTUR$3 OR VENIPUNCTUR$3 OR VENESECTION OR VENISECTION).TI.
4. 1 OR 2 OR 3
5. (BLOOD AND DONOR$1 AND (SELECT$3 OR ACCEPT$3 OR ELIGIB$5 OR INELIGIB$5 OR DEFERRAL OR DEFERRED OR RECRUIT$4 OR REINSTAT$5 OR RETENTION OR RETAINING OR RETURN$3 OR CARE OR HEALTH OR CRITERIA OR SCREEN$3 OR REJECT$3 OR EXCLUD$3 OR INCLUD$3)).TI.
6. (BLOOD AND (DONATION$1 OR DONOR$1) AND (REACTION$1 OR SAFETY OR COMPLICATION$1 OR SIDE ADJ EFFECT$1 OR ADVERSE ADJ EFFECT$1 OR ADVERSE ADJ EVENT$1 OR FAINT$3 OR VASO ADJ VAGAL OR VASOVAGAL OR RISK$1)).TI.
7. ((HEMOVIGILAN$2 OR HAEMOVIGILAN$2) NEAR (DONOR$1 OR DONATION)).TI,AB.
8. 5 OR 6 OR 7
9. HYPERTENSION#.W..DE.
10. (HYPERTENSI$2 OR HIGH ADJ BLOOD ADJ PRESSURE$1 OR ANTIHYPERTENSI$2 OR ANTI ADJ HYPERTENSI$2).
11. (ACE ADJ INHIBITOR$1 OR CALCIUM ADJ CHANNEL ADJ BLOCKER$1 OR NORMOTENSIVE OR MEDICATION OR DRUG$1).TI.
12. 9 OR 10 OR 11
13. DIABETES-MELLITUS#.DE.
14. DIABET$2.TI,AB.
15. 13 OR 14

16. 12 OR 15
17. 4 AND 16
18. 8 OR 17

EMBASE (Dialog DataStar)

1. BLOOD-DONOR.DE.
2. (BLOOD ADJ DONOR$1 OR BLOOD ADJ DONATION OR DONAT$3 ADJ BLOOD).TI,AB.
3. (ALLOGENEIC ADJ DONOR$1 OR AUTOLOGOUS ADJ DONOR$1 OR BLOOD ADJ COLLECT$3 OR BLOOD ADJ LETTING OR PHLEBOTOM$3 OR VENEPUNCTUR$3 OR VENIPUNCTUR$3 OR VENESECTION OR VENISECTION).TI.
4. 1 OR 2 OR 3
5. (BLOOD AND DONOR$1 AND (SELECT$3 OR ACCEPT$3 OR ELIGIB$5 OR INELIGIB$5 OR DEFERRAL OR DEFERRED OR RECRUIT$4 OR REINSTAT$5 OR RETENTION OR RETAINING OR RETURN$3 OR CARE OR HEALTH OR CRITERIA OR SCREEN$3 OR REJECT$3 OR EXCLUD$3 OR INCLUD$3)).TI.
6. ((DONATION$1 OR DONOR$1) AND BLOOD AND (REACTION$1 OR SAFETY OR COMPLICATION$1 OR SIDE ADJ EFFECT$1 OR ADVERSE ADJ EFFECT$1 OR ADVERSE ADJ EVENT$1 OR FAINT$3 OR VASO ADJ VAGAL OR VASOVAGAL OR RISK$1)).TI.
7. ((HEMOVIGILAN$2 OR HAEMOVIGILAN$2) NEAR (DONOR$1 OR DONATION)).TI,AB.
8. 5 OR 6 OR 7
9. HYPERTENSION#.W..DE.
10. (HYPERTENSI$2 OR HIGH ADJ BLOOD ADJ PRESSURE$1 OR ANTIHYPERTENSI$2 OR ANTI ADJ HYPERTENSI$2).
11. (ACE ADJ INHIBITOR$1 OR CALCIUM ADJ CHANNEL ADJ BLOCKER$1 OR NORMOTENSIVE OR MEDICATION OR DRUG$1).TI.
12. 9 OR 10 OR 11
13. DIABETES-MELLITUS#.DE.
14. DIABET$2.TI,AB.
15. 13 OR 14
16. 12 OR 15
17. 4 AND 16
18. 8 OR 17

Figure 1

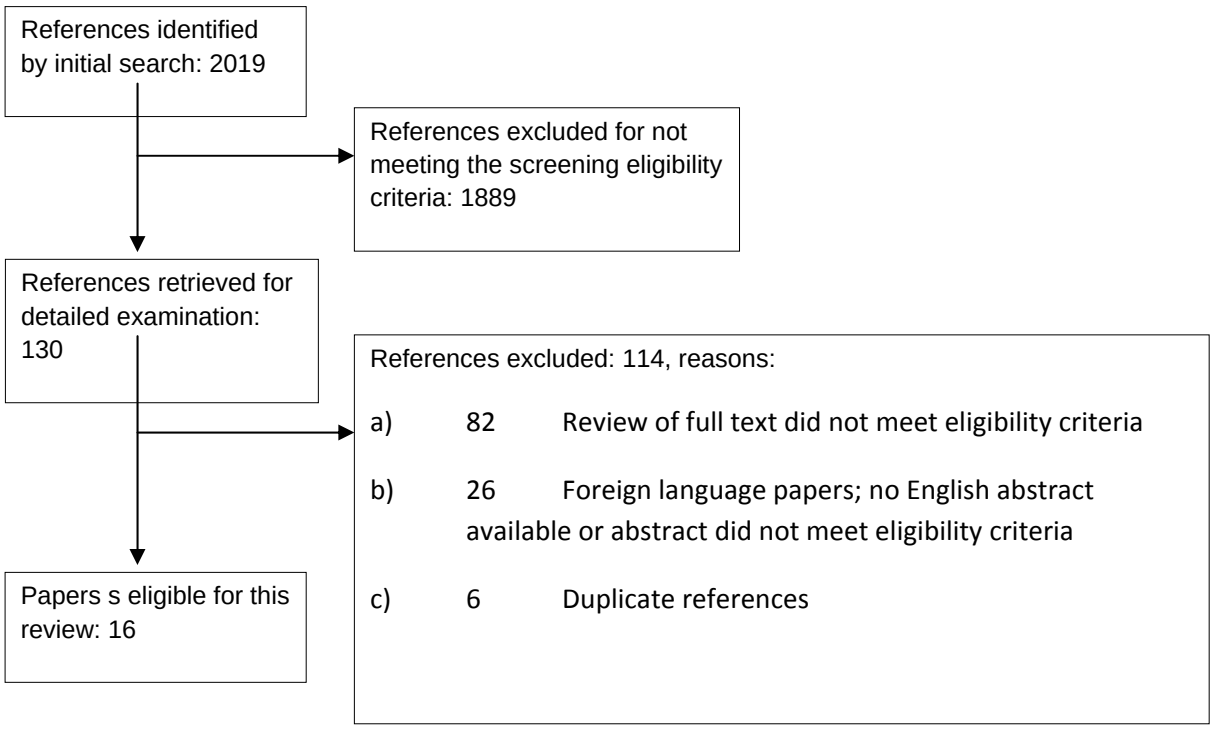
References identified by initial search: 2019
References excluded for not meeting the screening eligibility criteria: 1889
References retrieved for detailed examination: 130
References excluded: 114, reasons:
a) 82 Review of full text did not meet eligibility criteria
b) 26 Foreign language papers; no English abstract available or abstract did not meet eligibility criteria
c) 6 Duplicate references
Papers s eligible for this review: 16

Table 1: Summary of relevant literature

Reference	Objectives	Type of study	Population	Method	Observations/results	Is BP a risk factor in adverse reactions to phlebotomy?	Is phlebotomy safe in donors with type 2 diabetes?
Graham 1961[1]	To investigate vasovagal reactions in blood donors	observational study	414 consecutive donors at a hospital blood bank. Accepted if systolic BP 100-200, diastolic <100.	Adverse reactions recorded and analysed in relation to variables including baseline BP	No correlation between fainting and systolic or diastolic BP	No	n/a
Ogata et al 1980[2]	To identify factors predictive of vasovagal reactions in blood donors	observational study	10,547 donors bled in a hospital blood bank between 1976 and 1978	Characteristics of donors experiencing vasovagal reactions compared with those who did not	119 (1.13%) donors had vv reactions, 2 severe. Significant correlation with lower initial diastolic BP ($p<0.025$)	Low BP may predispose	n/a
Kaspirin et al 1992[3]	To determine if various demographic, physical and societal/emotional factors were predictive of reactions in donors	Case controlled study (unmatched controls)	217 homologous donors with moderate or severe reactions during a 12 month period, compared to randomly selected controls from 5630 non-reacting donors.	54 variables examined, 8 selected to be reporting, including BP.	Systolic and diastolic BP slightly but significantly lower in reactors (116.2 torr and 73.3 torr in reactors vs 119.4 torr and 75.5 torr $p<0.0001$). Differences too small to be of clinical value.	Low BP may predispose	n/a
Trouern-Trend et al 1999[4]	To define the contibutory role of sex, age, BP and pulse in vasovagal reactions with syncope in blood	Retrospective case-controlled multicentre study	1013 allogeneic donors with recorded syncopal reactions (from 1,250,000 donations) and non-reacting controls matched by sex, age and donation status. Random population	Logistic regression analysis to determine the significance of individual variables to syncopal reactions	High systolic BP (>150mmHg) was protective against syncope, BP overall was not an independent predictor. Donors with low pre-donation BP had higher reaction rates, but when adjusted for other variables,	No	n/a

	donors		control group also selected		was not significant.		
Franchini et al 2002[5]	To measure the frequency of adverse reactions to whole blood and apheresis donations and attempt to determine predictive factors	Retrospective observational study	116,952 consecutive blood and apheresis donors in a single centre.	Physical and demographic characteristics (age, gender, weight, whether first-time donor, predonation blood pressure), of donors experiencing adverse reactions compared with those of all donors.	1,960 adverse events recorded (1.7%). 19 severe reactions (0.02%), none life-threatening. Young age, first-time donation status and lower pre-donation blood pressure were independent risk factors for adverse reactions.	Low BP may predispose	n/a
Zervou et al 2005[6]	To estimate the type, incidence and causes of donor adverse reactions during and after blood donation	Prospective case controlled study	12,173 donors attending a single Greek blood bank during a 3 year period	Adverse reactions recorded. Reacting donors matched with non-reacting controls and variables compared.	107 (0.87%) of donors had an adverse reaction, 22 with loss of consciousness. Blood pressure not found to be a predictive factor	No	n/a
Tomasulo et al 1980[7]	To investigate the effect on donor adverse reactions of adopting more liberal criteria for donor acceptance	case controlled study	40,437 donors attending over 6 month period. 896 (2.2%) 'reactors' compared with matched non-reacting controls	Acceptance criteria modified, including modification of BP from 90-180/50-100 to <200/100, with no lower limit and no restriction on medication. Adverse reactions recorded	No donor with SBP 180-200 had a reaction, - probably 40-60 processed, based on survey of 14,000 donors. Reaction rate in 787 donors with SBP<100 was 3.7% c.f overall rate of 2.3 - 3.3%	No	n/a
Pisciotto et al 1982[8]	To determine whether donors taking anti-hypertensive medications experience a higher incidence of adverse	observational study	16,424 blood donors attending mobile blood collection units. Donors taking β-blockers were excluded from donating.	Observation and severity of adverse reactions recorded. Reaction rates in donors with history of hypertension compared with those without.	212 donors had a history of hypertension controlled by medication (reserpine, aldomet, hydralazine). Frequency of reaction in repeat donors taking medication was lower but not significantly different from repeat donors	No	n/a

	reactions than donors not taking them.				not taking meds. All adverse reactions in donors on anti-hypertensives were mild.		
Aubuchon & Popovsky 1991[9]	Assessment of safety of PAD in a non-hospital setting, and investigation of predictive factors for adverse reactions	Observational study	5660 PADs in 25 different blood centres. Included patients with cardiac risk factors. Collection took place in non-hospital setting without volume support or extensive monitoring. 886 patients did not meet the usual homologous blood donor health criteria, including 57 with hypertension, 21 with type 1 diabetes and 416 taking cardiac drugs	Data on adverse reactions submitted from 25 centres over 2 months. Categorised by type, severity and time after donation. Health histories of reactors reviewed. Proportions analysed using Z scores.	Overall reaction rate in patients not meeting usual homologous donor criteria was higher than those that did (4.3% cf 2.7%). When categorised by specific deviations, significant differences found in 3 criteria; age <17, weight <100 lbs, & pts with MS. Only 4 severe reactions.	No	n/a
Spiess et al 1992[10]	Pilot study of haemodynamic changes during phlebotomy in high risk patients. Not designed to develop risk stratification.	Cohort study	123 'high-risk' patients donating 224 units. 174 received volume replacement. Included 58 patients with poorly controlled hypertension requiring 2 or more medications, and 10 patients with diabetes (type unspecified)	Phlebotomy done with volume replacement. Haemodynamic monitoring; BP monitor, pulse oximeter, modified lead 2 ECG. Measurements at baseline, then every 5 mins after, sitting & standing (how long?).Subset (35) pts had continuous non-invasive cardiac output monitoring. Control group of 8 anaesthetists.	123 patients, 224 donations. In 49/224 (22%) there was a 20% decrease in systolic BP from baseline, syncope occurred in 5/224 (2.2%) and dysrhythmias in 7/224 (3.1%). Not analysed by risk factors	n/a	n/a
Hillyer et al	To determine the safety and outcome of blood	Retrospective observational	1393 consecutive donations. 207 classified as 'high risk autologous',	Donor characteristics and parameters evaluated including pre- and post-	HR donors were older. 3.9% of HR donors had adverse reactions (7 mild, 1 med, 0 sev),	No	yes

1994[11]	donation by high risk autologous donors c.f. others.	study	including 23 insulin dependent diabetics and 101 pts with hypertension on 2 or more drugs. 665 were 'non-high risk autologous' donors and 521 homologous donors meting all standards and criteria for allogeneic donation.	donation mean arterial pressure and heart rate, number and severity of of reactions. Three groups compared	c.f. 3.3% of NHR and 4.4% of homologous. First-time donors and donors taking cardiac glycosides had a higher likelihood of a reaction. None of the medical risk factors evaluated (including insulin dependent diabetes and hypertension on >2 drugs) was predictive of adverse reactions.		
Wiesbach et al 2006[12]	To investigate the occurrence of hypotension in the 24hr period after PABD in pts with and without hypertension	Cohort study	20 pts undergoing PABD with fluid replacement. 11 had known hypertension on treatment (3 also had IHD), 2 were previously undiagnosed, 7 were not hypertensive.	Ambulatory BP monitoring performed before PABD started and on every donation day in 2 repeated phlebotomies	25% of patients had changes in BP post-phlebotomy, especially during the night. No significant difference between hypertensive and non-hypertensive patients.	No	n/a
Thomas et al 1992[13]	To study the haemodynamic response to venesection in normal subjects and patients with coronary heart disease or hypertension	observational study	18 patients with coronary heart disease including 5 with hypertension, and 14 controls. 11 pts taking β-blockers, 11 on vasodilators, 3 on diuretics.	Baseline haemodynamic measurements (heart rate, ECG, BP, stroke vol) supine and standing. Continued at 1 min intervals during venesection and for 10 mins after, then with subject upright.	BP , stroke vol and cardiac index fell in both groups during venesection, but there were no significant differences between the 2 groups.	No	n/a
Zidek et al 1985[14]	To test whether resistant essential hypertension can be treated effectively by phlebotomy	observational study	15 pts with essential hypertension resistant to triple drug regime (usually diuretic, β-blocker, vasodilator/Ca anatagonist).	500 ml blood removed at monthly intervals and effect observed.	Repeated phlebotomies resulted in sustained decrease in BP, no side effects observed, in particular no signs of cerebral or cardiac ischaemia.	No	n/a

Bofill et al 1994[15]	To determine whether the presence of NIDDM influences the EPO response to repeated phlebotomies c.f. normal subjects	Case controlled study	22 pre-op diabetic patients & 22 matched non-diabetic controls	Patients donated between 1-5 units pre-op. Biochemical values measured at baseline and final.	Phlebotomy well tolerated in both groups.	n/a	Yes
Ferndandez Real et al 2002[16]	To evaluate insulin sensitivity and insulin secretion after blood-letting in patients with high-ferritin type 2 diabetes	randomised controlled study	28 male patients with high-ferritin type 2 diabetes	Patients randomised to blood-letting (500ml x3 at 2-weekly intervals) or observation.	Blood-letting group had decreased HbA1c, increased insulin sensitivity cf baseline at 4 months and 12 months. (? Relevance to normal donation intervals). No adverse events recorded.	n/a	Yes

Appendix 2

Expert advice on acceptance of donors with treated hypertension

Advice was obtained by Dr Mark Butler from Prof J K Cruikshank, Professor of Cardiovascular Medicine and Clinical Epidemiology, Consultant Physician, Manchester Royal Infirmary, and by Dr Stainsby from Dr Simon Thomas, Consultant Physician and Reader in Therapeutics, Regional Drug and Therapeutics Centre, Newcastle upon Tyne.

Prof Cruikshank wrote that, '…it would be medically safe to accept donations from donors on anti-hypertensive medication other than diuretics. None of the anti-hypertensive agents in regular use should compromise a patient's ability to compensate for a 1 unit donation.' Regarding possible direct toxicity to the recipient, his view was that 'that unit of blood will have very little active drug in it by the time it reaches the recipient.'

Dr Thomas' opinion regarding donor safety was that '……it would not be unreasonable to consider allowing blood donation in patients with stable cardiovascular disease or those taking cardio-active medications, provided that they do not suffer from symptoms of postural hypotension generally.' He also recommended audit of adverse events and suggested that 'measurement of lying and standing blood pressure before and after donation might be sensible as a limited short term measure.'
Regarding recipient safety, Dr Thomas calculated the likely dose of an antihypertensive drug in a unit of whole blood to be between 300 and 100 times lower than a therapeutic dose, and hence very unlikely to cause haemodynamic changes.

Endorsement of current UK policy not to routinely measure blood pressure pre-donation was obtained in 2002 by Dr Frank Boulton from Prof Bryan Williams, Professor of Medicine, University of Leicester Faculty of Medicine and Biological Sciences, and President of the British Hypertension Society, and from Prof Eoin O'Brien, Professor of Cardiovascular Pharmacology in Dublin.

Expert advice relating to donors with type 2 diabetes taking oral hypoglycaemics

Advice from Prof David Matthews, Chair of the Oxford Centre for Diabetes, Endocrinology and Metabolism, was as follows;

'Those with Type 2 diabetes need not be excluded if they are on diet alone, metformin alone or thialodinediones or insulin to control their blood glucose. One should be cautious with those on sulphonylureas as residual concentrations of these in the blood might cause hypoglycaemia in the recipient – however this is a theoretical possibility and I have no evidence to suggest that this would be a serious risk. It is likely that the risk (if any) from suphonylureas would only exist for a few hours following ingestion. The usual other exclusions would apply.

Dr Simon Thomas advised that for the sulphonylurea gliclazide, plasma concentrations around 1.5 mg/l cause hypoglycaemic effects. He estimated that a unit of whole blood from a donor taking gliclazide is likely to contain 10- to 100-fold less than a single daily therapeutic dose, and is very unlikely to produce hypoglycaemia.

Appendix 3

Experience of other blood services

1. Hypertension

This was researched by Dr Mark Butler, who undertook a web search followed by personal contact with Dr Richard Pembrey (Australian Red Cross Blood Service), Dr Richard Charlewood (NZ Blood Service) and Dr German LeParc, Chief Medical Officer, Florida Blood Services (contacted via AABB). Their full responses are copied into Appendix 2, but the following extracts are of particular note.

'A 2002 study of 72,059 whole blood donations at the American Red Cross (ARC) showed no statistical association between low pre-donation systolic or diastolic blood pressure and adverse reaction. In addition, ARC reviewed pre-donation blood pressure on all donors with adverse reactions that resulted in hospitalization from January 1999 to December 2002. This review showed no over-representation of low blood pressure or antihypertensive use in those donors.
A review of donor fatality reports from FDA obtained under FOIA shows no low pre-donation donor blood pressure. '

'Health Canada's decision (*to accept donors taking antihypertensive medication*) is based on the fact that there is no known link between reactions from giving blood and the use of medication to control high blood pressure. A recent study *(2000)* conducted with autologous donors at Héma-Québec's permanent centre in Montreal, has shown that donors who take anti-hypertensive medication are no more at risk than other donors.'

Responses received by Dr Mark Butler to the following letter;

Dear

The National Blood Service (UK) is currently reviewing the National Donor Selection Guidelines (DSG) for the acceptance/deferral of potential and existing whole blood donors taking prescribed medication including ACE inhibitors and/or calcium channel blocking agents for treatment of arterial hypertension.

The current guidelines (DSG 202, November 2005) recommends that only current and potential donors taking diuretics and beta-blockers alone or in combination are eligible to donate blood, provided that they satisfy the other donor selection criteria on the DSG.

The National Blood Service does not routinely measure blood donor's blood pressure. The American Blood Services does not preclude current or potential blood donors taking medication for hypertension, irrespective of what the medication might be.

I would be grateful if you could inform us as to the safety of taking blood donations from whole blood donors taking calcium antagonists and/or ACE inhibitors for arterial hypertension; particularly whether they have an increased risk of immediate or delayed adverse events (such as vaso vagal episodes, cardiovascular reactions etc) following whole blood donation. I would be grateful if you could inform us also, whether there is any evidence that the very small quantity of drug in the donation may cause any adverse clinical effect in patients who are transfused this blood.

1 Response from Dr Tony Keller, Chair, Australian Red Cross Blood Services Donor and Patient Safety Review Committee (sent via Dr Richard Pembrey)

Dear Richard,

I am sorry for the delay in reply but have been reviewing our records. We have addressed ACE inhibitors at DPARC 12 months ago but not in relation to bradykinin levels. Our concerns related to an article in the New England Journal and an editorial concerning possible teratogenic effects of ACE inhibitors. It was noted that this concern related to patients taking ACE inhibitors and not blood donors.We sought advice from international Blood Services- none were intending to introduce restrictions based on ACE inhibitors. International advice indicated that the levels in a blood donation were considered too low to have any effect. This issue was put onto the Abo's Medical Subgroup Issue list and was to be reviewed in 12 months which is about now. I will follow this up.

With regard to hypotensive reactions in apheresis donors these events appear to be very uncommon. Certainly severe vasovagal events are lower that in whole blood donors. In plateletpheresis donors there were 2 severe vasovagal and 2 severe citrate reactions in 27,000 procedures). I do not have exact figures for plasmapheresis but will investigate further.

Although we ask about drug intake at interview we do not record all donor medications. This would have to be done prospectively. Currently ACE inhibitors are acceptable as long as the underlying condition eg hypertension would not preclude.

2 Response from Dr German LeParc, Chief Medical Officer, Florida Blood Service

In response to your inquiry regarding the use of antihypertensives by prospective blood donors, I have the following comments to offer:

- The AABB "Standards for Blood Banks and Transfusion Services" requires that blood pressure be ≤180 mm Hg systolic and ≤100 mm Hg diastolic. These levels have been the requirement since 1987. This particular standard was reviewed in 2002 and again in 2003, and the BBTS [Blood Banks and Transfusion Services] Standards Program Unit found no scientific evidence to warrant changing the standard.
- The Code of Federal Regulations (CFR) requirements for blood pressure state that “systolic and diastolic blood pressure must be within normal limits” [21 CFR 640.3(b)(2)], and that “standard operating procedures for donor-qualifying tests and measurements must specify maximum and minimum values” [606.100(b)(2)]. However, they have not enforced the rule for minimum values for blood pressure.
- To the best of my knowledge, blood pressure is not a requirement for donor qualification in the European Union Commission Directive 2004/33/EC.
- The Council of Europe Guide states: "If pulse and blood pressure is tested then the pulse should be regular and between 50 and 100 beats per minute. It is recognized that recording the blood pressure may be subject to several variables but as a guide the systolic blood pressure should not exceed 180 mm of mercury and the diastolic pressure 100 mm."
- A number of researchers have published articles in peer-reviewed journals showing a lack of correlation between the use of antihypertensives or low pre-donation systolic or diastolic blood pressure and adverse donor reactions.

- A 2002 study of 72,059 whole blood donations at the American Red Cross (ARC) showed no statistical association between low pre-donation systolic or diastolic blood pressure and adverse reaction. In addition, ARC reviewed pre-donation blood pressure on all donors with adverse reactions that resulted in hospitalization from January 1999 to December 2002. This review showed no over-representation of low blood pressure or antihypertensive use in those donors.
- A review of donor fatality reports from FDA obtained under FOIA shows no low pre-donation donor blood pressure.
- At Florida Blood Services, it is our policy to allow blood donations by donors who are taking ACE inhibitors or calcium channel blockers, as long as the blood pressure is no lower than 90/60 (The values were set arbitrarily as a guideline that eliminates the need for physician clearance).
- When there were questions regarding the suitability of donors taking ACE inhibitors or calcium channel blockers for aphaeresis donations (quite a few years ago), we performed a survey of ABC members and found that no restrictions were put on aphaeresis donors on those medications.
- We do take donors on both types of medications and have not seen increased reaction rates for either aphaeresis or whole blood donations. Neither did we observe increased incidence of citrate toxicity in those taking calcium-channel blockers. And while extracorporeal circulation during aphaeresis may increase kininogen activation, we have not found an increase in hypotensive episodes, compared to the population that does not take ACE inhibitors or angiotensin receptor blockers.

3 Response from Dr Richard Charlewood (on behalf of Dr Peter Flanagan, Medical Director, NZ Blood Service)

Peter Flanagan has passed on your email regarding antihypertensives, particularly ACE inhibitors and calcium channel antagonists.

Our policy does not make particular exception for ACE inhibitors, calcium channel antagonists or diuretics, but rather considers whether the donor has a normal blood pressure at the time of donation and has not changed medication in the past three months. If the donor meets these two requirements, we would accept the donor. For beta blockers we add a requirement that that the donor has not had any episodes of postural hypotension with a pulse of at least 60/min, diastolic of at least 70 mmHg and systolic of 100-160 mmH. We do not normally check donors' blood pressures, but do so if the donor has a history of hypertension, whether on medication or not.

I am not aware that we have an increased incidence of adverse events with hypertensive donors though it has to be said our system currently does not actively seek that information. Similarly, because we do not record whether a donor has a history of hypertension in our blood management system (Progesa), our haemovigilance program is currently not able to provide any evidence that drugs from the donors are causing adverse events in the recipients. However, pure hypotensive episodes, (i.e. not associated with NHFTR or anaphylactoid reactions) are unusual. In 2005, we received only 4 reports of pure hypotension. Although there is most likely a significant amount of under-reporting, there still would seem to be a large discordance between the number of donors on anti-hypertensives and the number of hypotensive reports.

Ottawa, April 18, 2000 - Following on a decision by the Bureau of Biologics and Radiopharmaceuticals at Health Canada, Canadian Blood Services (CBS) announced today that donors who control their high blood pressure with medication will soon be able to resume donating blood throughout Canada. Following a joint request made by CBS and Héma-Québec, the Bureau of Biologics and Radiopharmaceuticals at Health Canada, granted permission to both blood operators in Canada to allow donations by those who control their blood pressure with medication. Potential donors must still have normal vitals signs in order to donate. Health Canada's decision is based on the fact that there is no known link between reactions from giving blood and the use of medication to control high blood pressure. A recent study conducted with autologous donors at Héma-Québec's

permanent centre in Montreal, has shown that donors who take anti-hypertensive medication are no more at risk than other donors. As well, in the United States, donors are not deferred for taking this type of medication. Donors who presently take medication to control their blood pressure and have been deferred, or those Canadians taking this medication who would like to become blood donors will be able to donate once the operational changes have been put in place.

4. Other Blood Services' guidelines on individuals with diabetes mellitus:

Australian Red Cross- Information for donors on website accessed on 1/11/2007:

Diabetes -"If you have no complications from your diabetes such as eye, blood vessel related or kidney problems and your diabetes is well controlled through *diet or oral medication*, you will be able to donate. If, however, you are free from complications, well controlled, your insulin dosages are stable and you have not used bovine (cattle-derived) insulin in the past, you will generally still be able to donate (www.donateblood.com.au)

American Red Cross – accessed on 1/11/2007

"Diabetes: deferred only if received bovine insulin from UK, eastern Europe, or western Europe" "If you have a chronic condition such as diabetes or high blood pressure, "healthy" also means that you are being treated and the condition is under control".(www.redcross.org)

New Zealand Blood Service- information on donor eligibility criteria for diabetes provided by Dr Dhana Gouder on behalf of Dr Peter Flanagan (Medical Director).

'If diabetes is under control by diet or oral medication the donor is accepted.

- If the donor is on insulin **or** the diabetes is uncontrolled then the donor is permanently deferred. On most occasions the decision to accept or defer is based on the response during the donor interview. Only occasionally we may need to request for relevant clinical and laboratory data.'