ORIGINAL ARTICLE

Keep in a cool place: exposure of medicines to high temperatures in general practice during a British heatwave

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SUMMARY

Exposure of medicines to high temperatures in storage or in transit could reduce their efficacy, and most licences specify storage at 25°C or less. To assess whether this criterion was being met, maximum temperatures in a general practice drug cupboard and in drug bags placed in car boots were recorded for two weeks during a British heatwave (average peak daily ambient temperature 26°C). Also, ten neighbouring dispensing pharmacies were questioned about their temperature-control policies.

On every day of the study, maximum temperatures in the drug cupboard and in the car boots exceeded 25°C. Mean daily maxima (range) were: drug cupboard 30.7 (27.5–37.0); silver car 37.5 (32.0–43.5); dark blue car 41.8 (35.0–49.5). None of the local dispensaries had air conditioning or kept a temperature log.

In the course of a British summer, medicines were exposed to temperatures that might in theory have reduced their efficacy. This aspect of quality control deserves more attention.

INTRODUCTION

Family doctors in the UK store medicines either on practice premises or in bags for emergency use on home visits. Manufactured drugs, in general, are licensed for storage at temperatures up to 25°C.[1] At higher temperatures there is the risk that their efficacy will be adversely affected, and the quality of drugs carried by family doctors for emergency use—for example, benzylpenicillin for suspected bacterial meningitis—needs to be above suspicion. Box 1 lists some of the agents commonly carried in this way.

The temperature conditions of medicines were investigated in a suburban primary care setting during an English heatwave.

Box 1 **Agents commonly carried in doctors' bags**

Adrenaline	Furosemide
Benzylpenicillin	Glucose
Cefotaxime	Hydrocortisone
Chlorphenamine	Naloxone
Chlorpromazine	Pethidine
Diamorphine	Prochlorperazine
Diazepam	Sodium chloride
Diclofenac	Water for injection

METHODS

Three mercury maximum/minimum thermometers were purchased and checked by comparison of maximum temperatures recorded after 24 hours on the same shelf of the practice drugs cupboard. They agreed within 0.5°C. Two of the thermometers were then put in doctors' bags (Gladstone, burgundy coloured), which in turn were placed in the boots of two cars (A, silver coloured; B, dark blue), which occupied similar positions in the car park. The third thermometer was installed on the top shelf (41 cm below ceiling height) of a locked metal drugs cupboard in the practice treatment room. The day's maximum temperature was recorded at 1900 h each day from 4 to 15 August 2003, inclusive—a time of warm weather. Over the same period, the maximum ambient air temperature at the Coleshill Weather Station, 8 km from the practice, was obtained from the national UK meteorological website.

On 13 August the ten geographically closest dispensing pharmacies were contacted by telephone and were asked: Does your dispensary have air conditioning? Do you measure temperatures in your dispensary?

RESULTS

Table 1 shows the maximum temperatures for the drugs cupboard and the boots of the two cars, together with maximum ambient air temperatures during the days of the study. On every day, at every drug storage site, temperatures exceeded 25°C. The telephone survey indicated that none of the ten local pharmacies had air conditioning or monitored dispensary temperatures.

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DISCUSSION

The journey of a medicine begins at the site of manufacture and passes through warehouses, pharmacies, and sometimes other environments before reaching the end user. Temperature conditions in the earlier stages have received attention, but little work has been done in primary care settings and community pharmacy settings in the UK. A previous study, by Rudland and Jacobs,[2] did draw attention to high temperatures in the boots of doctors' cars. The findings of the present study suggest that temperature quality control in primary care and community pharmacies (if ours are typical) leaves much to be desired. Where air conditioning is not standard practice, medicines are at the mercy of the ambient temperature; and conditions in car boots are particularly disturbing. The difference between the cars was of interest: although the vehicles were not identical models, the paint colour was probably the relevant feature: car B was dark blue, and more likely to absorb heat than the silver car A.

In all three environments, drugs were exposed to temperatures exceeding 25°C. Do these deviations from the recommended storage temperatures matter in practice? Looking at one of the drugs commonly carried, adrenaline, Rudland and co-workers found no significant alterations in activity by high ambient temperatures.[3,4] However, some other products do seem temperature sensitive. For example, the capsules of certain brands of cefalexin degraded more rapidly in hot conditions and this caused 'serious fluctuations' in absorption.[5]

Ampicillin, erythromycin, furosemide for injection and benzylpenicillin stored in a tropical climate showed significant reductions in activity at one year.[6] Aspirin follows first-order kinetics with regard to temperature degradation, and a similar finding was recorded for diclofenac tablets exposed to high ambient temperatures (dissolution rate was reduced significantly in as little as three months, with resultant reduction in maximum plasma concentration achieved).[7]

There is a duty to ensure that medicines are kept in an environment that maintains their efficacy. The manufacturer will be responsible for shortcomings only if storage has occurred as stipulated in the Summary of Product Characteristics.[8] In almost all cases the specified temperature is 25°C or less. The effect of temperature is seen in the rate of oxidation or hydrolysis: for every 10°C increase in temperature there is generally an exponential increase in the rate of reaction.[9] (Drug stability can also be affected by *low* temperatures, especially liquid preparations liable to freezing.)

This research highlights some important areas in medicines management. Manufacturers need to offer more drug stability data in relation to temperature. Even if the immediate stability of stored medicines is not seriously affected there may well be an effect on shelf life or expiry date. To rectify this, practices and pharmacies may have to consider arrangements for cooling. As to the carriage of medicines by healthcare professionals in their cars, simple precautions are to avoid leaving drug bags in the boot or to use cool bags.

The present observations, though made in exceptional weather conditions for the English Midlands, highlight the need for further work on storage conditions for medicines in primary care and in community pharmacies.

Table 1 **Maximum temperatures (°C)**

Date (August 2003)	Drug cupboard	Car A	Car B	Ambient
4	34.0	40.5	45.0	30
5	30.0	38.0	41.0	27
6	37.0	42.0	46.5	31
7	30.5	38.0	42.0	26
8	30.0	40.5	44.0	26
9	36.5	43.5	49.5	34
10	29.5	32.0	35.0	22
11	27.5	33.0	37.5	22
12	29.0	34.0	37.5	24
13	28.5	37.0	42.0	24
14	28.0	35.0	41.0	23
15	27.5	37.0	40.5	23

REFERENCES

1 *US Pharmacopeia*, Vol 26. Rockville, MD: USP, 2000

2 Rudland SV, Jacobs AG. Visiting bags: a labile thermal environment. *BMJ* 1994;**308**:954–6

3 Rudland SV, Annus T. Adrenaline activity is not significantly altered by high ambient temperatures. *Emerg Med* 1997;**9**:109–11

4 Rudland SV, Annus T, Dickinson J, Langdon S. Adrenaline degradation in general practice. *Br J Gen Pract* 1997;**47**:827–8

5 Molokhia AM. Effect of storage on the bioavailability of cephalexin from its capsules. *Res Commun Chem Pathol Pharmacol* 1984;**45**:219–24

6 Ballereau F, Prazuck T, Schrive I, *et al*. Stability of essential drugs in the field: results of a study conducted over a two-year period in Burkina Faso. *Am J Trop Med Hyg* 1997;**57**:31–6

7 Risha PG, Vervaet C, Vergote G, Bortel LV, Remon JP. Drug formulations intended for the global market should be tested for stability under tropical climatic conditions. *Eur J Clin Pharmacol* 2003;**59**:135–41

8 [http://emc.medicines.org.uk] accessed 21 April 2004

9 *US Pharmacopeia*, Vol 28. Rockville, MD: USP, 2002:2232–3